Offshoring Production and Intra-industry Trade

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This very preliminary version: July 2012

Introduction

The pharmaceutical industry's ambition to increase access to foreign markets and to reduce production costs motivated the industry's pressure on the U.S. government to make the implementation of intellectual property rights (IPR) abroad a priority. As pharmaceutical markets in developed countries present poor opportunities of further growth, and as the cost of discovering new drugs is increasing, U.S. pharmaceutical companies have been devising strategies to develop their presence in new markets thanks to an increase in trade and foreign direct investments (FDI).

The increase in foreign patent protection has enabled pharmaceutical companies to relocate part of their research and development (R&D) and production facilities abroad, resulting in a change in the industry's global organization. U.S. companies increasingly offshore production and R&D efforts to countries that offer lower production costs and better access to growing markets (Pore, Pu, Pernenkil, & Cooney, 2008). The increase in production abroad takes the form of FDI through a foreign affiliate (offshoring) or contracting to another company (offshore outsourcing).[1] Foreign patent protection increases the fragmentation of the production

[1] Offshoring is also known as fragmentation, vertical specialization, vertical integration of the production process or "slicing the value-added chain" in the literature (Bernard et al., 2007).

process, which leads to an increase in the United States' trade of pharmaceuticals: both exports and imports are likely to increase. Exports increase thanks to growth in sales and exports of intermediate goods to affiliates or licensed companies. Imports increase since part of the foreign production supplies the domestic market, while the rest of the production supplies the market in which affiliates or licensed companies are settled, as well as third markets (Baltagi, Egger, & Pfaffermayr, 2007).

This article builds on the recent literature in international trade theory, which focuses on intra-firm trade and production offshoring (e.g. R. Baldwin & Venables, 2010; Bernard, Jensen, Redding, & Schott, 2007; Helpman, Melitz, & Yeaple, 2004; Melitz, 2003; Yeaple, 2006). Offshoring production by American firms tends to generate an increase in the United States' imports, which has an impact on the country's intra-industry trade (IIT), i.e. two-way trade of products from the same category. The literature finds a general increase of IIT in developed countries, especially in vertically differentiated products (e.g. Fontagné, Freudenberg, & Gaulier, 2006). Offshoring production tends to generate a growth in two-way trade of intermediate goods, which explains in part this increase in vertical IIT (e.g. Türkcan & Ates, 2011).

The share of countries with which the United States both imports and exports pharmaceuticals has indeed increased since the end of the Uruguay Round and the implementation of patent protection in foreign countries. In particular, two-way trade of vertically differentiated products has grown. However, IIT in the pharmaceutical industry remains quite low compared to one-way trade, and the fragmentation of the production process is captured by the growth in one-way trade with a few specific countries. This article introduces a measure of IIT intensity to try to capture the impact of an increase of intra-firm trade on IIT.

Two countries in particular have become large offshoring centers for U.S. firms at the end of the 1990s and early 2000s: Ireland and Singapore. The examples of these two countries show

that American companies will offshore production in markets that offer intellectual property rights protection, adequate infrastructure, highly qualified (and English-speaking) workers, and favorable corporate tax policies. Furthermore, Ireland enables U.S. firms to have easier access to European markets. In Singapore, they obtain easier access to Asian markets. Strong patent protection matters for where U.S. pharmaceutical firms decide to offshore production. For instance, right after the United States' free trade agreement with Singapore came into force in January 2004, U.S. trade data showed a strong increase in imports of pharmaceuticals from Singapore. IIT with this country remains low however. U.S. firms are now settling in emerging countries such as China and India to have increased access to Asian markets. While these countries offer some advantages such as an increasing pool of highly qualified and English-speaking workers, weak intellectual property rights protection remains a challenge for pharmaceutical companies. With stronger IPR protection, U.S. IIT is likely to grow in the years to come, especially with countries that have a large market and in which local pharmaceutical companies are likely to conduct R&D efforts and grow.

Section 3.2. presents stylized facts on U.S. pharmaceutical offshoring activities and their impact on trade. Section 3.3. offers a review of the literature on international trade theories to justify an analysis of IIT in pharmaceuticals. Section 3.4. conducts an IIT analysis and studies trade patterns of the U.S. regarding pharmaceuticals. Section 3.5. presents future perspectives for trade trends following the industry's global reorganization. Section 3.6. concludes.

Offshoring in the U.S. pharmaceutical industry

The pharmaceutical industry is a highly globalized industry at all stages of the value chain. Firms fragment production processes by offshoring the activities of manufacturing, R&D and clinical trials. The following section focuses on stylized facts regarding the U.S.

pharmaceutical industry's fragmentation process, and its impact on trade. In particular, this fragmentation process generates widespread intra-firm trade: in 2009, 80% of U.S. imports and 48% of U.S. exports of pharmaceuticals was intra-firm trade (Lanz & Miroudot, 2011). The U.S. pharmaceutical industry is one of the three industries (with the automobile and transport equipment industries) that has the highest share of intra-firm trade (Lanz & Miroudot, 2011).

- **Increase in foreign direct investments**

The value of foreign direct investments by U.S. multinational pharmaceutical firms grew from 29.66 billion dollars in 1999 to 62.27 billion dollars in 2010 (U.S. Bureau of Economic Analysis, 2012). As a result, the value of total assets of all foreign affiliates of U.S. pharmaceutical firms grew from 88.95 billion dollars in 1999 to 279.99 billion dollars in 2009. The number of employees in foreign affiliates of U.S. pharmaceutical firms also grew since the end of the Uruguay Round, from 209,600 in 1999 to 262,800 in 2009.

All major U.S. pharmaceutical companies conduct production activities abroad (Table 3.1.). A large part of these activities take place in developed countries, but some also take place in developing countries and emerging economies. U.S. pharmaceutical multinational firms increasingly engage in *complex FDI*. Firms that engage in complex FDI choose to offshore production to reduce costs in serving the domestic market (lower production costs), the market in which its affiliates are settled (by saving on trade costs through local production), and third markets (Baltagi et al., 2007). The tripling in ten years of total sales by all foreign affiliates of U.S. pharmaceutical companies reflects the two latter FDI purposes. Total sales by all foreign affiliates of U.S. pharmaceutical companies grew from 106.4 billion dollars in 1999 to 348.1 billion dollars in 2009. U.S. pharmaceutical companies also offshore activities through FDI to

reduce production costs and serve the U.S. market, resulting in the increase in U.S. pharmaceutical imports.

Table 1. Foreign activities of the 21 largest American pharmaceutical companies, 2009

Company	Revenues (million of US dollars)	Pharmaceutical activities (outside the USA)
Johnson & Johnson	63,747	Presence in the Netherlands, China, India, Ireland, Japan, Puerto Rico, Canada, United Arab Emirates, Slovenia, Czech Republic, Vietnam, Turkey, Thailand, Taiwan, South Africa, Slovakia, Singapore, Saudi Arabia, Italy, Mexico, Spain, Colombia, France, Australia, New Zealand, Poland, Greece, Austria, Finland, UK, Hungary, Indonesia, Germany, Argentina, Brazil, Portugal, Egypt, Romania, Russia, Venezuela, Norway, Sweden, Denmark, Philippines, South Korea, Hong Kong, Belgium, Switzerland Manufacturing in the UK, Puerto Rico, Ireland, etc.
Pfizer	48,296	Major plants located in Belgium, France, Germany, Ireland, Japan, Puerto Rico.
Abbott Laboratories	29,528	Plants in Germany, Singapore, Ireland, Argentina, etc. Presence in more than 60 countries, including China, Singapore, India, Ireland, Italy, Canada, Germany.
Merck	23,850	Presence in more than 50 countries. Sales and marketing structure and research projects in India, etc. Plants in Ireland, Singapore, Egypt, Puerto Rico, Australia, etc.
Wyeth	22,834	Part of Pfizer since the end of 2009.
Bristol-Myers Squibb	21,366	Facilities in Brazil, China, Ecuador, England, France, Ireland, Italy, Japan, Mexico and Puerto Rico.
Eli Lilly	20,378	40,000 employees abroad, major research and development facilities in eight countries, clinical trials in more than 50 countries. Manufacturing in Brazil, China, Egypt, France, Germany, Ireland, Italy, Japan, Mexico, Puerto Rico, Spain, UK.
Schering-Plough	18,502	Merged with Merck in November 2009.
Amgen	15,003	Locations in Puerto Rico, Canada, Mexico, Brazil, Austria, Belgium, Bulgaria, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Lithuania, Netherlands, Norway, Poland, Portugal, Slovakia, Spain, Sweden, Switzerland, UK, Australia, New Zealand, UAE, Hong Kong, India, Japan Manufacturing in the Netherlands and Puerto Rico.
Gilead Sciences	5,336	Manufacturing in Canada, Ireland. Present in Canada, the UK, Australia, New Zealand, Austria, Belgium, Denmark, France, Germany, Greece, Ireland, Italy, Norway, Portugal, Spain, Sweden, Switzerland, Turkey.
Mylan	5,138	Manufacturing in India, China, New Zealand, etc.
Genzyme	4,605	Manufacturing in the UK, Belgium, Ireland, Switzerland, etc.
Allergan	4,403	Manufacturing in Ireland, India, etc.
Biogen Idec	4,098	Affiliates in 25 countries. Manufacturing in Denmark.
Forest Laboratories	3,836	Manufacturing in Ireland, UK.
Hospira	3,630	Manufacturing in Australia, Italy, Germany.
Watson Pharma.	2,536	Distribution, R&D, manufacturing, etc. in Australia, Brazil, Canada, China, India, Ireland and Malta.
Celgene	2,255	Manufacturing in Switzerland.
NBTY	2,180	Manufacturing in Canada and the UK.
Cephalon	1,975	Manufacturing in France.
Perrigo	1,822	Manufacturing in the UK, Israel and Mexico.

Source: Fortune 500 (2009) for the list of the largest pharmaceutical companies in terms of sales, and corporate websites for information on activity locations.

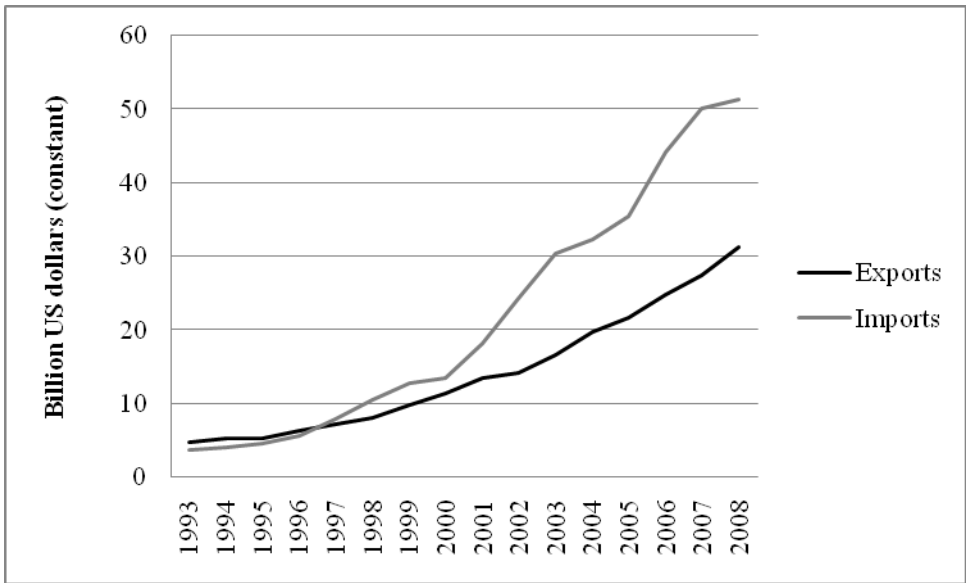
Offshoring manufacturing and its consequences on U.S. trade of pharmaceuticals

The increase in U.S. pharmaceuticals activities abroad has resulted in a large increase in intra-firm two-way trade. The value if U.S. imports of pharmaceutical products shipped to U.S. parents by foreign affiliates nearly quadrupled in less than ten years, growing from 6.4 billion dollars in 1999 to 24.6 billion dollars in 2008. The value of U.S. exports of pharmaceuticals shipped from the U.S. to foreign affiliates nearly tripled over the same period of time, growing from 7.8 billion dollars in 1999 to 22.1 billion dollars in 2008.

This increase in offshoring explains to some extent the United States' large trade deficit in pharmaceutical products, which totaled 18.1 billion dollars in 2008, just before the economic crisis (Figure 3.2.). More specifically, the United States' trade data suggests that the implementation of foreign IPR enabling larger offshoring of the production process may have had an impact on the country's imports of pharmaceuticals. The United States' trade deficit appeared in 1997, one year after the TRIPS Agreement came into force, because of the high growth in U.S. imports. The average annual growth rate of imports reached 19.8% between 1993 and 2008, compared to 13.4% for exports.[2]

[2] Unless otherwise specified, all American trade data used in this paper comes from the *USA Trade Online* database published by the US Bureau of the Census: Foreign Trade Division (2009).

Figure 1. The United States' Trade of Pharmaceutical Products, 1993-2008



Source: U.S. Bureau of the Census (2009).

The trade gap is mainly due to the import of a few specific categories of products. In 2006, exports totaled 25.2 billion dollars, while imports totaled 42.3 billion dollars (Table 3.2). The top five categories of products which the United States exported the most were worth 13.6 billion dollars (53.87% of total exports). The number one category of exported products was a final product category, "*medicaments in measured doses for retail sale*" (5.3 billion dollars, 21.01% of total exports). The top five categories of products that the United States imported the most totaled 21.7 billion dollars, i.e. 51.24% of total imports. Imports of cardiovascular medicaments totaled 11.7 billion dollars, and were largely responsible for the U.S. trade deficit. This category of pharmaceutical products included several blockbuster drugs of the early 2000s.

For instance, the three drugs that generated the largest sales worldwide in 2009 were treatments for cardiovascular conditions.

Table 2. Top imports of pharmaceutical products to the United States and trade gap, in dollars 2006

Category	Imports	Exports	Trade gap
Cardiovascular medicaments, not elsewhere specified or included	11,692,718,451	1,748,337,354	-9,944,381,097
Medicaments in measured doses for retail sale, not elsewhere specified or included	3,280,523,862	5,303,133,068	2,022,609,206
Medicaments with hormones or products of 2937, not elsewhere specified or included	2,468,614,721	630,210,164	-1,838,404,557
Blood fractions not elsewhere specified or included	2,336,654,871	3,447,759,090	1,111,104,219
Antidepressants, tranquilizers, other psych agents, not elsewhere specified	1,919,325,031	713,567,100	-1,205,757,931
Antineoplastic and immunosuppressive medicaments	1,882,713,204	2,066,065,302	183,352,098
Anti-infective medicaments	1,776,242,099	868,346,637	-907,895,462
Medicaments affect central nervous system, not elsewhere specified or included	1,667,231,862	281,763,829	-1,385,468,033
Medicaments affect eyes/ears/respiratory sys not elsewhere specified or included	1,570,334,770	217,384,419	-1,352,950,351
Medicaments primarily affect digest system not elsewhere specified or included	1,417,696,786	114,818,176	-1,302,878,610
Vaccines for human medicine	1,227,502,859	1,029,280,629	-198,222,230
Medicaments containing insulin but not containing antibiotics	1,140,281,194	242,106,570	-898,174,624
Total	32,379,839,710	16,662,772,338	-15,717,067,372

Source: data from US Bureau of the Census: Foreign Trade Division, 2009

The United States imports most of its products from European countries: the U.K., Germany and Ireland have been the three countries exporting the most products to the United States since 1993. Ireland became one of the top three in 2001, when it exported for 2.1 billion dollars compared to 678 million dollars in 2000. In 2006, Ireland exported pharmaceutical products worth a total of 6 billion dollars to the United States. Since 2001, Ireland has become the number one exporter of cardiovascular medicaments to the United States. This type of drug has gone from representing 5% of total U.S. imports in value in the 1990s, to about 10% in 2000 and 2001. It has become the largest category imported in the United States in total value (18.11%

in 2003 to 27.61% in 2006). Lipitor, the cholesterol-lowering drug which posted the largest sales revenues in 2009, is manufactured by Pfizer in Ireland, and exported to the United States. Zocor, manufactured by Merck, another U.S. firm, is also manufactured in Ireland.

However, the United States' share of imports from Western Europe is decreasing (Table 3.3.).[3] In 2006, 73% of the United States' imports originated from Europe, after a record high of 81.2% in 2002. Japan's share is also declining, to 3.1% of total American imports, after a record high of 10.6% in 2000. Canada's share is increasing slightly to 8.2% in 2006 from 6.7% in 2005, but down from 9.6% in 1997. While Israel's pharmaceutical industry has existed for several years, its share of exports to the United States more than doubled in two years, rising from 2.8% in 2004 to 5.9% in 2006, as Israel is becoming one of the major producers of generic drugs. Overall, 21 countries totaled 97% of the United States' imports in 1997. The share of these countries' exports to the United States remained reasonably stable until 2004, before dropping to 90.8% in 2006.

Table 3. Shares of U.S. imports of pharmaceutical products by country, 1997-2006

Year	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Western Europe	77,3%	81,1%	79,1%	77,4%	77,8%	81,2%	79,6%	79,8%	77,2%	73,0%
Including Ireland	*2,7%*	*4,3%*	*5,6%*	*5,6%*	*13,3%*	*24,4%*	*20,2%*	*18,6%*	*17,2%*	*14,1%*
Japan	6,5%	6,5%	9,7%	10,6%	8,6%	7,5%	7,6%	6,5%	5,0%	3,1%
Canada	9,6%	7,2%	6,2%	6,7%	7,1%	5,6%	6,7%	6,8%	6,7%	8,2%
Australia	0,5%	0,4%	0,6%	0,5%	1,0%	0,6%	0,5%	0,5%	0,6%	0,6%
Israel	3,1%	2,2%	2,0%	2,3%	3,2%	2,5%	2,6%	2,8%	4,1%	5,9%
Subtotal	97,0%	97,4%	97,5%	97,6%	96,8%	97,4%	96,9%	96,4%	93,5%	90,8%
Singapore	0,1%	0,1%	0,1%	0,0%	0,0%	0,0%	0,0%	0,3%	3,3%	5,7%
Other	2,9%	2,5%	2,4%	2,4%	2,2%	2,6%	3,1%	3,3%	3,2%	3,5%
Total	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%

Source: US Bureau of the Census (2009).

[3] Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxemburg, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and the United Kingdom.

Singapore is becoming a major producer of pharmaceuticals. Its exports to the United States grew from 0.03% of total U.S. imports in 2003 to 5.7% in 2006, following the implementation of the U.S.-Singapore Free Trade Agreement in January 2004. In 2004, Singapore was the third largest exporter of cardiovascular medicaments, behind Ireland and France (Plavix, a major cardiovascular drug is manufactured by the French company Sanofi-Aventis and the American firm Bristol Myers Squibb). In 2006, Singapore became the second largest exporter of cardiovascular medicaments to the United States, still behind Ireland.

Finally, the share of other countries in the United States' imports of pharmaceuticals remained low in 2006, representing only 3.5% of total imports. However, the growing strength of patent protection in developing and emerging economies is likely to further stimulate the U.S. pharmaceutical companies' offshoring of manufacturing activities abroad.

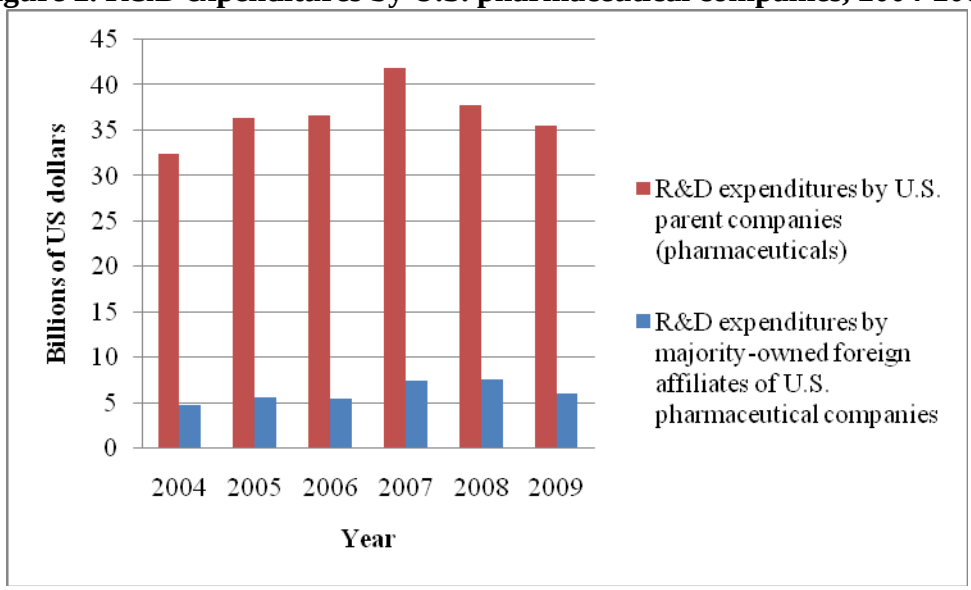
Offshoring R&D

Foreign patent protection is also likely to stimulate U.S. firms' offshoring of R&D activities. The United States is currently the largest global center for R&D in pharmaceuticals: 33.6% of total R&D expenditures conducted in the U.S. by all majority-owned U.S. affiliates of foreign companies, in all sectors, were directed at the pharmaceutical industry. The U.S. attracts R&D from foreign firms that want to benefit from returns to scale: 25% of R&D performed by pharmaceutical companies in the United States was conducted by majority-owned U.S. affiliates of foreign companies in 2005 (Anderson, 2008).

U.S. companies are increasingly conducting R&D efforts in their foreign affiliates. In 2007, majority-owned foreign affiliates of U.S. pharmaceutical companies spent 7.1 billion

dollars in R&D efforts, compared to 4.8 billion in 2004 (Figure 3.3.).[4] However, U.S. pharmaceutical companies continue to spend the largest amounts in R&D in the United States: more than 41 billion dollars in R&D were spent by U.S. parent companies in 2007. R&D expenditures dropped both in the United States and abroad following the beginning of the 2008 economic crisis

Figure 2. R&D expenditures by U.S. pharmaceutical companies, 2004-2009



Source: U.S. Bureau of Economic Analysis (2012)

The location choice for FDI in R&D by pharmaceutical companies depends on its purpose. If companies are looking to *expand* their knowledge base, they will tend to settle near universities, but if they are looking to *exploit* their knowledge base, they will tend to settle in locations in proximity of manufacturing facilities and near existing or growing markets (Kuemmerle, 1999).

[4] No data available before 2004.

Offshoring clinical trials

Offshoring production brings companies closer to new target markets. The emergence of new markets is fostering the increase in fragmentation at all stages of the production process. The lower costs of labor and clinical trials, as well as short development time for drugs in countries such as India and China are an attractive force for U.S. pharmaceutical companies (Pore et al., 2008). Pharmaceutical companies are increasingly offshoring clinical trial activities in developing and emerging markets, such as India, China, Argentina, Brazil, Taiwan, South Africa, Israel, and Eastern European countries (Cockburn, 2008). This increase in the offshoring of clinical trials started in the mid-1990s (Glickman et al., 2009). It is likely that IPR protection abroad has enabled pharmaceutical companies to offshore even clinical trials.

Literature review

The traditional theory of trade based on comparative advantage and factor endowments was dominant in the economics literature on international trade for a large part of the twentieth century. However, some economists revived the research on international trade in the 1980s by changing assumptions of the Heckscher-Ohlin (HO) model which dominated the literature since the 1930s (see Baldwin, 2008). By introducing imperfect competition and increasing returns to scale, the "new" theory of international trade was able to explain the growth in IIT (Krugman, 2008). Building on these models, the "new new" theory of international trade focuses on intra-firm trade and differences in productivity to explain why only a few firms decide to export and/or invest abroad to offshore production (Helpman et al., 2004; Melitz, 2003).

The traditional theory of trade

The traditional (or classical) theory of international trade is based on David Ricardo's model of comparative advantage: nations specialize in the production of goods for which they have a relative advantage in the production process (Ricardo, 1821). Nations therefore specialize completely: they export goods for which they have a comparative advantage, and import other goods. The Heckscher-Ohlin (HO) model (Heckscher, 1919; Ohlin, 1933) develops Ricardo's idea of comparative advantage, by including factor endowments. The model predicts that countries will specialize in the production of goods for which they have a comparative advantage in terms of factor endowment. A country will therefore export goods that use its abundant and cheap factors of production, and import goods that require factor endowments that are scarce in the country.

This theory of trade is based on strong assumptions: international trade is supply-based (consumer tastes are not taken into account), the theory assumes constant returns to scale along with perfect competition, countries exhibit identical levels of technology in production, and factors are mobile within a country but not across countries. The weaknesses of the HO theory became a focus of trade economists when it became apparent that it was unable to explain the development of intra-industry trade in the second half of the twentieth century (e.g. Balassa, 1966; Grubel & Lloyd, 1975).

The "new theory of trade" and intra-industry trade

Beginning in the 1980s, the "new" trade theory emerged to find an explanation for the growth in IIT, especially between identical economies (e.g. Lancaster, 1980). The new trade theory tends to be demand-based, and assumes economies of scale as well as imperfect competition and product differentiation to explain the growth in intra-industry trade, without

being based on comparative advantage (Markusen, 1995). Indeed, countries with similar demand structures tend to generate similar industries (Linder, 1961). They therefore trade similar, although differentiated, goods. Countries do not specialize in the production of goods according to differences in endowments as in the traditional theory, but to take advantage of economies of scale (Krugman, 1980). According to the new trade theory, international trade tends to develop more between similar countries (i.e. among developed nations that have similar factor endowments), while the traditional trade theory would explain that more distant countries in terms of factor endowments should trade more with each other (Helpman & Krugman, 1985). Consumers' love for variety and the trade in differentiated but similar products can therefore explain IIT.

By introducing elements of industrial organization with imperfect competition as an explanation for trade, economists started to focus in the 1980s on the role played by multinational firms in trade (e.g. Batra & Ramachandran, 1980; Helpman, 1984; Markusen & Venables, 1998, 2000). The first general equilibrium theory to explain why firms might decide to offshore production activities is based on this new trade theory (Helpman, 1984). The new trade theory started to explain trade thanks to the development of foreign direct investment and outsourcing parts of the production process through licensing.

To the "new new theory of trade" and intra-firm trade

In the mid-1990s, economists started to pay closer attention to the roles that firms play in trade, especially since only a few large firms actually participate in export activities (Bernard et al., 2007). A theoretical framework was needed to explain why only the few most productive firms were the ones that decided to export (e.g. Bernard & Bradford Jensen, 1999). In the seminal article of this "new new" trade theory, Melitz (2003) shows that firms' heterogeneity in terms of

productivity explains modern trade: firms exhibiting high productivity enter the export market, since they are the only firms able to cover the high fixed costs necessary for export activities. Firms with even higher productivity tend to enter foreign markets through FDI and offshore outsourcing (i.e. licensing to a non-affiliated firm in a foreign country), rather than simply export goods (Helpman et al., 2004). Because offshoring production generates larger fixed costs than exporting, only the most productive firms will decide to offshore production.

Multinational firms can enter new markets through three strategies, based on the level of local technology protection: exports, FDI, and licensing (An, Maskus, & Puttitanun, 2008). By reducing a firm's fixed costs, patent protection encourages firms to enter foreign markets through FDI rather than exports, or through licensing contracts rather than FDI (Maskus, Saggi, & Puttitanun, 2003). Indeed, FDI generates lower variables costs for a firm compared to exports (Helpman et al., 2004). An increase in the degree of patent protection in foreign countries suggests a higher degree of offshoring and outsourcing of the production process. A firm's decision to perform offshore production through FDI or licensing depends on the extent to which a firm wants to control the production process (Antràs, 2005).

Multinational firms' decisions to settle in foreign markets depend on their need for protection and the availability of protection (Nicholson, 2007). Multinational firms in knowledge-based industries tend to offshore production through FDI when IPR protection is low, and outsource production offshore through licensing when IPR protection is high (Nicholson, 2007). FDI is therefore more likely to happen when IPR protection is at an intermediate level, whereas licensing is more likely to happen when IPR protection is high. U.S. pharmaceutical companies, which have high needs in terms of IPR protection, have been pushing for the enforcement of IPR to increase its activities abroad and benefit from a drop in costs. For instance, without IPR

protection, foreign managers of a subsidiary could decide to launch a rival firm using the technology learnt thanks to the multinational firm (Markusen, 2001).

The development of FDI as a way of entering foreign markets explains to some extent the growth in trade of intermediate goods. Fragmentation of the production process in different countries characterizes modern trade: affiliates of multinational firms trade and transform intermediate goods before shipping the finished good to the home country (Blonigen, 2005).[5] The emergence of the global value chain can be characterized as a shift from trade in goods to trade in tasks (IDE-JETRO and WTO, 2011). As Picci (2010) notes in a paper on the internationalization of R&D, "*[a]lmost all contemporary products are the result of some form of international collaboration and trade*." However, the lack of IPR protection stalls the development of the fragmentation process, since it tends to reduce FDI (Branstetter, Fisman, & Foley, 2006; Smith, 2001; Wakasugi, 2007).

One of the institutions that has enabled the increase of trade in intermediates is the World Trade Organization (Felbermayr & Kohler, 2010).[6] More specifically, the protection of intellectual property rights through this institution may explain to some extent the development of trade. Since free trade agreements are supposed to increase patent protection abroad, they are likely to affect location strategies of pharmaceutical firms.

Through an increase in complex FDI, patent protection enables the relocation of part of the production to service the U.S. market. If U.S. companies decide to offshore or license part of their production process, patent protection is therefore likely to increase U.S. imports. The U.S. government is therefore more likely to sign free trade agreements with countries in which

[5] Escaith, Lindenberg, & Miroudot (2010) for instance, show the important impact of the economic crisis on world trade, because of the vertical integration of the production process.
[6] Other institutions include, for example, export promotion institutions (Volpe Martincus, Estevadeordal, Gallo, & Luna, 2010).

pharmaceutical companies want to relocate through FDI to supply the U.S. market.[7] Although the South's exports to the United States could also increase because IPR protection encourages technology transfer through licensing, thereby reducing marginal production costs of firms, "excessively strong" IPR reduces competition and welfare (Yang & Maskus, 2009). Some evidence suggests that China, an example of a country with the reputation of high imitative threat, has undergone a surge of FDI inflows thanks to an increase in IPR protection (Awokuse & Yin, 2010).

By reducing the costs of accessing local markets, patent protection might enable the settlement of US multinationals in foreign countries. But patent protection is not the only determinant of location choice for U.S. multinational firms. For instance, U.S. multinational firms' location choices in China are a function of the size of the market, production costs, industrial agglomeration, geographical location, and technological intensity in the host sector (Mucchielli & Yu, 2011).[8] Yeaple (2003) finds that U.S. outward FDI is a function of a host country's abundance in skilled-labor, and market access opportunities it represents. This is especially true for decisions to offshore innovation activities, when U.S. firms face a shortage of skilled labor (Lewin, Massini, & Peeters, 2009). A stable business environment in the host country is also an important factor (Tobin & Rose-Ackerman, 2005).

Intra-industry trade and intermediates

Although trade in intermediates has gained more attention with economists' focus on intra-firm trade, theoretical models of IIT also take into account trade in intermediates (R.

[7] Bilateral investment treaties (BITs) are also likely to be signed with countries from which U.S. companies want to provide local markets. There is some evidence that BITs might increase FDI (Egger & Pfaffermayr, 2004; Tobin & Rose-Ackerman, 2005).

[8] For instance, location choice of French multinational companies is positively related to a country's market potential, cultural proximity to the country of the firm's headquarters, access to intermediate goods, and the firm's financial network abroad, but negatively related with "distant countries with higher factorial prices" and (Mayer, Mejean, & Nefussi, 2010).

Baldwin & Taglioni, 2011). Trade fragmentation takes the form of IIT to some extent, and the standard tool to measure IIT, the Grubel and Lloyd index (Grubel & Lloyd, 1975), can therefore be used as a measure of trade integration (Fukasaku, Meng, & Yamano, 2011). Recent developments in the empirical literature on trade include research using measures of IIT to analyze the growing importance of trade in intermediates (Türkcan & Ates, 2011).

A complete IIT analysis must distinguish between the trade of products that are similar in terms of their characteristics (horizontal product differentiation or HIIT), the trade of similar products but of different qualities or at different stages of the production process (vertical product differentiation or VIIT), and unilateral (inter-industry) trade (Fontagné & Freudenberg, 1997). VIIT integrates to some extent trade in intermediates, and empirical studies using disaggregated trade data do find an increase in VIIT since the end of the twentieth century (Ando, 2006; Wakasugi, 2007; Kang, 2011; Türkcan & Ates, 2011). The consequence of the increased activities of multinational firms through the global value chain has been the growth in the value of intra-firm trade, although the extent of this growth tends to be quite different depending on countries and industries (Lanz & Miroudot, 2011). The literature is therefore growing on the specificities of each country or region, and between industries. While some of these papers focus on the determinants of the development of VIIT between different regions of the world (Ando, 2006; Kang, 2011; Wakasugi, 2007; Yoshida, Carlos Leitão, & Faustino, 2009), others focus on VIIT in specific industries (Chang, 2009; Fukao, Ishido, & Ito, 2003; Türkcan & Ates, 2011).

Türkcan and Ates (2011) study the determinants of the growth in the United States' VIIT in the automobile industry. They find that a larger part of U.S. trade in the automobile industry tends to involve technologically linked, but different, varieties of intermediates. They further find a positive correlation between VIIT and FDI. Through their study of the electrical machinery industry in East Asia, Fukao et al. (2003) confirm that FDI to offshore production generates an

increase in VIIT. However, Chang (2009) studies the determinants of the growth in IIT in the information technology (IT) industry, and finds that growth in HIIT dominates growth in VIIT between Asian countries and the U.S., during the period 1996-2005. The fact that some Asian IT firms are competitive world leaders alongside U.S. firms can explain this result to some extent. In this case, the main reason behind firms' decisions to perform FDI is a market seeking strategy.

Intra-industry trade and pharmaceuticals

The U.S. government's trade policy for pharmaceuticals also suggests that the American pharmaceutical industry wants to access foreign markets to both reduce costs and increase sales in foreign markets. Indeed, following the end of the Uruguay Round, U.S. pharmaceutical firms have increasingly offshored production to reduce costs while benefitting from a larger pool of qualified labor, and to access new markets more easily (Pore et al., 2008). While the cost reduction purpose is likely to increase VIIT, the sales purpose is likely to increase HIIT.

Offshoring and VIIT

The share of VIIT in pharmaceuticals may increase due to the reduction in trade barriers. The U.S. pharmaceutical industry's efforts to increase foreign patent protection through the World Trade Organization (WTO) and bilateral or regional trade agreements were in part motivated by its ambition to build facilities in growing markets. Pharmaceutical firms also pushed for the elimination of tariffs on U.S. trade of pharmaceuticals to facilitate the imports of pharmaceuticals from abroad. In 1994, the United States signed the Pharmaceutical Tariff Elimination Agreement (also known as the Pharmaceuticals Zero-for-Zero Initiative), which came into force in 1995, when the WTO was created. With this agreement, the main pharmaceutical producing countries agreed to eliminate tariff barriers for pharmaceutical

products, and to not replace them with non-tariff barriers.[9] This agreement also covers pharmaceuticals imported from countries that did not sign the agreement, including developing countries. The initiative covers three types of products: dosage-form pharmaceuticals (that may be packaged for retail sale or not), bulk active pharmaceutical ingredients (that still need to be processed into dosage-form pharmaceutical products) and chemical intermediates (generally organic chemicals that are used to produce active pharmaceutical ingredients).[10] The initiative therefore facilitates the import of both final and intermediate pharmaceutical products in the United States.

The share of VIIT in pharmaceuticals may increase for more reasons than just the reduction in trade barriers (through the elimination of tariffs and increase in patent protection abroad). Biopharmaceutical firms for example see a growth of location possibilities thanks to the drop in trade barriers, but also thanks to an increase in the supply of skilled and relatively cheap labor and infrastructure in new large markets (Cockburn & Slaughter, 2010).

Spillover effects and HIIT

However, the growth of these large markets (mainly India and China), may generate an increase in the share of HIIT if offshoring R&D activities leads to spillover effects on local firms. Some evidence suggests that this may happen: technology transfer and R&D spillover effects through trade and FDI are strong, in both developed and developing countries, and in all types of industries (e.g. Almeida & Fernandes, 2008; Bernstein & Mohnen, 1998; Ciruelos & Wang, 2005; Haruna, Jinji, & Zhang, 2010; Keller, 2004; Parameswaran, 2009; Xu & Chiang, 2005).

[9] The original signatories of the agreement are Australia, Austria, Canada, the Czech Republic, the European Communities, Finland, Japan, Norway, the Slovak Republic, Sweden, Switzerland, and the United States. All finished pharmaceutical products qualify for zero-tariff, whereas intermediates and active ingredients do not automatically qualify (Office of the USTR, 2012).

[10] See "Pharmaceutical Products and Chemical Intermediates, Fourth Review□: Advice Concerning the Addition of Certain Products to the Pharmaceutical Appendix to the HTS" (USITC, 2010) for a list of products covered by the initiative.

Due to the TRIPS agreement and stronger IPR protection in countries from the South, the rate of technology transfer increases through multinational firms from the North (Dinopoulos & Segerstrom, 2010). The growing presence of U.S. firms in emerging markets is likely to increase productivity in these markets through technology diffusion (Keller, 2004). In India, for instance, the local pharmaceutical industry "*followed a trajectory from duplicative imitation to creative imitation to move up the value chain of pharmaceutical R&D. Finally as a result of changes in patent law the industry is learning to develop capabilities in innovative R&D*" according to Kale and Little (2007). Thanks to government efforts to attract FDI in the pharmaceutical sector, Ireland has shifted from attracting FDI from the largest pharmaceutical multinational firms for manufacturing purposes and then for R&D purposes. As a result, Ireland was able to develop its own biopharmaceutical industry (Johnston, Henry, & Gillespie, 2006).

Spillover effects in R&D also occur in the pharmaceutical industry (Feinberg & Majumdar, 2001; Furman, Kyle, Cockburn, & Henderson, 2006; Henderson & Cockburn, 1996; Papageorgiou, Savvides, & Zachariadis, 2007). However, the relocation of R&D to low-cost countries remains limited, and innovative activity is concentrated in a few specific countries where knowledge spillovers and patent protection levels are highest (Cockburn, 2008). Furthermore, despite the active trade in intermediates, active pharmaceutical ingredients as well as finished products, only a few countries (such as Ireland and Puerto Rico) have become large manufacturing centers for supplying global markets (Cockburn, 2008). These two effects might limit the extent of both VIIT and HIIT.

An analysis of U.S. IIT in pharmaceuticals

Growth in the United States' IIT of pharmaceuticals: the Grubel and Lloyd index

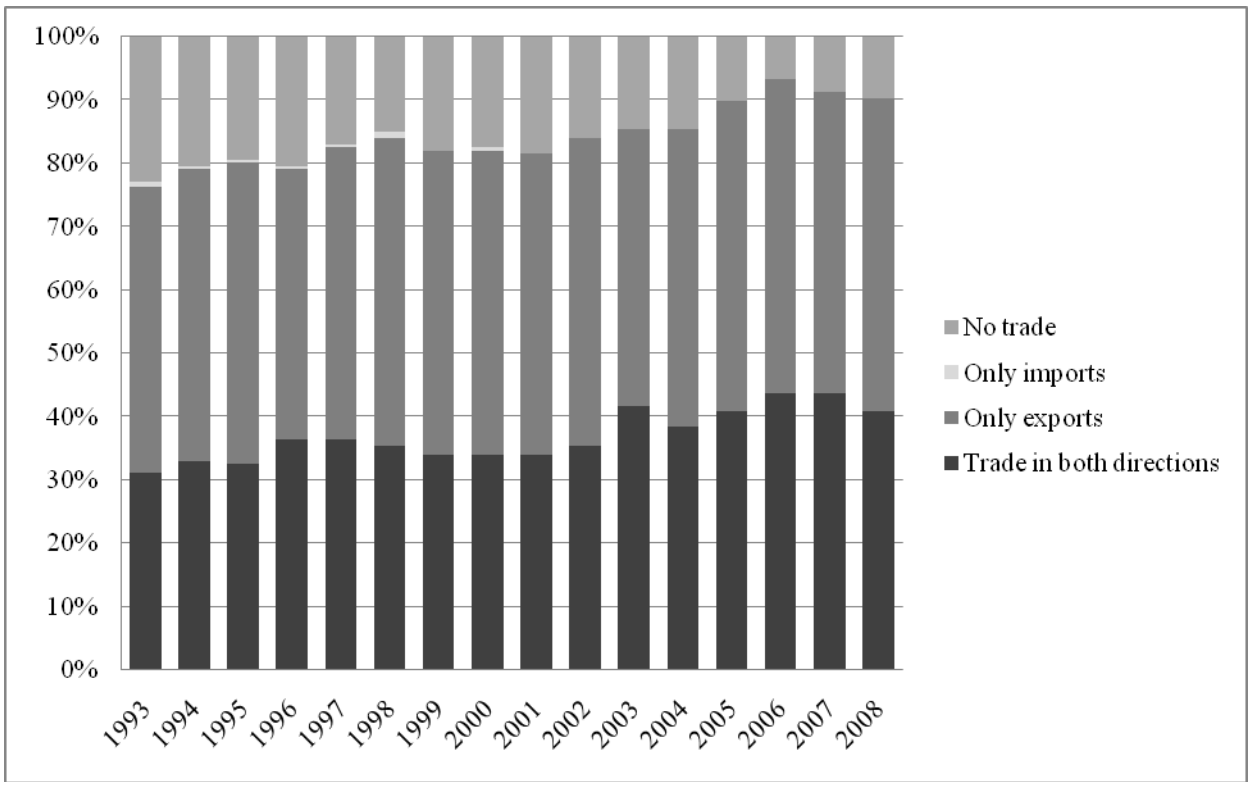
The Grubel and Lloyd index (1975) is the main instrument that measures intra-industry trade. Its basic version measures the share of overlapping trade between one country and the rest of the world, considered to be one trade partner:

$$GL_j = 1 - \frac{|X_j - M_j|}{X_j + M_j}$$

with X_j and M_j the exports and imports in industry j by a given country.

The index has at least two biases: a geographic bias and a product bias (Fontagné & Freudenberg, 1997). The geographic bias arises because while the United States' two-way trade in pharmaceuticals is growing, the U.S. both exports and imports pharmaceuticals with less than half of the countries throughout the world (see Figure 3.4.). With nearly half of the countries in the sample of 206 countries, it only exports but does not import any product (unilateral trade, only exports). However, these exports represented only 1.25% of total exports in value in 2006. Most countries in this category are developing or emerging markets. The category "only imports" concerns only a very limited number of countries during the 1990s, and no countries in recent years. Finally, with 10% of the countries, the U.S. does not trade any pharmaceuticals at all (no trade). The Grubel and Lloyd index might therefore yield a geographical bias by giving a disproportionate weight to the few countries with which the U.S. does perform bilateral trade.

Figure 3. Direction of U.S. pharmaceutical trade, percentage of countries, 1993-2008



Source: data from STAT-USA and the Foreign Trade Division, U.S. Census Bureau (2009).
Note: 206 countries are included in the database.

The basic Grubel and Lloyd index might also generate a product bias, because only a fraction of trade with other countries deals with the import and export of the same category of products. But the pharmaceutical products category includes very different types of products. The *USA Trade Online* database published by the U.S. Bureau of the Census: Foreign Trade Division (2009) yields 71 different product categories within its "Pharmaceutical" import and export database (at the 10-digit level).

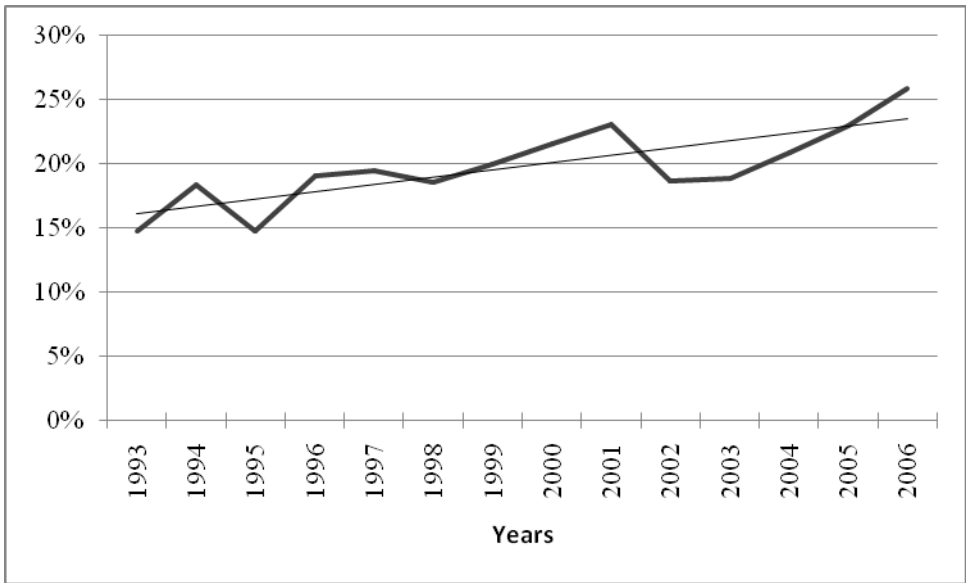
To avoid the geographic and product biases, Fontagné and Freudenberg (1997) argue that an average Grubel and Lloyd index yields a more detailed study of the nature of trade between the United States and each of its partners, for each category of pharmaceutical products at the most detailed level:

$$GL_{n,fe} = 1 - \frac{\sum_{kan}\sum_{ie\,f}|X_{kie} - M_{kie}|}{\sum_{kan}\sum_{ie\,f}(X_{kie} + M_{kie})}$$

where X_{ktit} represents the value of U.S. exports and M_{ktit} the value of U.S. imports, with trading partner k, among the United States' n trading partners, for product type i from industry j, during year t.

IIT as measured by the average Grubel and Lloyd index increased from 14.8% in 1993 to 25.91% in 2006 (Figure 3.5.).

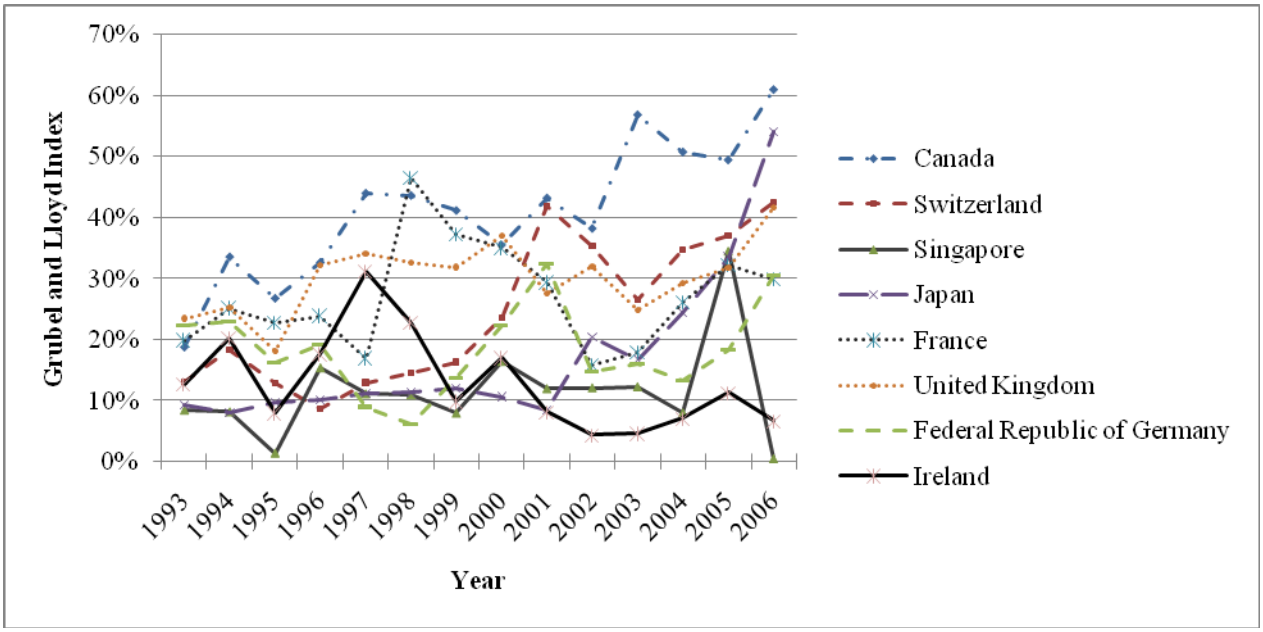
Figure 4. The average Grubel and Lloyd index, U.S. trade in pharmaceuticals, 1993-2006



Source: data from STAT-USA and the Foreign Trade Division, U.S. Census Bureau (2009).
Note: trade data between the United States and 237 trade partners.

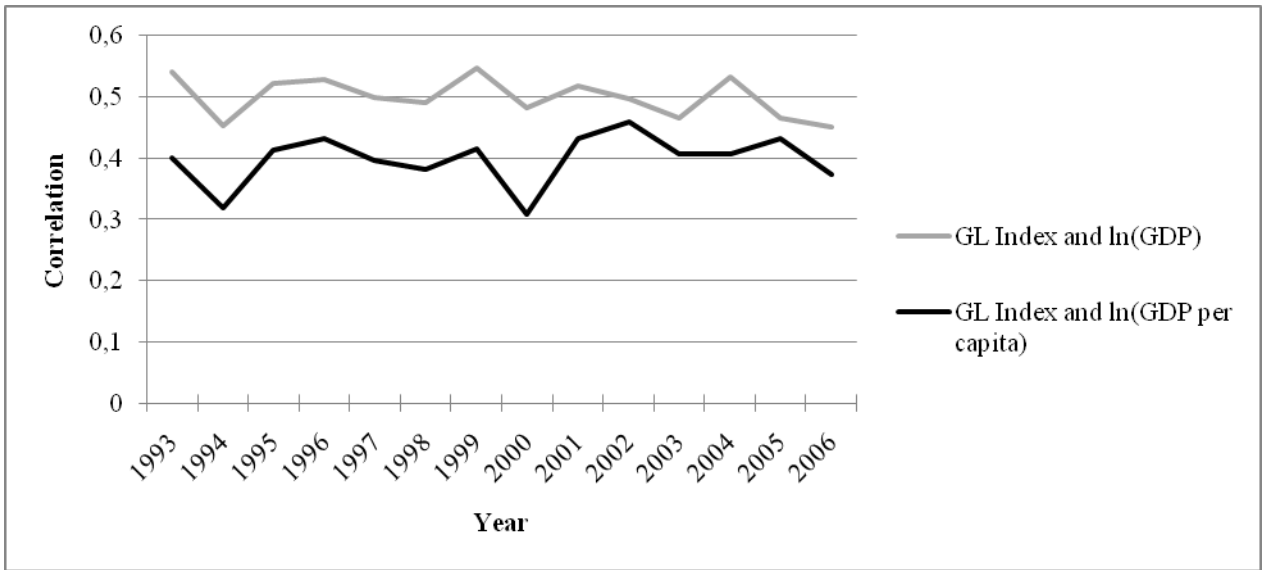
The countries that present the highest level of IIT as measured by the average Grubel and Lloyd index are mostly developed countries. Some developed countries display especially high average Grubel and Lloyd indexes (Figure 3.6.). The average Grubel and Lloyd index for trade in pharmaceuticals with Canada has been the highest with more than 60% in 2006.

Figure 5. The average Grubel and Lloyd index, advanced vs. non-advanced economics, U.S. trade in pharmaceuticals, 1993-2006



Ireland's and Singapore's average Grubel and Lloyd indexes show a peak in the year of implementation of U.S. firms, followed by a drop. In 2006, the average Grubel and Lloyd indexes for these two countries were lower than 10%. IIT as measured by the average Grubel and Lloyd index therefore does not capture the impact of offshoring of manufacturing activities. The average Grubel and Lloyd index is however quite correlated with a country's GDP: the index tends to show that IIT is higher with larger economies.

Figure 6. Correlation between the average Grubel and Lloyd index for U.S. pharmaceuticals, GDP and GDP per capita, 1993-2006.



Growth in the United States' intensity of bilateral trade in pharmaceuticals: a new measure of IIT

One of the reasons why the average Grubel and Lloyd index may be unable to capture the impact of offshoring on IIT, is because the index does not measure the intensity of IIT when bilateral trade exists for a given product category. Some countries may be trading bilaterally only a few categories of pharmaceuticals with the United States, but IIT may be high for these categories. The average Grubel and Lloyd index would therefore be low, when in fact IIT is quite intensive for a few product categories.

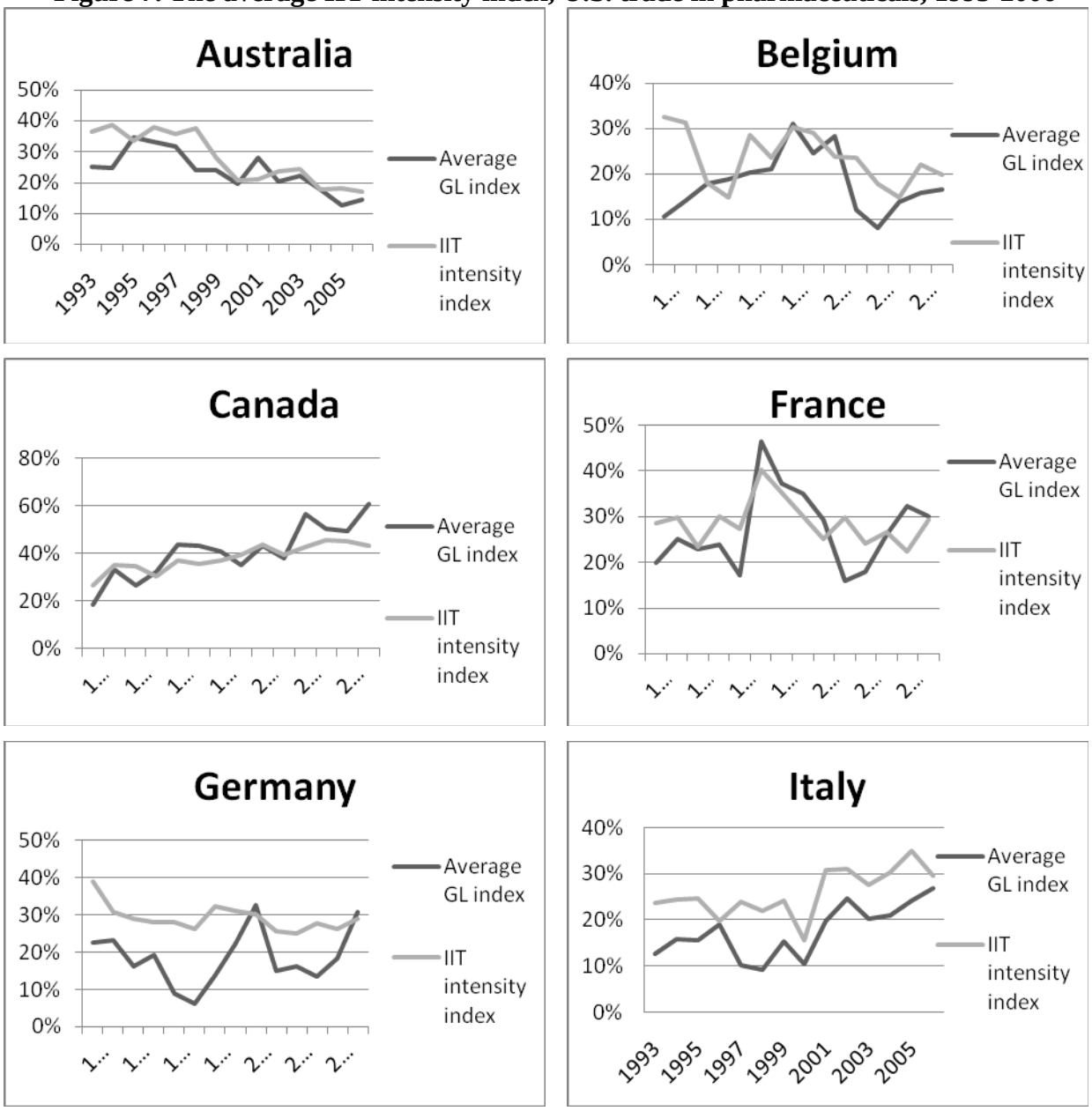
This article therefore introduces a measure of IIT intensity, GL_{kijt}, which is a country's average of the Grubel and Lloyd indexes of the products that actually register bilateral trade, i.e. when $X_{ijt} > 0$ and $M_{ijt} > 0$:

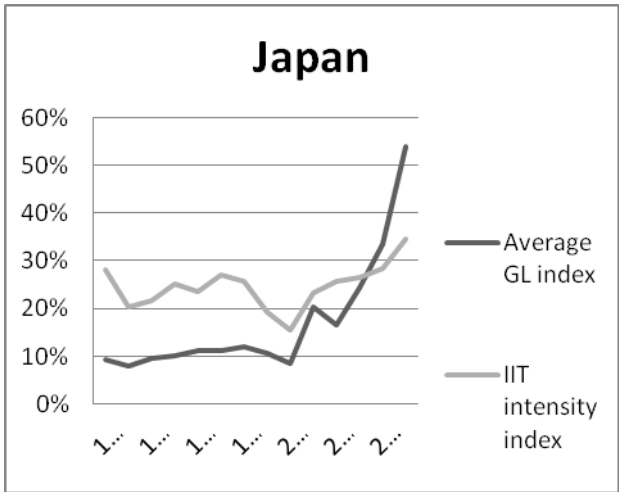
$$\widetilde{GL_{k,ltc}} = \Sigma_{i=1}\left(1 - \frac{|X_{itc} - M_{itc}|}{X_{itc} + M_{itc}}\right) \Big/ l_{ktc}$$

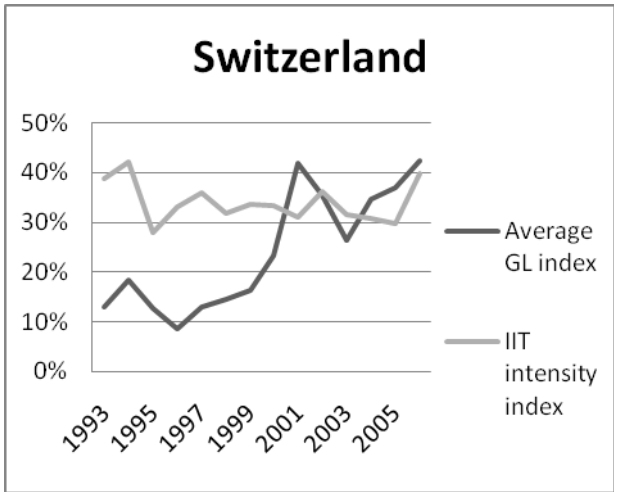
with l_{ktc} the number of pharmaceutical products i that country k both exports and imports in year t. This new index therefore measures the intensity of bilateral trade for the products that are traded by the two countries.

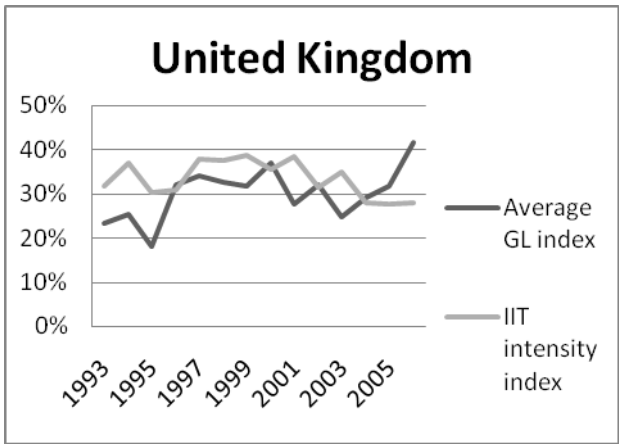
Advanced economies tend to have high correlation of their average Grubel and Lloyd indexes and their IIT intensity indexes (Figure 3.8.). However, non-advanced economies and countries that are manufacturing offshoring bases for the U.S. pharmaceutical industry tend to have much higher IIT intensity indexes compared to their average Grubel and Lloyd indexes. The fact that Ireland has been specializing in the production of specific pharmaceutical products appears to explain an increase in IIT intensity, but a drop in the average Grubel and Lloyd index.

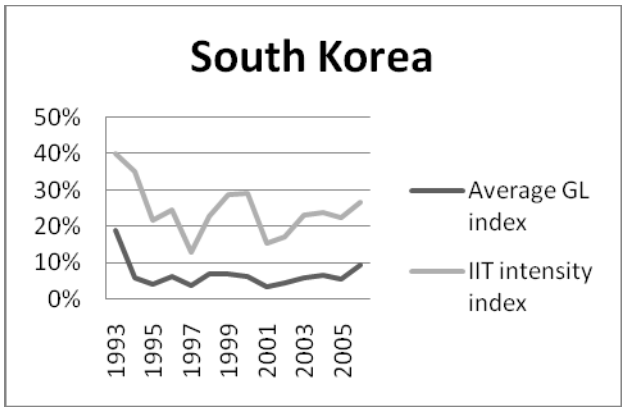
Figure 7. The average IIT intensity index, U.S. trade in pharmaceuticals, 1993-2006

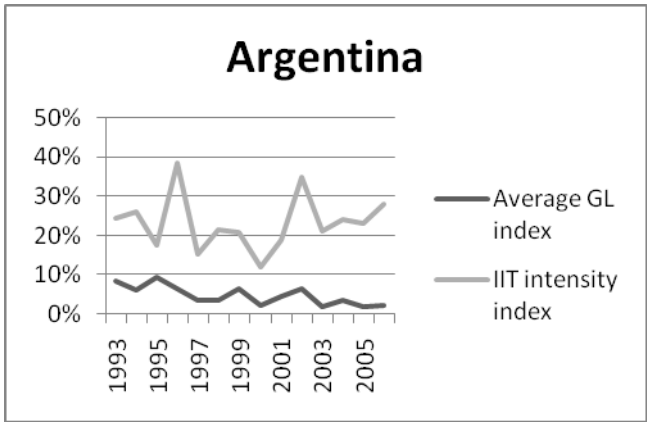


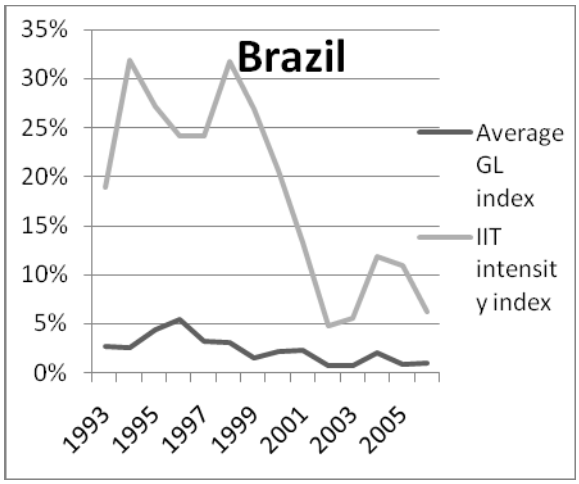

Japan
60%
50%
40%
30%
20%
10%
0%
Average GL index
IIT intensity index

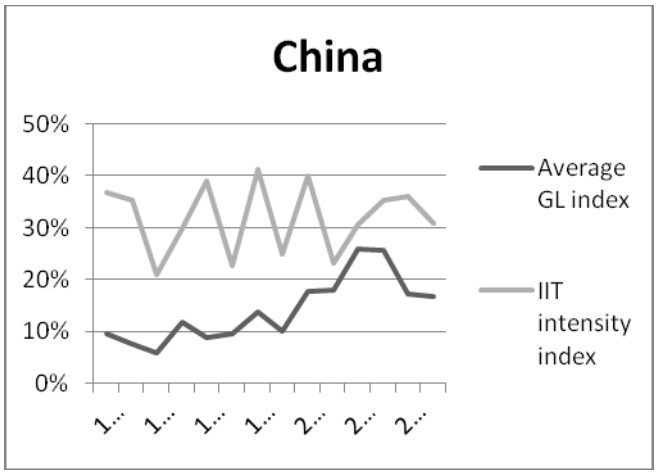

Switzerland
50%
40%
30%
20%
10%
0%
1993
1995
1997
1999
2001
2003
2005
Average GL index
IIT intensity index

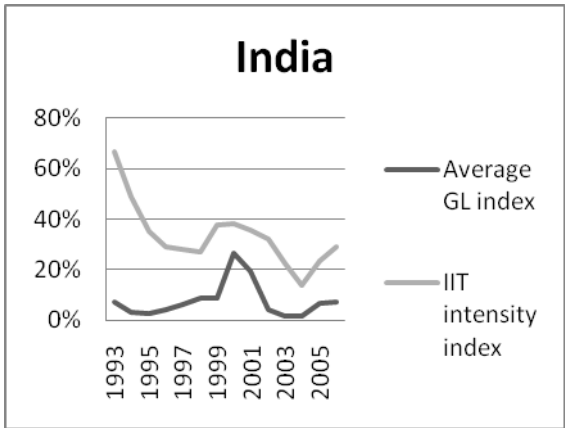

United Kingdom
50%
40%
30%
20%
10%
0%
1993
1995
1997
1999
2001
2003
2005
Average GL index
IIT intensity index

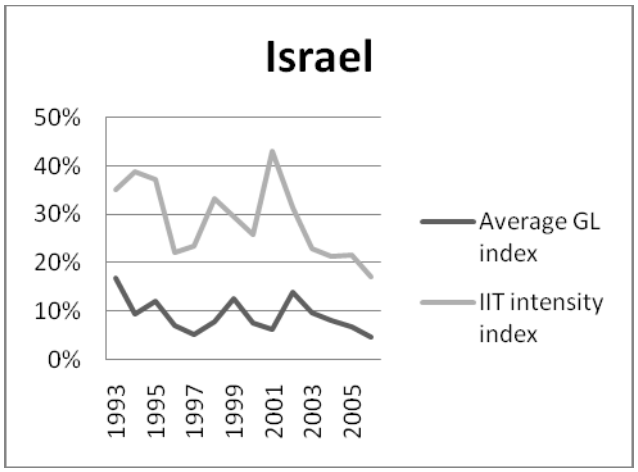

South Korea
50%
40%
30%
20%
10%
0%
1993
1995
1997
1999
2001
2003
2005
Average GL index
IIT intensity index

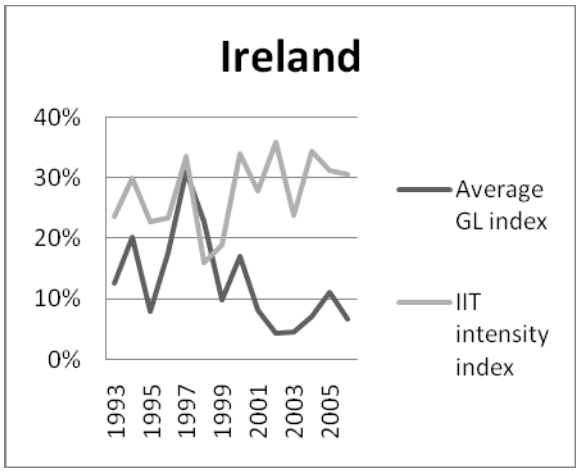

Argentina
50%
40%
30%
20%
10%
0%
1993
1995
1997
1999
2001
2003
2005
Average GL index
IIT intensity index

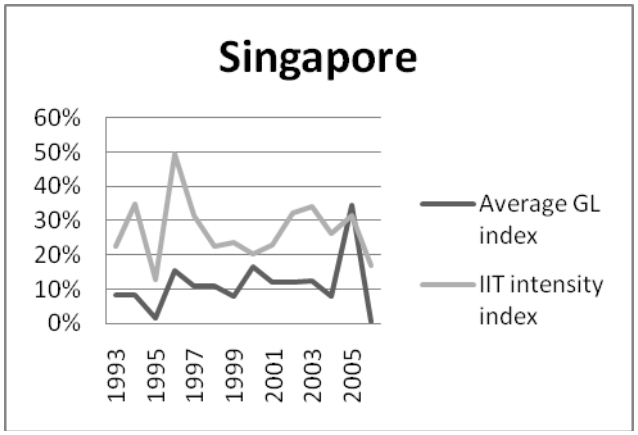

Brazil
35%
30%
25%
20%
15%
10%
5%
0%
1993
1995
1997
1999
2001
2003
2005
Average GL index
IIT intensit y index











VIIT versus HIIT

Economists from the Centre d'études prospectives et d'informations internationales (CEPII), such as Abd-El-Rahman (1986), have developed tools to distinguish the nature of

reciprocal trade. The products are considered to be horizontally differentiated if the ratio of exports' and imports' unit prices is such that:

$$\frac{1}{1.15} \leq \frac{UV_{kit}^{X}}{UV_{kit}^{M}} \leq 1.15$$

with UV_{kit}^{M} the unit price of imports, UV_{kit}^{X} the unit price of exports, with the trade partner k of the United States, for the product i belonging to the pharmaceutical industry, during year t. Economists from the CEPII consider that goods that show similar characteristics must have similar prices. Here, the price is considered to be more or less equal to the unit value of the good exported or imported. X_{kit}^{HVD} defines exports of horizontally differentiated products, and M_{kit}^{HVD} defines imports of horizontally differentiated products. Otherwise, products are considered to be vertically differentiated. X_{kit}^{DVD} defines exports of vertically differentiated products, and M_{kit}^{DVD} defines imports of vertically differentiated products.

Other tools from the CEPII show with which countries the United States exports and imports significant quantities of pharmaceutical products. Indeed, with some countries, trade is considered to be unilateral because the United States exports much more than it imports. Only if the following rule is respected can trade be considered to be bilateral:

$$\frac{Min(X_{kit}, M_{kit})}{Max(X_{kit}, M_{kit})} > 10\%$$

Otherwise, trade is considered to be unilateral. The 10% threshold is arbitrary but gives nonetheless a pretty good idea of trade's nature.

Other tools are:

- the share of bilateral trade of vertically differentiated products, which is defined by:

$$BTVD_{n,j,t} = \frac{\sum_{k \in n} \sum_{i \in j} (X_{kit}^{DVD} + M_{kit}^{DVD})}{\sum_{k \in n} \sum_{i \in j} (X_{kit} + M_{kit})}$$

- the share of bilateral trade of horizontally differentiated products, which is defined by:

$$BTHD_{n,j,t} = \frac{\sum_{k \in n} \sum_{i \in j} (X^{BHD}_{kit} + M^{BHD}_{kit})}{\sum_{k \in n} \sum_{i \in j} (X_{kit} + M_{kit})}$$

- the share of unilateral trade of pharmaceutical products, which is defined by:

$$UT_{n,j,t} = 1 - BTVD_{n,j,t} - BTHD_{n,j,t}$$

Most trade (58.50%) is considered to be unilateral trade when the 10% threshold of trade overlap is applied (Table 3.4.). But VIIT has increased, growing from 19.72% of trade in 1995 to 37.98 in 2006, after reaching a peak of 40.31% in 2005. The share of HIIT has also increased, although it remains small: HIIT represented 0.95% of the United States' pharmaceutical trade in 1995, compared to 3.52% in 2006.

Table 4. Shares of bilateral (vertically and horizontally differentiated) and unilateral trade, 1995-2006

Year	$BTVD_{n,j,t}$	$BTHD_{n,j,t}$	$UT_{n,j,t}$
1995	19.72%	0.95%	79.33%
1996	30.13%	0.96%	68.91%
1997	28.35%	1.95%	69.70%
1998	27.90%	0.66%	71.44%
1999	30.67%	2.79%	66.53%
2000	35.17%	5.71%	59.13%
2001	34.31%	3.91%	61.79%
2002	34.20%	1.42%	64.38%
2003	35.12%	1.09%	63.79%
2004	40.09%	1.10%	58.81%
2005	40.31%	4.08%	55.61%
2006	37.98%	3.52%	58.50%

Note: the 10% threshold defines bilateral trade

Finally, as in Fontagné and Freudenberg (1997), Table 3.5. shows the share of pharmaceutical trade flows between the United States and the rest of the world according to different thresholds of trade overlap, for 2006. Only 17.6% of total trade in value involves trade where the overlap exceeds 50%. This result also suggests that real trade overlap for the same product type is quite low, and most trade in pharmaceuticals is actually unilateral.

Table 5. Share of trade overlap by threshold, 2006

Trade overlap	Share of total trade	Cumulated share
]90+	2.4%	2.4%
]80-90]	1.4%	3.8%
]70-80]	3.3%	7.1%
]60-70]	3.9%	11.0%
]50-60]	6.6%	17.6%
]40-50]	5.9%	23.5%
]30-40]	4.3%	27.8%
]20-30]	4.1%	31.9%
]10-20]	9.6%	41.5%
]0-10]	52.5%	94.0%
0.0	6.0%	100.0%

At the aggregate level, IIT analysis does seem to capture the impact of the increase in offshoring activities of U.S. pharmaceutical companies to some extent. The growth in VIIT is correlated with an increase in the fragmentation of the production process. Furthermore, the small increase in the share of HIIT may also reflect the growth in offshoring. As worldwide markets in pharmaceuticals are growing, the shares of the United States' VIIT and HIIT in pharmaceuticals may also increase in the future.

Perspectives for future U.S. IIT in pharmaceuticals

The U.S. pharmaceutical industry has pushed for stronger patent protection abroad in free trade agreements to offshore parts of its production process. While strong patent protection is a necessary condition to reduce the costs of offshoring, other criteria are also necessary. Ireland and Singapore are interesting examples for other countries to follow. Indeed, pharmaceutical companies seem to implement their businesses in foreign countries where patent rights are protected, but more generally where the foreign government creates a business-friendly environment. A country's political will to cater to the pharmaceutical industry seems to

significantly increase U.S. imports. Finally, inadequate infrastructure and a government's lack of political will or inability to provide an efficient health care system are significant impediments to trade.

Ireland's success

In the mid twentieth century, the Irish government initiated the development of the pharmaceutical industry. It decided the country should specialize in pharmaceuticals as a highly skilled industry that would enable Ireland to be competitive in the twenty first century. The national Industrial Development Agency therefore encouraged foreign (mostly American) companies to invest in Ireland. In the 1960s, several firms set foot there, including Squibb-Linson (now Bristol Myers Squibb) and Pfizer Pharmaceuticals, following the Danish based Leo Laboratories that settled in the 1950s. Others followed quickly, including Eli Lilly, Schering-Plough, Merck Sharp and Dohme, SmithKline-Beecham and Jannsen Pharmaceuticals. At the end of the century, biopharmaceutical companies including Wyeth Biopharma and Genzyme started settling in Ireland as well.

The pharmaceutical industry in Ireland has therefore developed thanks to foreign companies' massive investments in the country. Eight out of the top ten pharmaceuticals in the world have operations in Ireland (IBEC, 2012). In only a few years, Ireland has grown to become a major producing country for foreign pharmaceutical firms. At first, the country served as a manufacturing center for active ingredients. Then, as the local industry grew to a critical mass, the country served as a manufacturing platform of finished products. By attracting foreign pharmaceutical firms, Ireland managed to develop its own major pharmaceutical company, Elan, a biotechnological company with locations in Ireland, the United States, the United Kingdom, Japan and Bermuda. The industry is highly integrated, and product development is carried out for

Irish and other plants. Both branded and generic drugs are manufactured in Ireland. The country has become a major manufacturing and global sales base, and is the largest net exporter of pharmaceutical products in the world (IBEC, 2010).

Ireland has invested massively in its research and development infrastructures and trained its staff to become highly qualified medical and pharmaceutical researchers. The government seems to have managed to maintain a supply of very qualified labor corresponding to the specific needs of the pharmaceutical industry. The industry employed more than 24,000 people in the pharmachemical industry in 2009, compared to 5,200 in 1988 (IBEC, 2010). Half of those employed have third level graduate degrees. The industry has become R&D oriented, and collaborates often with local universities and hospitals. The government also offers funds to help the industry (the Government's Research Technology and Innovation Initiative supported by the European Regional Development Fund). Ireland also offers advantageous tax incentives for companies that settle there.

The main U.S. pharmaceutical companies have operations in Ireland. Most have manufacturing plants in Ireland. Pfizer first located its activities in Ireland in 1969 and employs 5,000 people in eleven locations in 2012 (Pfizer, 2012). It manufactures active pharmaceutical ingredients, solid dose pharmaceuticals, sterile injectibles, nutritionals, vaccines and biopharmaceuticals. Some of Pfizer's best selling drugs and vaccines (Lipitor, Viagra, Sutent, Enbrel and Prevenar) are manufactured in Ireland and are exported to global markets, including the United States. It also holds commercial activities for several of its businesses (Human Prescription, Animal Health and Consumer Health products), a center for Global Financial Services centre as well as a global Treasury operation. Pfizer's total capital investment in Ireland amounts to more than 7 billion dollars.

Other large U.S. pharmaceutical companies have large operations in Ireland. Abbott's Ireland Pharmaceutical Operations is a facility that manufactures active pharmaceutical ingredients and drug products (Abbott, 2012a). One of Merck's eight facilities in Ireland supplies over 10 active pharmaceutical ingredients to other facilities to 20 countries around the world which take care of the formulation to the final dosage form. The plant's production is responsible for nearly 1.5 billion dollars worth of net sales worldwide (MSD, 2012). Overall, the Merck Sharp & Dohme Corporation and Schering Plough have invested around 2.2 billion euros in Ireland since the 1970s.[11] All U.S. firms, including largely pharmaceutical firms, exported above 100 billion euros worth of products from Ireland into world markets in 2010 (American Chamber of Commerce Ireland, 2012).

Singapore's success

Singapore's government also led an active policy to attract U.S. pharmaceutical companies. As a member of the WTO, Singapore has incorporated the protection of intellectual property rights in its legal framework. Singapore has also signed a bilateral free trade agreement with the United States in 2003, which offers more guarantees regarding the protection of intellectual property rights than the TRIPS agreement. Singapore is quickly becoming a major production center for pharmaceutical products as well as a biomedical center. Many companies are settling subsidiaries there (Pfizer, Schering-Plough, Merck, Abbott, Novartis, Sanofi-Aventis, GSK, etc.).

The development of the local industry is the result of strong intellectual property rights and political will. The government offers very attractive tax incentives and is supplying a highly

[11] Merck and Schering-Plough merged in 2009.

skilled workforce, thanks to manpower training initiatives. It encouraged the development of the Tuas Biomedical Park, a 183 hectare manufacturing hub for the biomedical industry (plus an adjacent 188 ha. site to be developed). The park is a way for companies to benefit from economies of scale, as companies can share major infrastructures specifically developed for the park. The Tuas Biomedical Park caters to bulk active pharmaceutical and biopharmaceutical manufacturers. Many companies are still building their infrastructures there. The Tuas Park is part of Singapore's biomedical science initiative. As the Asian market is expected to be the fastest growing regional market in the years to come, foreign firms find that Singapore offers many advantages for accessing new markets. Singapore's infrastructures guarantee the enforcement of property rights and are compliant with international health standards. These newer plants are also very flexible, which is not necessarily the case of older plants in Europe or the United States.

All companies benefit from infrastructures and other advantages, such as low transportation costs to find ingredients, and a shared large pool of skilled workers. Singapore is ideally located for the export of products to the rapidly growing Asian markets. The government of Singapore also promoted the Biopolis, a major biomedical sciences research campus, which opened in 2003. Singapore thus manages to lower operating costs for pharmaceutical companies. As is the case for Ireland, Singapore offers many English-speaking highly qualified employees.

Trends in growing pharmaceutical markets

Although Singapore is a rich country, neighboring nations are tagging along in the development of a pharmaceutical market in Asia. China, for instance, is following Singapore's example. As the avian influenza triggered a major scare in many countries, China decided to

develop its own vaccine production centers. China, like other countries, is increasingly reluctant to depend on foreign countries for its pharmaceutical supplies, and is developing its own infrastructures to become self sufficient. More and more companies are now investing massively in China, as the country has entered the WTO and is committed to respecting pharmaceutical companies' property rights. Until recently, many companies hesitated to invest in China because they feared piracy.

GlaxoSmithKline for instance, has invested in a facility that produces anti infective drugs. It targets the Chinese market. The company has developed a treatment against hepatitis B, a disease that many Chinese are believed to suffer from (an estimation of 120 million people). GSK currently employs 3,000 people and has four manufacturing facilities in China. Many other companies are settling operations in China, including Sanofi-Aventis. Once again, it appears that a strong government commitment to respecting property rights and government will to develop the industry is at the origin of the industry's expansion in the country.

The same goes for India. The Indian pharmaceutical and biotechnological industry is now expanding and investing in foreign countries. Bharat Biotech International Limited, a developer and manufacturer of vaccines and bio-therapeutics, for instance, invested in a new facility in Malaysia. In Malaysia, the government offers tax incentives to promote investments, which suggests the country should also develop its industry in the years to come. Bharat manufactures vaccines along with other drugs, and is able to produce a vast range of biotech products, including cardiovascular drugs. According to Kale & Little (2007), "*the Indian pharmaceutical industry has followed a trajectory from duplicative imitation to creative imitation to move up the value chain of pharmaceutical R&D. Finally as a result of changes in patent law the industry is learning to develop capabilities in innovative R&D. The basic and intermediate technological*

capabilities gained from imitative learning gave these firms a solid base for development of competence in advanced innovative R&D."

Finally, large Latin American countries are also growing bases for U.S. offshoring activities in the pharmaceutical industry. For example, Abbott's plant in Argentina produces more than 150 tablets and more than 120 million capsules, 75% of which is exported to more than 14 Latin American countries and Canada (Abbott, 2012b).

Conclusion

The pharmaceutical industry's success in lobbying for foreign patent protection has enabled it to offshore part of its production process abroad and to reduce costs. However, current trade statistics do not manage to fully take into account the impact of the fragmentation of the production process on trade (IDE-JETRO and WTO, 2011). The analysis of IIT for the U.S. pharmaceutical industry manages to capture the growth in the offshoring to some extent at the aggregate level. However, disaggregating trade data in finer categories of products tends to reveal only unilateral trade, and thus does not show the extent of offshoring.

The cases of Ireland and Singapore seem to indicate that some factors are essential to attract FDI from U.S. pharmaceutical companies. Patent protection is important to attract FDI. However, companies are also interested in benefitting from economies of scale, and tend to choose locations where they have easy access to English-speaking, highly qualified and cheap labor. A dynamic R&D environment also attracts U.S. firms. Easy access to growing markets through proximity and high quality distribution networks also appears to be an important factor in attracting U.S. firms. When more data will be available, an econometric analysis will be conducted to see to what extent strong patent protection is actually important for offshoring.

Furthermore, more data should enable a more complete analysis of VIIT and HIIT as the offshoring process continues.

Finally, attracting U.S. firms is likely to generate positive externalities on emerging economies. Indeed, through the transfer in technology thanks to FDI, emerging economies are more likely to stimulate the development of local companies. This development is likely to generate larger levels of IIT in the United States.

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