

## **The Influence of TRIPS on Global Trade in Pharmaceuticals, 1994-2005**

Mercedes Delgado

Innovation Policy and Economy Post-Doctoral Fellow, National Bureau of Economic Research  
Post-Doctoral Fellow, Harvard Business School, Institute for Strategy and Competitiveness  
[mdelgado@hbs.edu](mailto:mdelgado@hbs.edu)

Margaret Kyle

Assistant Professor, London Business School  
Faculty Research Fellow, National Bureau of Economic Research and Centre for Economic Policy Research  
[mkyle@london.edu](mailto:mkyle@london.edu)

Anita M. McGahan\*

Professor, Strategic Management, Rotman School, University of Toronto  
Senior Institute Associate, Harvard University, Institute for Strategy and Competitiveness  
Senior Economist, Center for Global Health, Massachusetts General Hospital  
[amcgahan@rotman.utoronto.ca](mailto:amcgahan@rotman.utoronto.ca)

March 5, 2008

This paper examines changes in the patterns of global trade in biopharmaceuticals before and after the implementation of the WTO TRIPS agreement on intellectual property. The purpose of the analysis is to explore the patterns for evidence consistent with the objective of TRIPS to promote “the transfer and dissemination of technology” particularly from advanced to least-developed countries. The evidence suggests that, during the period of TRIPS implementation between 1994 and 2005, global trade in biopharmaceuticals and other products dependant on intellectual property increased relative to sectors unaffected by TRIPS, but the results also suggest that trade in technology-intensive products has not grown dramatically between developed and less developed countries. To explore alternative explanations for the patterns, the statistical analysis is supplemented with brief case analyses of the impact of TRIPS in South Africa, the UK, India, and Brazil.

\* Corresponding author. Thanks to Michael Porter for providing us with access to the ICCP data on cluster definitions and the UN Comtrade database. We are grateful to Iain Cockburn, Matthew Slaughter, and the NBER Biopharmaceuticals Location project for encouragement and comments.

Copyright © 2007, 2008, Mercedes Delgado, Margaret Kyle, and Anita McGahan. All rights reserved.

Between 1994 and 2005, intellectual-property protection on pharmaceuticals was formally implemented in 40 developing countries that previously had not offered patent protection (Westerhaus and Castro 2006). This major change in global trade policy occurred as the result of bilateral and multi-lateral agreements, the most significant of which established the World Trade Organization (WTO) on April 15<sup>th</sup>, 1994. Annex 1C of the WTO agreement dealt with the “trade-related aspects of intellectual property rights,” or TRIPS, and had the following objective:<sup>1</sup>

“The protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology....”

The agreement covered a range of topics related to intellectual property, and yet among the most important was the phased implementation, by the end of 2005, of patent protection for up to 20 years in developing countries that previously had no patent laws. The benefits of patent protection, i.e. to stimulate the dissemination and development of drugs, were balanced against the costs, i.e., to provide patent-holders with monopoly rights on their technologies (Taylor 1993, 1994). In subsequent amendments, countries were given access to compulsory licensing as a “relief valve” that would assure access to life-saving medicines in special circumstances, but only with a compensating payment to the patent holder.

Prior studies have addressed the efficacy of TRIPS in achieving its objectives in the pharmaceutical industry. Several important studies have dealt specifically with the influence of TRIPS on the incentives for research and development in pharmaceutical companies on diseases that are prevalent among the poor (Chen and Puttitanum 2002, Chien 2003, Jack and Lanjouw 2003, Lanjouw and Cockburn 2001). Overall, the results of these studies suggest that the evidence of new research on neglected diseases as a response to TRIPS incentives is inconclusive.

A complementary line of research has demonstrated how research on neglected diseases may be stimulated by TRIPS in concert with additional policies. Glennerster and Kremer (2000)

---

<sup>1</sup> Part 1, Article 7 of Annex 1C of the Marrakesh Agreement to establish the World Trade Organization available at [http://www.wto.org/english/docs\\_e/legal\\_e/27-trips\\_03\\_e.htm](http://www.wto.org/english/docs_e/legal_e/27-trips_03_e.htm) (accessed June 21, 2007)

and Kremer and Glennerster (2004) suggest that the introduction of government guarantees for the purchase of vaccines against malaria and HIV/AIDS would stimulate investments in drug development. Maurer (2006) promotes a model of “open innovation” on neglected diseases in which firms, individuals, and other types of institutions pursue basic research collaboratively and thereby create even stronger incentives for the commercialization of drugs based on commonly created knowledge.

In this paper, we investigate a question that reflects one of the specific objectives of TRIPS: to promote “the transfer and dissemination of technology” regardless of its degree of patentability, patent history, or the presence of incentives. The purpose is to explore whether the implementation of TRIPS between 1994 and 2005 has led to greater cross-border trade in pharmaceuticals as compared with other sectors of the global economy, and to evaluate specifically whether increased trade in medicines occurred in the 40 developing countries that did not have patent protection prior to TRIPS. The dataset for the trade analysis is the United Nations’ Statistics on Trade as screened and developed at the Institute for Strategy and Competitiveness at Harvard University. The cross-sectional analysis reveals several interesting regularities. In particular, it shows a modest increase in cross-border trade in pharmaceuticals above the levels in other sectors, and a moderate increase in the 40 developing countries that had no patent protection prior to TRIPS above the levels in other countries. A range of explanations arise for these results, including, for example, the emergence of new treatment protocols that lower the costs of administering unpatented drugs in developing countries.

To inform subsequent research on various features of cross-border trade in pharmaceutical for neglected diseases, we follow suggestions by Kuhn (1962) and Eisenhardt (1989) and turn to several cases examples. The cases are not representative of the problems in cross-border trade in pharmaceuticals, but rather illustrate some of the issues that arise in complex situations where TRIPS has been applied. The first case on the stock-price response to Wellcome’s introduction of AZT pre-dates TRIPS and illustrates why, in part, the industry had avoided investments in drugs for neglected diseases. The second case on South Africa discusses how the issuance of compulsory licenses and parallel importing under TRIPS emerged. The third case discusses the role of India’s Cipla as a generic manufacturer and exporter of drugs for neglected diseases, and highlights the sources of revenue to the company. The final case deals with the emergence of a local pharmaceutical industry in Brazil during the years of TRIPS implementation and illustrates how local development reflected opportunities for export from the

country. The conclusions emphasize that, while new medicines for neglected diseases are critical to promote global health, the delivery of medicines across international borders depends on more than only patent incentives.

## **Background**

The TRIPS agreement provoked objections almost immediately after it was enacted. In South Africa, these objections became part of a national debate about HIV/AIDS (discussed below). Around the world, the controversy over TRIPS stemmed from the idea that countries with high degrees of impoverishment would be hit with large bills for essential medicines, and that payments would yield extraordinary profits for large, first-world pharmaceutical corporations. Even when compulsory licenses were issued by member countries, the affected pharmaceutical companies had rights to payments that would reflect the value of the drugs and that would be adjudicated by the WTO. On the other side, critics noted that the historically small level of investment in neglected diseases had reflected the lack of profit protection for innovators. Representatives of the pharmaceutical industry also noted that history included instances where firms were punished financially for introducing drugs for neglected diseases (such as when Wellcome's stock price dropped upon the announcement of the launch of AZT) because of the potential pressures on the firms to distribute drugs at low prices.

A partial resolution to the controversy occurred in December 2002 when an interpretive memo was issued by the WTO called the "Doha Declaration," which "allows countries to issue compulsory licenses during national emergencies such as HIV/AIDS, malaria, tuberculosis, and other epidemics. In these circumstances, a local third-party manufacturer may produce the necessary drugs for domestic use and *reasonable* compensation must be paid to the patent holder" (Loff 2002, emphasis added). Yet the Doha Declaration highlighted another problem, which was that compulsory licenses were initially ineffective for countries without the manufacturing capacity to produce medicines (Westerhaus and Castro 2006). The "Paragraph 6" amendment in August 2003 allowed for "parallel imports" in which countries could import essential medicines if they lacked the production capacity for self-manufacture (Khor 2005).

These amendments were only partial solutions for a number of reasons. First, the criterion of "national emergency" is difficult to apply in situations where infectious diseases such as HIV/AIDS create chronic, semi-permanent health crises. Second, some observers expressed

concern about a retaliatory environment where compulsory licensing would deter foreign direct investment. Third, the profits accruing to the large, first-world pharmaceutical firms, even as a reward for assuming the risks of product failure, continued to be a source of bitterness. Fourth, the standing of the Doha Declaration as a permanent amendment to TRIPS turned on how it was interpreted. The “Paragraph 6” amendment was explicitly temporary. Thus, the longevity of the policies remains in question, and the uncertainty discourages commitments of manufacturing capacity even among third parties. Furthermore, observers on both sides of the controversy have noted that the uncertainty alone may diminish cross-border trade in drugs.

In 2008, several questions about TRIPS itself are also unresolved. The Doha round of WTO negotiations has stalled and the future of TRIPS as a broad framework for international trade policy is in question. According to an agreement among WTO members in late 2005, the “parallel imports” provision enacted in August 2003 would have become permanent if two-thirds of the WTO’s 148 member states had ratified it before December 1<sup>st</sup>, 2007, but this did not occur. The efficacy of compulsory licensing and parallel imports in the first place also been called into question by observers who note that these provisions have been enacted only a few times (Westerhaus and Castro 2006, p. 1232):

“[O]nly four countries – Malaysia, Indonesia, Zambia, and Mozambique – have thus far issued compulsory licenses for ARV production, all of them in 2004. [para break] No country has yet made use of the provisions instilled in the temporary waiver, even though many low- and middle-income countries face public health emergencies.”

These concerns have been compounded by the complicated dynamics that surround newly salient exporters of pharmaceuticals from developing countries such as India and Brazil. In India, the generic pharmaceutical manufacturer, Cipla, quickly ramped up to export generic drugs for neglected diseases to countries that had declared public emergencies and sought parallel imports. Yet the company also came under considerable criticism for profiteering (discussed below as the third case). In Brazil, a conventionally research-oriented pharmaceutical industry developed locally, but the research did not tend toward neglected diseases. Instead, as the final case below demonstrates, the Brazilian pharmaceutical companies pursued lucrative export markets for global diseases such as diabetes and cancer rather than locally relevant neglected diseases. We interpret these results as evidence of a complex set of interacting responses to the incentives created under TRIPS.

A first purpose of this paper is to evaluate systematically whether the level and patterns of international trade in pharmaceuticals changed significantly after TRIPS was implemented. The cross-sectional evidence available to analyze this question is crude, and does not allow us to discern whether any apparent increase in trade is due to higher prices, larger volumes, or shifts in the composition of the traded medicines. Nonetheless, we proceed with caution to identify whether any change in pattern is evident. In particular, we investigate how trade in biopharmaceuticals between advanced, developing and least-developed countries shifted between 1994, before TRIPS was implemented, and 2006, after implementation in almost all WTO countries. Our hope is that this finding will inform the policy debate about whether TRIPS should be renewed and strengthened.

A second purpose is to inform subsequent research by conducting case analyses on specific situations affected by TRIPS to shed light on obstacles to the effective transfer and dissemination of technologies. These case studies are descriptive rather than prescriptive. The results are intended to suggest areas for further study.

### **Theorized Relationships**

Patent systems provide temporary monopolies on property rights as an incentive for innovation. Scherer (2007) estimates that the average cost to pharmaceutical companies of new-drug development (after accounting for research dead-ends and clinical trails) increased dramatically into the hundreds of millions during the 1980s and 1990s despite alleged decreases in the costs of basic science. The rationale for pharmaceutical patents is that no firm can justify investing on this scale without the assurance of ex post property rights, given the relative ease with which a chemical can be copied.

The life-saving nature of medicines and the profitability associated with scale in risk-taking has made the assignment of property rights in pharmaceuticals particularly controversial. The controversy stems from the suggestion that the patent system may not be effective for facilitating the transfer and dissemination of technologies to poorer countries for several reasons.

First, the markets for life-saving drugs for neglected diseases are attenuated by the absence of institutions such as private and social insurance and other risk-sharing mechanisms

(Kremer 2000, Barder Kremer and Williams 2006, Gallup and Sachs 2000). Insurance is important because it distributes the burden of payment across the population and provides some assurance to private pharmaceutical companies of revenues even when some patients are destitute. The absence of risk-sharing mechanisms dampens the incentive for innovation in neglected diseases and may mean that the patent system does not function as effectively to spur innovation in this context as in first-world markets where various forms insurance create revenue on drugs even when patients are destitute.

Second, when innovation does occur, market-clearing prices in resource-poor settings may be too low. Even when a drug exists for a particular treatment, firms may choose not to market it in very poor countries because the expected revenues would not even cover the fixed costs of launch (Vachani and Smith 2004, Hamoudi and Sachs 1999).

Third, missing infrastructure in developing countries may further impede the effective distribution of medicine for neglected diseases (Lennox and Ehrenpreis 2003). The WTO memos in 2002 and 2003 highlight the role of licensing legislation and manufacturing facilities. Other institutions that are crucial to market mechanisms include clinics where indications are diagnosed, therapies prescribed, and compliance monitored; and facilities for transporting, storing, dispensing, billing and accounting for medicines.

Fourth, the costs of cross-border trade or international reference pricing in pharmaceuticals may be perceived as significant regardless of the application to neglected diseases (Carmignani 2003, Kyle 2007). A perception of high costs would arise if firms anticipated that the export of products at low prices to some countries could undermine exports at high prices to traditional purchasers in advanced countries. Kyle (2007a, 2007b) shows that this concern is evident in the behavior of the leading pharmaceutical companies of Western Europe, which do not pursue opportunities even in European markets because of the threat of parallel trade, reference pricing, or restrictive price controls.

Fifth, basic research on neglected diseases may be hampered by lack of information among researchers regarding patient experience on a number of levels. Researchers may not have good statistical information on previously prescribed therapies or compliance. Detailed clinical case analysis may not be available. Information about interactions and related conditions may be missing (see Hermans, Loffler and Stern 2007).

Sixth, informational spillovers which are common in the pharmaceutical research process may be uncommon when the research relates to neglected diseases. Scientific conferences, publication outlets, and communities of practice may be relatively sparse, which may in turn increase the costs of innovation.

Seventh, the costs and hazards of clinical trials may be perceived as relatively higher for neglected diseases than for non-neglected diseases. Firms may have difficulty in predicting the costs of clinical trials, administering trials, finding control groups, and assuring compliance with home-country protocols.

Eighth, the leading pharmaceutical companies may perceive that compulsory licenses may be issued on their successful inventions regarding neglected diseases, and thereby face a dampened incentive to innovate in the first place (Pecoul et al 1999). Stiglitz (2004) suggests that this perception has led leading pharmaceutical manufacturers to encourage bilateral agreements that supersede TRIPS and protect their patented HIV/AIDS drugs from generic competition.

As a result of these theorized relationships, the effectiveness of the current WTO legislation in promoting the transfer and dissemination of medicines into resource-limited settings may be blunted. We examine data on international trade in pharmaceuticals to develop information about whether the implementation of TRIPS (including the 2002 and 2003 amendments) has been associated with change in the patterns of trade in medicines across international boundaries. In particular, we first examine whether international trade in pharmaceuticals has increased during the period of TRIPS implementation relative to trade in other sectors that were not specifically targeted by TRIPS. We also conduct cross-sectional analysis on 1993-2006 pharmaceutical trade between developing and least-developed countries to evaluate whether the patterns of trade changed significantly.

These intertemporal and cross-sectional analyses yield insight about changes in trade patterns, but are limited as tests of the efficacy of TRIPS. Definitive inferences require a structural analysis of each of the theorized relationships described above. Because of data limitations, we cannot conduct these tests directly. Yet to shed light on the most important issues for further study, we reflect on several of these theoretical relationships in the case analyses. In each situation, we highlight information regarding how the pharmaceutical industry responded to



the local conditions that are theorized above as relevant. The conclusion identifies the opportunities for further research to support the ongoing debate about WTO policy regarding incentives for pharmaceutical research on neglected diseases.

## **Data**

The panel dataset for comparing changes in patterns of global trade originates as the United Nations Commodity Trade Statistics database (UN Comtrade). The UN Comtrade data, expressed in nominal local currency, is adjusted into real dollars using GDP deflators (i.e., through currency conversion using the exchange rates reported by the nation, or if national data is unavailable, derived from contemporaneous monthly market rates).

In the UN Comtrade data, the coverage by country differs somewhat over time, with a broad trend toward more comprehensive coverage in more recent years. The 1991 data covers 75 countries, the 1995 data covers 122 countries, and the 1997 data covers 135 countries. Only countries that were either WTO members or observers are included in the empirical analysis.

The UN data has one special feature that makes it particularly attractive for the purpose of this analysis: trade that is imported and then re-exported from a country is generally identified separately and has been excluded. In particular, imports to a nation that are only in transit prior to export are excluded. By contrast, any trade that involves value added within a country is included at the gross amount. For example, the value of automotive exports from the United States are not net of imports of steel used in the manufacture of automobiles, but steel imported to the US only for transit to Canada is generally excluded from the data.

To conduct our analysis, we compare the increase in trade in the biopharmaceutical sector for particular countries in a particular year with the increase in trade from the same countries in a control group of non-Intellectual Property (IP)-intensive products that do not involve either biopharmaceuticals or related activities or other R&D intensive sectors. To define the relevant biopharmaceuticals products and the control group we use the benchmark industry cluster definitions from the International Cluster Competitiveness Project (ICCP) at the Institute for Strategy and Competitiveness at Harvard. This project employs the methods described in Porter (2003) to identify 36 clusters and 206 subclusters of trading activity in 163 countries. Cluster boundaries are determined by the location correlation of employment in the industries that are

candidates for inclusion in a particular cluster (e.g., as explained on the project’s website at <http://data.isc.hbs.edu/iccp/index.jsp>, the computer hardware and software industries are tied into the same cluster because employment in each industry is strongly correlated geographically). The advantage of the ICCP cluster definitions is its reliance on employment data to establish affinities between industries despite the idiosyncrasies of the standard system.

Table 1 shows the core biopharmaceuticals cluster (Panel I) and other constituent subclusters and SITC industries represented in the broadly defined biopharmaceuticals cluster as established by the ICCP. In the ICCP definition, the core Biopharmaceuticals cluster includes the Biopharmaceuticals Product subcluster and Health and the Beauty Products subcluster. The broad biopharmaceuticals cluster definition includes products from linked clusters, such as analytical instruments, chemical products, medical devices, , and food processing. Our analysis is confined only to the core activities listed under the “biopharmaceuticals products” sub-cluster. For robustness, we have replicated the analysis using the broad biopharmaceuticals cluster definition.

The purpose of the control group is to provide a benchmark that captures the amount of trade between countries independently of TRIPS. For example, imagine that trade between the Netherlands and China increases dramatically both within biopharmaceuticals and other non-IP sectors. It would be reasonable to consider that the increase in biopharmaceuticals may have occurred in parallel with the other sectors even if TRIPS had not been implemented. To allow for the possibility of enhanced trade between countries independently of TRIPS, we compare all levels of trade in biopharmaceuticals with those in the control group. The control group excludes the broad biopharmaceuticals cluster described in Table 1 and other R&D intensive clusters, including aerospace engines, aerospace vehicles and defense, communications equipment, and information technology (broadly constructed to include computers, electronics and peripherals). Thus, the control group for each country represents all trading activity for the country except in biopharmaceuticals and these additional IP-intensive clusters.

For each country, using the ICCP cluster definitions, we isolate from the UN Comtrade data two complementary datasets: one on exports by year and cluster for specific countries, and the other on imports by year and cluster for specific countries. In each instance we capture information on trading partners, i.e., the originating countries for automotive cluster imports into the United States in a particular year, and also the target countries for automotive cluster exports from the United States in a particular year. If the reported exports from one country into another

do not coincide with the imports reported for the receiving country, then we rely on the methods developed by Feenstra et al (2005) to achieve reconciliation. There are many valid reasons for these differences, including the fact that the data are reported independently by administrations of two different countries (see <http://comtrade.un.org/kb/article.aspx?id=10166>). The reconciliation that we employ (which Feenstra et al (2005) developed for the NBER-UN export dataset) generally emphasizes the accuracy of import reports over export reports except when they are not available.<sup>2</sup>

A crucial step in the analysis is the classification of countries by year as “advanced,” “developing,” and “least developed.” To complete this step in the construction of the dataset, we used the United Nations’ designations for each year, but confined the dataset only to include members and observer countries in the World Trade Organization (because only these countries would be bound by TRIPS). Of the 165 WTO member and observer countries in the dataset, 41 were classified by the UN as “advanced,” 91 were classified as “developed” (including Russia, were observers), and 32 were least-developed countries (Bangladesh, Benin, Bhutan, Burkina Faso, Burundi, Cambodia, Cape Verde, the Central African Republic, Chad, Ethiopia, Gambia, Guinea, Lesotho, Madagascar, Malawi, Maldives, Mali, Mauritania, Mozambique, Myanmar, Nepal, Rwanda, Samoa, Sao Tome and Principe, Senegal, Sierra Leone, Sudan, Togo, Uganda, the United Republic of Tanzania, Vanuatu, Yemen and Zambia). The source information for this classification is available at:

[http://www.wto.org/english/tratop\\_e/devel\\_e/d1who\\_e.htm](http://www.wto.org/english/tratop_e/devel_e/d1who_e.htm). According to the WTO’s rules, members declare their status as advanced, developing or least-developed, but other members may challenge the declared status for WTO review. In 2000 and 2001, the WTO reviewed the legislation of developing WTO members whose transition periods expired on 31 December 1999.<sup>3</sup>

The statistical regularities evident in the analysis of trade patterns raise a series of questions about the micro-dynamics of biopharmaceutical responses to the implementation of TRIPS, including the impact of changes in pricing, company strategy, complementary infrastructure development, and product mix. To explore these questions, we examined the circumstances of trade in the four case situations identified earlier: Wellcome’s introduction of

---

<sup>2</sup> There are countries that are not available some years. For these countries we estimate both their exports and imports using other countries reported imports from and exports into the country. We drop countries that have never reported trade in the UN Comtrade data.

<sup>3</sup> [http://www.wto.org/english/tratop\\_e/trips\\_e/tripfq\\_e.htm#Transition](http://www.wto.org/english/tratop_e/trips_e/tripfq_e.htm#Transition)

AZT, the South African debate, India’s Cipla and developments in the Brazilian pharmaceutical industry. For each of these countries, we combed public records (such as newspapers, the trade press, and the policy press) to enrich the perspective available through the trade statistics and to develop hypotheses for further research.

## Methods

We begin with a descriptive analysis of trade patterns over time for countries with different levels of income. We are interested first in comparing a country’s total exports (imports) in biopharma to other IP-intensive products that may be affected by TRIPS and to a control group of products that should not be affected by IP-related TRIPS in particular. These provisions involved specific protections in computing, semiconductor, and other high-technology businesses. Thus, the “control group” for each country includes all sectors except those specifically named in TRIPS, and the “other IP” group includes sectors named specifically in TRIPS except for biopharma. We define each country as an advanced, developing, or least-developed country using the United Nations’ and WTO’s categorizations. We estimate the following equations for each sector (biopharma, other IP, and control), where  $i$  indexes country,  $t$  indexes year,  $s$  indexes sector, and  $l$  indexes country type (advanced, developing, or least-developed):

$$(1a) \text{LogBiopharmaImport}_{it} = \sum \alpha_{lt} I_{lt} + \sum \gamma_l \text{PostTRIPS}_{it} + \varepsilon_{it}$$

$$(1b) \text{LogOtherIPImport}_{it} = \sum \alpha_{lt} I_{lt} + \sum \gamma_l \text{PostTRIPS}_{it} + \varepsilon_{it}$$

$$(1c) \text{LogControlImport}_{it} = \sum \alpha_{lt} I_{lt} + \sum \gamma_l \text{PostTRIPS}_{it} + \varepsilon_{it}$$

$$(2a) \text{LogBiopharmaExport}_{it} = \sum \alpha_{lt} I_{lt} + \sum \gamma_l \text{PostTRIPS}_{it} + \varepsilon_{it}$$

$$(2b) \text{LogOtherIPEXport}_{it} = \sum \alpha_{lt} I_{lt} + \sum \gamma_l \text{PostTRIPS}_{it} + \varepsilon_{it}$$

$$(2c) \text{LogControlExport}_{it} = \sum \alpha_{lt} I_{lt} + \sum \gamma_l \text{PostTRIPS}_{it} + \varepsilon_{it}$$

where  $I_{lt}$  is a vector of country type-year dummy variables, and  $\text{PostTRIPS}$  is a dummy variable indicating whether country  $i$  has implemented TRIPS. Since the error terms in the three sector equations are likely to be correlated, we estimate equations 1a-1c and 2a-2c using Seemingly Unrelated Regression (SUR). We also cluster the standard errors by country. This allows each sector to have different country type-year effects in addition to a different estimated

impact of TRIPS on exports or imports. The coefficients of interest are  $\gamma_l$ : we expect this to be of greater economic importance for the biopharma and IP-intensive sectors than for the control group, and we are interested in whether this varies by country type.

As an alternative, we also estimate the following:

$$(3) \text{LogImport}_{ist} = \sum \alpha_{it} I_{it} + \sum \gamma_{ls} I_{lst} \text{PostTRIPS}_{it} + \varepsilon_{ist}$$

$$(4) \text{LogExport}_{ist} = \sum \alpha_{it} I_{it} + \sum \gamma_{ls} I_{lst} \text{PostTRIPS}_{it} + \varepsilon_{ist}$$

This specification constrains the country type-year effects to be the same for all sectors and includes a country type and sector-specific TRIPS effect.

The equations above capture how the dollar volume of exports and imports changed over time for advanced, developing and least-developed countries. This provides some insight into how liberalized trade affected the balance of trade for a country in different industry sectors. For example, if TRIPS removed the fear of having technology appropriated by imitators in poorer countries, we would expect an increase in IP-related imports in developing and least-developed countries relative to our control group after the implementation of TRIPS. However, this analysis does not show whether the flow of trade between countries of each type changed over time. These flows are of central interest in an assessment of the efficacy of TRIPS, which had as an objective to enable the transfer and dissemination of technology from biopharmaceutical firms (almost all of which were headquartered in advanced countries at the time of implementation) to least-developed countries. Thus, the level of trade between advanced and least-developed countries is of special interest in the assessment. Of course, increases in the level of trade between advanced and developing countries may also conform to the objectives of TRIPS.

We turn next to an analysis of bilateral trade between countries. We use the same approach as Rose (2004) in estimating the well-established gravity model of trade between two countries, and rely on differences in the timing of TRIPS implementation across pairs of countries to identify the effect of TRIPS on pharmaceutical trade. As before, we compare three sectors of trade: biopharma, other IP, and our control group. We use the following specification to estimate trade between countries  $i$  and  $j$  in sector  $s$  in year  $t$ :

$$(5a) \text{LogBiopharmaTrade}_{ijt} = \beta_X X_{ijt} + \gamma_1 \text{BothTRIPS} + \gamma_2 \text{OneTRIPS} + \varepsilon_{ijt}$$

$$(5b) \text{LogOtherIPTrade}_{ijt} = \beta_X X_{ijt} + \gamma_1 \text{BothTRIPS} + \gamma_2 \text{OneTRIPS} + \varepsilon_{ijt}$$

$$(5c) \text{LogControlTrade}_{ijt} = \beta_X X_{ijt} + \gamma_1 \text{BothTRIPS} + \gamma_2 \text{OneTRIPS} + \varepsilon_{ijt}$$

X includes variables typically used in gravity models, such as the real GDP and real GDP per capita of the pair of countries, dummy variables indicating if the pair of countries shares a language or border (land border or small body of water border), a dummy variable denoting the existence of a free trade agreement in year  $t$ , and the (log of) great circle distance between the capital cities in kilometers.<sup>4</sup> We include dummy variables for each type of country pair (advanced-advanced, advanced-developing, advanced-LDC, developing-developing, developing-LDC, and LDC-LDC), which are allowed to vary by year. As before, we estimate the 5a-5c system of equations using SUR, and we cluster the standard errors by country pair. And as before, we estimate an additional specification as follows, including year-sector dummy variables in X:

$$(6) \text{LogTrade}_{ijst} = \beta_X X_{ijt} + \gamma_1 \text{BothTRIPS} + \gamma_2 \text{OneTRIPS} + \varepsilon_{ijst}$$

We complement the statistical analysis with four case analyses, which are descriptive rather than normative or prescriptive. The objective is to draw on secondary literature and protagonist reports to explore issues related to TRIPS in specific settings. The four represented cases are salient rather than representative. The purpose of the analysis is to complement the statistical analysis with detailed information that yields hypotheses for further study.

## Results

---

<sup>4</sup> Real GDP and real GDP per capita are sourced from the IMF data, and are deflated using the US Price Deflator for Gross Domestic Product (2006 is the base year). The common border and common language variables are sourced from Jon Haveman's web page and updated by the authors (see <http://www.macalester.edu/research/economics/PAGE/HAVEMAN/Trade.Resources/TradeData.html>). Distance is also sourced from Jon Haveman's web page. This dataset contains information for 137 countries (9451 pairs of countries). Finally, the FTA variable includes regional trade agreements and key bilateral agreements. We have computed the FTA variable using WTO data. Specifically, member countries of WTO report on whether they have subscribed to any regional trade agreement (RTAs) that offers advantages over GATT's conditions ([http://www.wto.org/english/tratop\\_e/region\\_e/regfac\\_e.htm](http://www.wto.org/english/tratop_e/region_e/regfac_e.htm)). Other useful linkages for multilateral and bilateral trade agreements that we have used are <http://bilaterals.org/> and [http://www.sice.oas.org/agreements\\_e.asp](http://www.sice.oas.org/agreements_e.asp).

The results of the estimates of the analysis of biopharmaceutical exports and imports are presented in Table 2. Columns 2-4 correspond to exports of biopharma products, other IP products, and our control sectors; columns 5-7 correspond to imports for these sectors. Table 3 presents the results of estimating equation 4, where we stack all sectors together and constrain the country type-year effects to be the same for all sectors. Across all specifications, the implementation of TRIPS is associated with higher imports or exports of biopharma and IP-related products relative to the control sector. These differences are most pronounced (both in statistical significance and magnitude) for developed countries.

We graph the pattern of exports and imports over time using results from Table 2 in Figures 1 and 2, with a panel for each country type and within each panel, a line for each sector by TRIPS implementation. The figures account for the country type-year specific effects and allow a visual comparison of changes in trade across sectors. Biopharma and other IP-intensive products exports and imports grew slightly more in biopharma for all three country income levels relative to the control sector; however, these figures make clear that the growth in IP-related trade (biopharma and otherwise) has not been especially large. The only dramatic difference between countries that have implemented TRIPS and those that have not appears to be for developed countries, and this difference is driven a rather small number of countries (Russia and the Bahamas are the only UN-defined developed countries that had not implemented TRIPS by 2006).

We turn next to the analysis of bilateral trade. The results of estimating the system of equations 5a-5c above using SUR are presented in Table 4 (year and country pair dummies and interactions are included but not reported), and these results are graphed for three country pair types (developed-developing, developed-least developed, and developing-least developed) in Figure 3. Coefficients on gravity variables such as the existence of a common border or language, distance, and the product of the pair's real GDP and real per capita GDP have the expected signs. We are, as before, more interested in understanding differences across sectors associated with the implementation of TRIPS as well as differences between pairs of countries. Indeed, trade increases significantly in all sectors when both countries have implemented TRIPS, and this increase is greatest for biopharma products. The coefficient on the dummy variable for TRIPS implementation by both countries is statistically different for biopharma and other IP trade than for the control group (in the specifications that include distance, the coefficient is different

for biopharma and for other IP as well). Similarly, the results from the pooled regression of trade across the three sectors, which are presented in Table 6, show that the implementation of TRIPS by both countries is associated with greater trade in biopharma and other IP products than in the control group. As well, the effect of TRIPS is stronger when both countries have implemented its rules than when just one half of the pair has done so. These specifications include country pair-type dummies interacted with year dummies and standard errors are clustered by country pair.

The results in Tables 2-5 are robust to a number of alternative specifications, such as weighting by GDP (country real GDP in Tables 2-3 and country-pair total real GDP in Tables 4-5), restricting the sample to countries with positive trade in biopharma, and changing the definitions of the biopharma, other IP and control sectors.<sup>5</sup>

### **Case Evidence**

The exploration of specific cases that shed light on the issues and complexities of TRIPS is roughly chronological. The first case on Wellcome's introduction of AZT pre-dated adoption of the TRIPS agreement by several years. The second on the South African controversy over TRIPS occurred virtually simultaneously with the agreement that established the WTO in 1994. The third on India's Cipla reflects developments after the implementation of the Doha and Paragraph 6 amendments on compulsory licensing and parallel imports. The final case on the Brazilian pharmaceutical industry deals with recent developments.

*Wellcome's introduction of AZT.* In September 1986, the British pharmaceutical company, Wellcome PLC, in conjunction with the US FDA, ended testing in placebo control groups of azidothymidine (AZT) as a treatment for HIV. The drug had saved so many lives in the test group that administration of a placebo was deemed unethical. Despite the drug's serious side effects, its efficacy led the FDA to announce January 1987 hearings to expedite approval for the treatment of AIDS. Once introduced, AZT would be the only available treatment.

A few days in advance of the FDA's hearings, the company's stock price jumped 15%. The *New York Times* reported the prospect of a large market for AZT as "AIDS hope" among

---

<sup>5</sup> Specifically, in the sensitivity analysis we use the broad biopharmaceuticals definition specified in Table 1, and we use a narrower IP group of products that excludes electrical and electronic components, assemblies and peripherals.



investors and analysts, and quoted a Warburg analytical report as saying “We identify Wellcome as our single most attractive major capitalization recommendation of pharmaceutical companies based anywhere in the world” (Lohr, 1987).

Despite investor enthusiasm and Wellcome’s ability to set a price in the US without direct intervention from the government, the company’s ability to realize “AIDS hope” in financial-market value was stymied. The annual retail price of a year’s course of AZT therapy was estimated at \$10,000 upon introduction of the drug in February 1987 (Liedtka 1991). Wellcome’s share price jumped 24% at the time of AZT’s launch, but extensive criticism followed: activists demonstrated against the company’s pricing, the US Congress scheduled hearings on pricing, and the scientific community criticized AZT’s toxicity and potential for inducing drug resistance. The *Wall Street Journal* and *New York Times* debated the morality and policy implications of a profit-seeking motive when introducing a drug with important effects on public health.

Wellcome dropped its price on AZT by 20% in December 1987, and by another 20% and in September 1989 (Liedtka 1991). These decreases were accompanied by a series of actions taken by the firm to assure the public that the therapy would be available even to low-income patients. Yet despite these steps, activists, scientists, politicians, legislators and patients continued to criticize the company for the pricing and medical efficacy of AZT (Emmons and Nimgade 1991). Activists in AIDS groups, particularly ACT UP, staged dramatic demonstrations targeted particularly at the company’s investors. Scientific critics went so far as to suggest that the AZT incorrectly legitimized the transmission mechanism of HIV to AIDS.

By 1990, the firm’s profitability was well below the average for pharmaceutical companies (Emmons and Nimgade 1991, Liedtka 1991). Given Wellcome’s history as a charity (75% of its shares were held by the non-profit Wellcome Foundation) and of emphasizing research on neglected diseases, the pharmaceutical industry’s advocates entered WTO negotiations over TRIPS with extensive concerns about the incentives required to stimulate research within private companies on neglected diseases (Vachani and Smith, 1999). Indeed, the complications for pharmaceutical companies that pursued research on neglected diseases were reportedly enhanced significantly by the public outcry over AZT (IFPMA, 2003). Thus, the Wellcome experience points to one reason why WTO negotiators may have been focused on creating particularly strong incentives for pharmaceutical R&D under TRIPS.

**South Africa.** South Africa's country's ascension into the WTO as a developed country on January 1, 1995, coincided with the raging HIV/AIDS epidemic and the historic election of ANC candidate Nelson Mandela to the presidency in April 1994. In 1994, rates of HIV/AIDS infection in South Africa were estimated at 7.6%, but with shortfalls in prevention and treatment programs, the rate nearly doubled to 14.2% in 1996 (Abdelal, Spar and Cousins, 2002). A central tenet of the ANC dating to the 1950's "Freedom Charter" was the idea that ownership of South Africa's material resources – and particularly its mines, banks, and manufacturing enterprises – would be by and to the benefit of the country's people rather than to "monopolistic" interests. Thus, the institution of TRIPS under the WTO agreement was almost immediately paradoxical, as it required the implementation of patent protections on essential medicines precisely at the moment in time when the newly elected government was explicitly anti-monopolistic in economic policy, and when the HIV crisis swept across the country.

The first priority of the newly elected ANC government was to address the most basic needs of the poverty-inflicted populace: housing, water and basic economic opportunity. Under a set of controversial reform policies implemented in 1996, the government sought to create jobs and build infrastructure. The 1999 election of ANC candidate Thabo Mbeki to succeed Mandela represented a deepening commitment to accelerating the process of reform (Abdelal, Spar and Cousins 2003).

In 1998, the pro-enterprise approach of the ANC was met with a lawsuit filed against the government by a group of 40 pharmaceutical companies, which sought to overturn a law signed by Mandela in 1997 allowing the importation of generic AZT drugs (and other pharmaceuticals) even without compensation to the patent-holder. This practice of the parallel importing of generic drugs violated the TRIPS agreement, according to the pharmaceutical companies (see Kennedy (2001) for a chronicle of articles on the suit). Another facet of the law, compulsory licensing, was also identified as a violation.

A series of protests against the pharmaceutical industry's position began almost immediately and escalated over the course of the subsequent two years. In a legendary action, the 1999 meeting of the WTO in Seattle was entirely disrupted by activists protesting TRIPS and the pharmaceutical-industry position. The protests ultimately led to the extension of South Africa's

two policies – compulsory licensing and parallel importing – under the WTO as the Doha and Paragraph 6 amendments to TRIPS, although the time required for their adoption was significant.

*India.* The attention drawn to the plight of the destitute poor with HIV under the WTO talks was soon followed by yet another controversy involving Indian generic pharmaceutical manufacturer, Cipla Limited. Cipla responded to the position of the leading pharmaceutical companies by offering to export generic copies of the critical HIV/AIDS “cocktail” for \$350 per year through Medicins Sans Frontieres, the Nobel-Prize-winning doctors’ group that provides healthcare to the poor in Africa. India, a country not yet required to comply with the WTO’s TRIPS standards because of its standing as a developing country, would serve as the place where the generics would be manufactured. The medicines would be distributed to least-developed countries in Africa where the HIV epidemic constituted a health emergency.

Cipla’s position had both a direct, immediate consequence and a more subtle impact on the debate over TRIPS. The direct consequence related to the WTO’s requirements for compliance among ascending member countries. Representatives of the countries argued that, without domestic pharmaceutical manufacturing capabilities, compulsory licensing was futile and that parallel importing from Cipla was essential for obtaining the medicines (Westerhaus and Castro 2006).

Cipla’s offer also had a major impact on a shift of sentiment among policy-makers away from concerns about the intellectual-property rights of leading pharmaceutical companies and toward the AIDS crisis (Kennedy 2001) in part because the same drug cocktail was priced at more than \$10,000 in the United States. The low price on Cipla’s generic versions highlighted the contribution margin obtained on the \$10,000 retail US prices, where an estimated 40% of AIDS patients were not covered by insurance and where AIDS was associated with impoverishment.

As attention turned toward the global health crisis associated with AIDS, policymakers were confronted with yet another paradox in the Cipla proposal. The recipient group, Medicins Sans Frontieres, had the capacity to serve only several thousands of patients in sub-Saharan Africa, not the millions that had been infected. Cipla’s offer to sell the cocktail at \$600 to governments had met with few orders in part because even the \$600 annual price tag was a significant percentage of average per-capita income in many of the affected countries. The

problem highlighted the complexity of resolving the challenges of effective health delivery in these settings, and contributed to the momentum for founding of the Global Fund to Fight AIDS, Tuberculosis and Malaria in 2002 and to US President Bush's PEPFAR program, announced in his January 2003 State of the Union address

**Brazil.** The generic pharmaceutical industry in Brazil developed in parallel to the industry in India during the late 1990s and early 2000's, although under some significantly different conditions such as the country's economic contraction between 1998 and 2003. One of the major long-standing structural differences across the countries was the centralized role of the Brazilian government as a major distributor of drugs, administrator of health services, and engine of research and development. As a result of the coordinating role of the government, the Brazilian pharmaceutical companies followed a unique developmental course that involved research on drugs for export to lucrative first-world markets as well as drugs for domestic distribution.

By 2007, four major Brazilian generic pharmaceutical companies specialized in providing drugs to the domestic market, yet in a remarkable announcement made on May 4<sup>th</sup>, the country's President, Luiz Inacio Lula da Silva, declared the country in a national emergency over HIV and evoked Brazil's right to a compulsory license on Merck's Efavirenz, an antiretroviral medication. The announcement was striking in part because of the availability of the drug to the Brazilian government directly from the manufacturer, although at higher prices than were available through generic Indian pharmaceutical companies currently selling copies in other parts of the world. In April of 2007, the Brazilian Health Minister had sought to negotiate a lower price on the drug directly from Merck, but rejected the company's proposal of a 30% discount as insufficient. According to *Medical News Today* (May 9, 2007):

“Merck in a statement released Friday after Silva's announcement said that Brazil ‘has a greater capacity to pay for HIV medicines than countries that are poorer or harder hit by the disease.’ HIV/AIDS advocates worldwide praised Silva's move, while the U.S.-Brazil Business Council criticized the move as a step backward, according to the AP/Forbes (AP/Forbes, 5/4). Jeffrey Sturchio, a vice president at Merck, said that if Brazil ‘expropriates our intellectual property, it will have a chilling effect on whether companies research diseases of the developing world and in the long term will have an impact on the poorest countries.’ Sturchio added that emerging economies, such as Brazil, must help

the developed world in covering production costs of new drugs and in funding future drug innovation.”

Thus, the issuance of one of the only compulsory licenses pursued under TRIPS was construed as a negotiating tactic and tied directly to incentives for subsequent research on neglected diseases. A subtext in the tactic was the focus of the Brazilian research community – including both public and private pharmaceutical development initiatives – on developing drugs for treating diseases prevalent in first-world countries such as the US (Kyle and McGahan 2007). Thus, the issuance of one of the first compulsory licenses under TRIPS was associated with the development of a local pharmaceutical industry specifically oriented toward export into advanced nations.

### **Discussion and Conclusion**

The TRIPS agreement implemented in 1994 and modified in 2002 and 2003 had as one of its principal objectives the “transfer and dissemination of technology” to enhance social welfare. Our results overall point to a positive, though not overwhelming in magnitude, effect of TRIPS implementation on the dollar value of trade. This finding is somewhat consistent with Rose (2004, 2006), whose work does not show a large effect of GATT/WTO membership on trade. We also find rather small effects, but effects that vary across sectors in the expected way: TRIPS appears to have affected IP-intensive products and not our control sector, which gives us hope that our findings are not entirely spurious. Others (such as Subramanian and Wei (2006)) have also demonstrated that GATT/WTO membership had different effects on particular sectors.

Other effects of TRIPS may have occurred in the volume of products traded or the price of traded goods, and this is an important question for further research. If the dollar value of trade between developed and least-developed countries increased, but this reflects only the ability of IP-owners to increase prices on their products, it is not clear that TRIPS has met its policy objective. Deardorff (1992) presents a theoretical model showing that the benefits to patentholders from extending patent protection to additional countries are exceeded by losses in countries that adopt IP protection. McCalman (2001) estimates that the US has benefited most from the harmonization of patent protection required by TRIPS. In an empirical study of pharmaceuticals in India, Chaudhuri, Goldberg and Jia (2006) find that the introduction of TRIPS could lead to a social welfare loss in India because domestic producers, previously making

generic versions of drugs under patent outside of India, would be forced to withdraw from the market. Patentholders may have increased their exports to India, but this increase would not necessarily offset the reduction in domestic supply.

Our findings may obscure other possible changes related to TRIPS during this period. For example, if pharmaceutical manufacturers in advanced countries offered large volumes of essential drugs at very low prices to least-developed countries, then the aggregate value of trade may not have increased despite the greater accessibility of the drugs to disadvantaged populations. Intra-national biopharmaceutical capacity is not captured in the analysis. If leading biopharmaceutical manufacturers, headquartered principally in advanced countries, built manufacturing capacity in least-developed countries, or if they transferred technology through financial transactions (such as compulsory licenses) to locally headquartered firms in least-developed nations, then the objectives of TRIPS for technology dissemination may have been met. Further research on this possibility is needed to assess whether TRIPS was effective at stimulating the dissemination of technology into least-developed countries, and in particular whether any additional trade resulted in improved access to critical medicines. Unfortunately, the data used here can tell us nothing about whether any of the increase in biopharma trade reflects the introduction of important new treatments in poorer countries.

Finally, the intention of firms and governments in advanced countries to transfer and disseminate technology to least-developed countries may have been institutionalized, but the impact of new activity may not yet be evident in trade flows. The compulsory-licensing and parallel-import provisions of TRIPS were not adopted until 2002 and 2003, respectively. The statistical analysis reported in this paper deals with trade flows only through 2006, the last year for which data is available, and the case analysis is current only through early 2007. More time may be needed for these agreements to develop into an impact on trade flows.

The modest increase in trade during the period of TRIPS implementation also suggests that the presence of basic institutions that facilitate the effective use of essential medicines may be as important to trade as patent protection. Each of the four case studies emphasizes the intensive response to the incentives created under TRIPS, and the ongoing controversy associated with delivering medicines to impoverished patients at prices that compensate researchers adequately to induce further development of drugs for neglected diseases. Additional research is needed on whether the barriers to trade in biopharmaceuticals between advanced and least-

developed countries in part relate to the absence of infrastructure in the least-developed countries for administering, distributing, and monitoring the use of biopharmaceuticals.

Unless dramatic underlying shifts in prices and volumes are obscured by the aggregate data, the results here suggest that TRIPS has not yet sparked major changes in levels of biopharmaceutical trade to least-developed countries. Yet the case studies emphasize that the response to TRIPS is still in its infancy. Further research is needed to understand the impediments to the effective operation of the patent system in least-developed countries: What missing institutions and infrastructure impedes the effective dissemination of essential medicines? How can TRIPS policy be modified and supplemented to become more effective in achieving the objective of technology transfer? Or should TRIPS be abandoned in favor of a different system for disseminating essential medicines to the world's poor?

## References

Abbott, FM (2005), "The WTO Medicines Decision: World Pharmaceutical Trade and the Protection of Public Health," *Am J Int Law* 99, pp. 317-58

Abdelal, Rawi, Debora Spar and Katherine Cousins (2003), "Remaking the Rainbow Nation: South Africa 2002," HBS Case 702-35

Attaran, A (2004), "How Do Patents and Economic Policies Affect Access to Essential Medicines in Developing Countries," *Health Affairs* 23, pp. 155-66

Attaran A. and L Gillespie-White (2001), "Do Patents for Antiretroviral Drugs Constrain Access to AIDS Treatment in Africa?," *JAMA* 286, pp. 1886-92

Attfield, Robin, Johan Hattingh and Manamela Matshabphala (2004), *Third World Quarterly* 25:2, pp. 405-21

Bajpai, Nirupam and Jeffrey Sachs (2000), "India's Decade of Development," *CID Working Paper No. 46, Center for International Development at Harvard University* (May)

Barder, Owen, Michael Kremer and Heidi Williams (2006), "Advance Market Commitments: A Policy to Stimulate Investment in Vaccines for Neglected Diseases," *Economists' Voice* (February), pp. 1-6

"Brazil Requests Voluntary License for AIDS Drugs to Treat More Patients, Reduce Costs of Importing Patented Drugs," Kaiser Daily HIV/AIDS Report," available [www.kaisernetwork.org/daily\\_reports/rep\\_index.cfm?hint=1&DR\\_ID=2876](http://www.kaisernetwork.org/daily_reports/rep_index.cfm?hint=1&DR_ID=2876)

Cage, S (2005 Dec 6), "WTO OKs Measures to Improve Drug Access," Associated Press

Carmignani, Fabrizio (2003), "Political Instability, Uncertainty and Economics," *Journal of Economic Surveys* 17:1, pp. 1-54

Chien C (2003), "Cheap Drugs at What Price to Innovation: Does the Compulsory Licensing of Pharmaceuticals Hurt Innovation?," *Berkeley Technology Law Journal* 18, pp. 1-15

Chaudhuri, S., P. Goldberg and P. Jia (2006), "Estimating the Effects of Global Patent Protection in Pharmaceuticals: A Case Study of Quinilones in India," *American Economic Review* 96(5).

Chen, Yongmin and Thitima Puttitanun (2002), "Intellectual Property Rights and Innovation in Developing Companies," *Center for Economic Analysis* working paper 02-06, University of Colorado at Boulder (May)

Coriat, B., J Dumoulin, Yves-Antoine Flori, T Barnett, Y Souteyrand et al (2003), "Patents, Generic Drugs and the Markets for Antiretrovirals," in Coriat, Y Souteyrand, T Barnett, J Dumoulin et al, editors, *Economics of AIDS and Access to HIV/AIDS Care in Developing Countries: Issues and Challenges* (Paris: National Agency for AIDS Research), p. 27-37

Deardorff, A. (1992), "Welfare Effects of Global Patent Protection," *Economica* 59, pp. 35-51.

Dumoulin, Jerome, Yves-Antoine Flori, Philippe Vinard, and Thomas Borel (2003), "World Market Strategies for Drugs to Fight AIDS," in JP Maotti, B Coriat, Y Souteyrand, T Barnett, J



Dumoulin et al, editors, *Economics of AIDS and Access to HIV/AIDS Care in Developing Countries: Issues and Challenges* (Paris: National Agency for AIDS Research), pp. 213-44.

Emmons, Willis and Ashok Nimgade (1991), "Burroughs Wellcome and AZT (A), (B), and (C)," Harvard Business School case studies 792-004, 793-114, and 793-115

Eisenhardt, Kathleen (1989), "Building Theories from Case Study Research," *Academy of Management Review* 14:4 (October), pp. 532-550.

Feenstra, Robert C, Robert E Lipsey, Haiyan Deng, Alyson C Ma, and Hengyong Mo (2005), "World Trade Flows: 1962-2000" (January), NBER Working Paper No. 11040 at <http://www.nber.org/papers/w11040>

Gallup, John Luke and Jeffrey D Sachs, "The Economic Burden of Malaria," *CID Working Paper No. 52, Center for International Development and Harvard University* (July)

Glennerster, Rachel and Michael Kremer (2000), "A World Bank Vaccine Commitment," *Brookings Policy Brief* 57 (May), pp. 1-8

Hamoudi, Amar A. and Jeffrey D Sachs (1999), "Economic Consequences of Health Status: A Review of the Evidence," *Working Paper No 30, Center for International Development at Harvard University* (December)

Hermans, Raine, Alicia Loffler, and Scott Stern (2007), "The Globalization of Biotechnology: Science-Driven Clusters in a 'Flat' World," *The National Academies: Board on Science, Technology and Economic Policy* (January 8)

IFPMA (2003), "Neglected Diseases and the Pharmaceutical Industry," International Federation of Pharmaceutical Manufacturers Association, December, available at [http://www.ifpma.org/Documents/NR235/Brochure\\_Neglected%20Diseases.pdf](http://www.ifpma.org/Documents/NR235/Brochure_Neglected%20Diseases.pdf)

"India's Choice" (2005, January 18), editorial, *New York Times*

Jack, William and Jean O. Lanjouw (2003), "Financing Pharmaceutical Innovation: How Much Should Poor Countries Contribute?," *Center for Global Development Working Paper No. 28* (July 28)

Kennedy, Robert E (2001), "The Pharmaceutical industry and the AIDS Crisis in Developing Countries," HBS Case 702-010.

Khor Martin (2005 Oct 26), "Impasse on Talks on TRIPS and Health 'Permanent Solution'," Third World Network, [www.health-now.org/site/article.php?articleId=499&menuId=1](http://www.health-now.org/site/article.php?articleId=499&menuId=1)

Kim, Jim Y (2004, December 17), "WHO Letter to India's Health Minister on Patent Legislation," available at [www.cptech.org/ip/helth/c/india/ngodeclaration12292004.html](http://www.cptech.org/ip/helth/c/india/ngodeclaration12292004.html)

Kremer, Michael (2000), "Creating Markets for New Vaccines, Part 1: Rationale," NBER Working Paper 7716 (May)

Kremer, Michael and Rachel Glennerster (2004), *Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases* (Princeton University Press)

- Kuhn, Thomas S (1972), *The Structure of Scientific Revolutions* (University of Chicago Press)
- Kyle, Margaret K (2007), "Strategic Responses to Parallel Trade," NBER working paper W12968 available at <http://ssrn.com/abstract=971602>
- Kyle, Margaret K and Anita M McGahan (2007), "Investments in Pharmaceuticals Before and After TRIPS: How Public Policy, Technology and Globalization Shaped Drug Development," London Business School and University of Toronto manuscript (October)
- Lanjouw, Jean O and Iain M Cockburn (2001), "New Pills for Poor People? Empirical Evidence After GATT," *World Development* 29:2, pp. 265-89
- Lennock, Jean and Dag Ehrenpreis, "Good Health: A Cornerstone of Development," *Observer* 237 (May), pp. 28-31
- Liedtka, Jeanne (1991), "Burroughs Wellcome and the Pricing of AZT (A), (B), (C)". UVA-E-0074 Available at SSRN: <http://ssrn.com/abstract=908127>, 908128, 907129
- Loff, Bebe (2002), "No Agreement Reached in Talks on Access to Cheap Drugs," *Lancet* 360, p. 1951
- Lohr, Steve (1987), "Market Place; Wellcome's Bet on AIDS Drug," *New York Times* (January 12), p. D6.
- Lucchini, S., B Cisse, S Duran, M de Cenical and C Comiti et al (2003), "Decrease in Prices of Antiretroviral Drugs for Developing Countries: From Political 'Philanthropy' to Regulated Markets?," in JP Moatti, B Coriat, Y Souteyrand, T Barnett, J Dumoulin et al, editors, *Economics of AIDS and Access to HIV/AIDS Care in Developing Countries: Issues and Challenges* (Paris: National Agency for AIDS Research), pp. 169-211
- Maurer, Stephen M. (2006), "Choosing the Right Incentive Strategy for Research and Development on Neglected Diseases," *Bulletin of the World Health Organization* 84, pp. 376-81
- McCalman, P. (2001), "Reaping what you sow: an empirical analysis of international patent harmonization," *Journal of International Economics* 55, pp. 161-186.
- McNeil, Donald G, Jr, (2005, March 24), "India Alters Law on Drug Patents," *New York Times*
- Oliveira, MA, JAZ Bermudez, GC Chavez, and G Velasquez (2004), "Has the Implementation of the TRIPS Agreement in Latin America and the Caribbean Produced Intellectual Property Legislation that Favours Public Health?," *Bill World Health Organ* 82, pp. 815-21
- Pecoul, Bernard, Pierre Chirac, Patrice Trouiller and Jaques Pinel (1999), "Access to Essential Drugs in Developing Countries: A Lost Battle?," *Journal of the American Medical Association* 281, pp. 361-7.
- Porter, Michael E (2003), "The Economic Performance of Regions," *Regional Studies* 37:6-7 (August/October), pp. 549-578.

Rose, A. (2004), "Do We Really Know that the WTO Increases Trade?" *American Economic Review* 94(1), pp. 98-114.

Rose, A. (2006), "The Effect of Membership in the GATT/WTO on Trade: Where Do We Stand?" Working paper, University of California-Berkeley.

Rosenberg, Tina, (2001, January 24), "Look at Brazil," *New York Times*

Sachs, Jeffrey D (2005), "The Development Challenge," *Foreign Affairs* 84:2 (Mar/Apr), pp. 78-91

Scherer, F. M. (2007), "Pharmaceutical Innovation," Kennedy School of Government working paper RWP 007-004

Stiglitz, Joseph (2004, July 24), "New Trade Pacts Betray the Poorest Partners," *New York Times*

Subramanian, A. and S. Wei (2006), "The WTO Promotes Trade, Strongly But Unevenly," IMF working paper.

Taylor, M. Scott (1993), "TRIPS, Trade and Technology Transfer," *International Economic Review* 26:3 (August), pp. 625-37

Taylor, M. Scott (1994), "Trips, Trade and Growth," *International Economic Review* 35:2 (May), pp. 361-81

't Hoen, E (2003), "TRIPS, Pharmaceutical Patents and Access to Essential Medicines: Seattle, Doha and Beyond," in Coriat, Y Souteyrand, T Barnett, J Dumoulin et al, editors, *Economics of AIDS and Access to HIV/AIDS Care in Developing Countries: Issues and Challenges* (Paris: National Agency for AIDS Research), pp. 39-67.

"Trips "safeguards" key tools to lower drug prices," *Medicins Sans Frontieres* (1/11/2001)

Vachani, S. and N. Craig Smith (2004), "Socially Responsible Pricing: Lessons From the Pricing of AIDS Drugs in Developing Countries," *California Management Review* 47:1, pp. 117-44

Westerhaus, Michael and Arachu Castro (2006), "How Do Intellectual Property Law and International Trade Agreements Affect Access to Antiretroviral Therapy?," *PLoS Medicine* 3:8 (August), p. 1230-6, [www.plosmedicine.org](http://www.plosmedicine.org)

**Table 1: Broad Definition of the Biopharmaceuticals Cluster**

<b>I. Biopharmaceuticals Cluster</b>	
<b>Biopharmaceutical Products*</b>	Health and Beauty Products
- Provitamins, vitamins, derivatives	- Toilet waters and perfumes
- Antibiotics exc medicaments	- Preparations for hair
- Vegetable alkaloids exc medicaments	- Preparations for oral or dental hygiene
- Hormones and derivatives exc medicaments	- Toiletries, razors, razor blades
- Glycosides, glands, antisera, vaccines, sim.	- Scent, toilet sprays, and mounts & heads
- Other pharmaceutical goods	
- Medicaments containing antibiotics	
- Medicaments containing hormones	
- Medicaments containing alkaloid	
- Miscellaneous medicaments	
<b>II. Products related to the core Biopharmaceuticals Cluster</b>	
Diagnostic Substances	Dyeing, Tanning and Coloring Materials
- Blood-grouping reagents	- Synthetic colors, lakes; Synthetic tanning substances
- Opacifying preparations for X-ray exam	- Dyes, tanning extract,
- Prepared culture media	Packaged Chemicals
- Diagnostic, laboratory reagents	- Organic detergents; Lubricating preparations
Medical Equipment	Optical, Laboratory and Process Instruments
- Electro-medical equipment	- Compound optical microscopes
- X-ray, alpha, beta, gamma radiations apparatus & parts	- Instruments for analysis, measuring viscosity, expansion
Medical and Dental Instruments & Supplies	- Speed indicators, tachometers
- Hygienic pharmaceutical rubber articles	- Drawing, measuring instruments
- Misc. glass articles	- Gas, liquid measuring or checking instruments
- Modeling pastes	- Instruments for analysis, measuring viscosity, expansion
- Dental instruments & Other medical instruments	- Miscellaneous measuring, controlling and scientific instruments
- Therapeutic apparatus	- Automatic control instruments
Wheelchairs and Medical Furnishings	- Miscellaneous parts for machines, instruments
- Medical, barber's furniture	Specialty Foods and Ingredients
Ophthalmic Goods	- Flavors for industrial use
- Optical fibers, lenses and other elements,	Metal and Glass Containers
Organic Chemicals	- Glass containers
- Phenols, phenol-alcohols and derivatives	
- Monocarboxylic acids and derivatives	
- Carboxylic acids and derivatives	
- Amine-function compounds	
- Oxygen-function amino compounds	
- Other nitrogen-function compounds	
- Lactams; heterocyclic compounds	
Chemically Based Ingredients	
- Essential Oils, Additives for mineral oils	
- Albuminoidal substances, modified starches, glues	
- Other chemical products & preparations	

Note: Source: Prof. Michael E. Porter, International Cluster Competitiveness Project, Institute for Strategy and Competitiveness, Harvard Business School; Richard Bryden, Project Director. Underlying data drawn from the UN Commodity Trade Statistics Database and the IMF BOP statistics. Copyright © 2008 by the President and Fellows of Harvard College. All rights reserved (See <http://www.isc.hbs.edu/data.htm>).

\*In this paper, Biopharmaceutical Products (in Panel I) are our core biopharmaceutical definition used in Tables 2-5; the other products in Panel I and II are referred as “products related to biopharmaceuticals”

**Table 2: SUR estimation of exports and imports by sector**

	Exports			Imports		
	Biopharma	Other IP	Control	Biopharma	Other IP	Control
Intercept	12.921** (0.634)	14.486** (0.464)	17.426** (0.318)	13.544** (0.298)	15.213** (0.323)	17.435** (0.266)
Developing country	-5.826** (0.736)	-5.397** (0.539)	-2.934** (0.369)	-2.905** (0.346)	-3.515** (0.375)	-2.882** (0.309)
Least-developed country	-12.028** (0.904)	-8.089** (0.661)	-5.391** (0.454)	-4.201** (0.425)	-5.405** (0.461)	-4.572** (0.379)
Post TRIPS	2.448** (0.612)	3.888** (0.447)	1.537** (0.307)	1.793** (0.288)	2.633** (0.312)	1.534** (0.256)
Developing country * Post TRIPS	-1.831** (0.678)	-3.745** (0.496)	-1.724** (0.340)	-2.016** (0.319)	-2.678** (0.346)	-1.777** (0.284)
Least-developed country * Post TRIPS	-2.752 (1.498)	-3.880** (1.096)	-1.017 (0.752)	-0.947 (0.705)	-2.100** (0.764)	-1.247* (0.628)
Number of observations	2203	2203	2203	2202	2202	2202
R-sq	0.4843	0.5228	0.4677	0.4641	0.5232	0.5094

Y = log(real dollar value of exports/imports in sectors). The omitted category of country type is developed.

Standard errors are in parentheses. \*\*=significant at the 1% level, \*=significant at the 5% level.

All specifications include country type-year fixed effects (not reported).

**Table 3: OLS estimation of exports and imports**

	Exports		Imports	
Intercept	11.517** (0.387)	6.469** (0.246)	13.845** (0.283)	9.820** (0.076)
Other IP sector	2.581** (0.246)	2.581** (0.249)	0.911** (0.088)	0.913** (0.090)
Control sector	7.700** (0.270)	7.700** (0.273)	3.746** (0.069)	3.748** (0.070)
Post-TRIPS	3.617** (1.161)	1.143** (0.206)	1.886* (0.931)	-0.068 (0.065)
Other IP*Post-TRIPS	-0.868** (0.253)	-0.868** (0.256)	0.438** (0.096)	0.435** (0.098)
Control*Post-TRIPS	-2.111** (0.296)	-2.111** (0.299)	-0.138 (0.074)	-0.140 (0.075)
Developing country	-4.719** (0.470)	-2.038** (0.196)	-3.101** (0.339)	-0.421** (0.084)
Least-developed country	-8.503** (0.555)	-4.963** (0.303)	-4.726** (0.332)	-2.821** (0.097)
Developing country*Post-TRIPS	-2.434 (1.314)	-0.559** (0.167)	-2.146* (1.001)	-0.156 (0.083)
Least-developed country*Post-TRIPS	-2.550 (1.477)	-1.232* (0.472)	-1.431 (1.122)	0.069 (0.152)
Country fixed effects	No (clustering) 6609 0.6487	Yes 6609 0.8734	No (clustering) 6608 0.6456	Yes 6608 0.9531

Y = log(dollar value of exports or imports). The omitted categories of dummy variables are the biopharma sector and developed countries. Standard errors are in parentheses. \*\*=significant at the 1% level, \*=significant at the 5% level. All specifications include country type-year fixed effects (not reported).

**Table 4: SUR estimation of bilateral trade across sectors**

	Biopharma	Other IP	Control	Biopharma	Other IP	Control
Intercept	-25.333** (0.290)	-30.030** (0.271)	-25.602** (0.277)	-8.148** (0.354)	-18.675** (0.332)	-5.192** (0.289)
Both post-TRIPS	1.184** (0.058)	1.151** (0.054)	0.352** (0.055)	1.729** (0.067)	1.532** (0.063)	0.236** (0.055)
One Post-TRIPS	0.504** (0.046)	0.583** (0.043)	0.193** (0.044)	0.741** (0.055)	0.731** (0.052)	-0.007 (0.045)
Log(GDP <sub>i</sub> *GDP <sub>j</sub> )	1.215** (0.005)	1.381** (0.005)	1.552** (0.005)	1.415** (0.006)	1.541** (0.005)	1.414** (0.005)
Log(GDPPC <sub>i</sub> *GDPPC <sub>j</sub> )	0.106** (0.009)	0.264** (0.008)	-0.035** (0.009)	0.032** (0.010)	0.222** (0.010)	-0.082** (0.009)
Common border	4.836** (0.093)	4.290** (0.087)	3.988** (0.088)	0.606** (0.099)	1.277** (0.092)	0.568** (0.080)
Common language	2.994** (0.040)	2.184** (0.038)	2.316** (0.038)	3.078** (0.043)	2.170** (0.040)	1.582** (0.035)
Free trade agreement	3.556** (0.064)	2.492** (0.060)	2.684** (0.061)	0.540** (0.078)	0.276** (0.064)	0.123* (0.056)
Log(Distance in km)				-2.485** (0.019)	-1.778** (0.018)	-1.927** (0.016)
Number of observations	147734	147734	147734	117342	117342	117342
R-sq	0.5551	0.6431	0.6134	0.588	0.651	0.616

Y = log(real dollar value of trade between country i and country j). Standard errors are in parentheses.

\*\*=significant at the 1% level, \*=significant at the 5% level.

All specifications include country pair type-year fixed effects (not reported).

**Table 5: OLS estimates of bilateral trade**

	Model 1	Model 2
Intercept	-29.534** (0.463)	-13.554** (0.583)
Other IP	0.724** (0.034)	0.861** (0.044)
Control	6.645** (0.055)	7.787** (0.059)
Both Post-TRIPS	0.651** (0.105)	1.258** (0.111)
Both Post-TRIPS * Other IP	0.802** (0.046)	0.763** (0.054)
Both Post-TRIPS * Control	-0.069 (0.063)	-1.040** (0.066)
One Post-TRIPS	0.038 (0.076)	0.272** (0.087)
One Post-TRIPS * Other IP	0.727** (0.044)	0.786** (0.055)
One Post-TRIPS * Control	0.439** (0.059)	-0.124 (0.065)
Log(GDPi*GDPj)	1.383** (0.011)	1.457** (0.011)
Log(GDPPCi*GDPPCj)	0.112** (0.020)	0.057* (0.021)
Common border	4.371** (0.268)	0.817** (0.232)
Common language	2.498** (0.095)	2.277** (0.082)
Free trade agreement	2.911** (0.139)	0.313** (0.121)
Log(Distance in km)		-2.064** (0.039)
Number of Observations	443202	352026
R-sq	0.6585	0.681

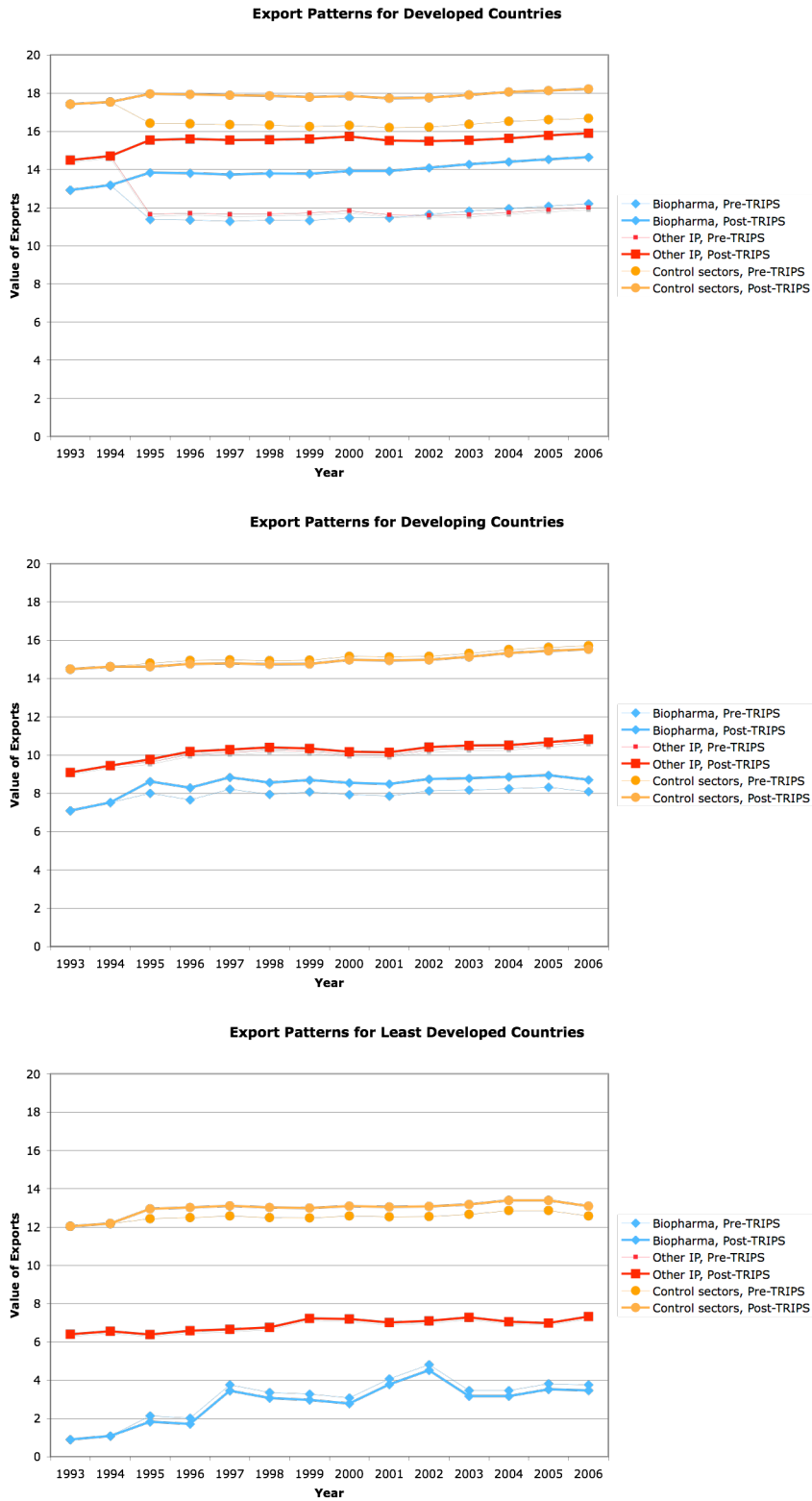
Y = log(real dollar value of trade between country i and country j). Standard errors are in parentheses. The omitted category of dummy variables is the biopharma sector.

\*\*=significant at the 1% level, \*=significant at the 5% level.

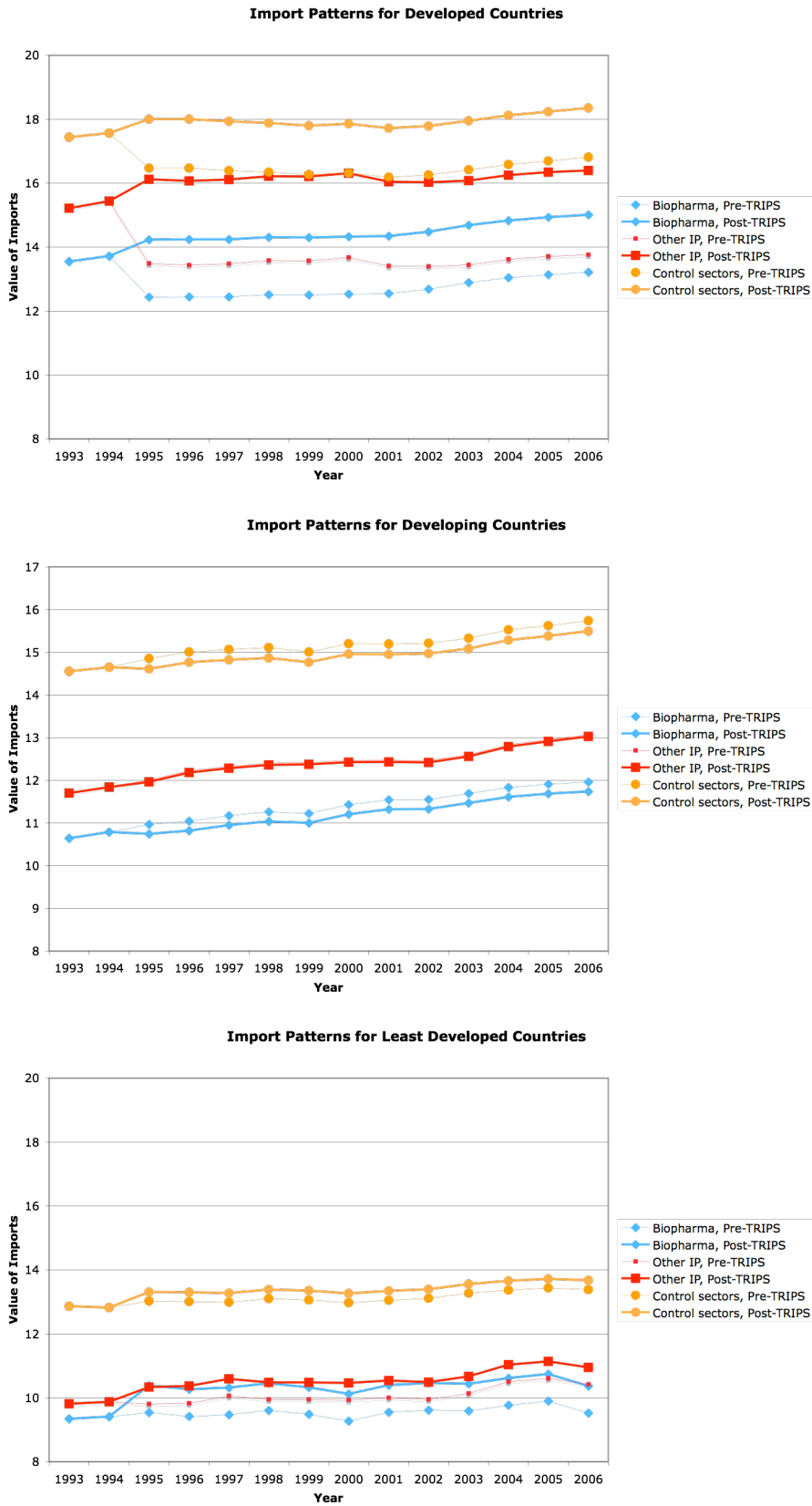
All specifications include country pair type-year fixed effects (not reported).



**Figure 1: Patterns of exports**



**Figure 2: Patterns of imports**



**Figure 3: Patterns of trade between different country pair types**

