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THE DIGITAL DIVIDE, LOCAL LEARNING AND INNOVATION IN THE DEVELOPING WORLD: THE REMARKABLE CASE OF PHARMACEUTICALS

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ABSTRACT

Although there is little direct growth and welfare effect in the developing world of the globalisation of the Internet, indirect effects through the impact of particular technologies or industries appear to be profound. The digital divide, or the divisions in the global Information and Communications Technologies (ICTs) market between developed and developing countries (including lower middle income countries), tends to line up with the income divide. However, there is another way of examining the impact of digitalisation of information and computerised calculations on development processes which will qualify that judgment. It is clear that, where policy encourages it, there are large information spillovers from multinational R&D companies to the production of brand and generic products in less developed countries. In other words, the interaction effects of collaboration across phases of production, researchers and countries, along with the lure of new markets and pressures for cost reduction felt both by the industry (patent-expiry laws) and developing countries (health needs), result in a self-sustaining growth process made possible by the revolution in computer-based technologies. This paper analyses learning effects made possible by the Internet in one particularly high technology industry, pharmaceuticals. The objective is to examine the way in which the digital communications revolution demonstrably stimulates innovation, marketing and management improvement in sectors oriented to the production of exports and the improvement of welfare in emerging markets in particular and developing countries in general.

KEYWORDS: Pharmaceuticals, Internet, Development

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INTRODUCTION

Although there is little direct growth and welfare effect in the developing world of the globalisation of the Internet, indirect effects through the impact of particular technologies or industries appear to be profound. The digital divide, or the divisions in the global Information and Communications Technologies (ICTs) market between developed and developing countries (including lower middle income countries),[2] tends to line up with the income divide. Granville, Leonard and Manning (2000) showed that the impact of Internet in the developing world is less extensive than in the advanced economies. However, in particular industries, the enabling feature of technology, the computerisation of calculations and the exchange made possible by the Internet, imparts crucial knowledge across the digital divide which in turn directly facilitates high technology industrial development. In the revolutionary transformation of pharmaceuticals innovation and production, for example, communications technologies play an integral part, and the developing world is both a beneficiary and a participant. Among the passive benefits countries receive are cost reductions and availability of drugs, which improve health of the populace. More active participation in pharmaceuticals production and trade renders export revenues and learning effects in drug discovery, but particularly in the marketing of generic drugs in domestic and global networks.[3] The primary advantages that emerging markets, even such a controlled one as India, bring to global pharmaceuticals production and trade are the large pool of low cost skilled professionals and abundant availability of low priced raw materials, making the cost of setting up a plant up to 40 per cent lower than in the developed countries, and bringing the cost of bulk drug production down by 60 per cent. India has experienced rapid and high growth in the production of pharmaceuticals at 14.6 per cent per annum and their export at 16 per cent per annum between 1998 and 2001 (Confederation of Indian Industry July 2000; Sept 2001).

This paper attempts to analyse learning effects made possible by the Internet in one particularly high technology industry, pharmaceuticals. The objective is to examine

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[2] A low income country is defined as having a GDP per capita below $755. A lower middle income country is defined as having a GDP per capita between $756-$2,995 In the Table, below, *GNI per capita (Atlas method, current US$)* shows the income divergence:

	1999
Low income	420
Middle income	1980
Lower Middle Income	1200
Upper Middle Income	4870
Low and Middle Income	1240

Source: *World Development Indicators* (April 2001).

[3] For example, beginning in 2000, Brazil and India conducted talks toward cooperative agreements to foster in both countries public private partnerships in pharmaceuticals developments and to enhance reciprocal trade through the WTO.

the way in which the digital communications revolution demonstrably stimulates innovation, marketing and management improvement in sectors oriented to the production of exports and the improvement of welfare in emerging markets in particular and developing countries in general.

The paper brings together two separate and seemingly conflicting strands of economic literature, that which is concerned with estimating the digital divide, in which conclusions—mostly reflecting problems of access—have been pessimistic, and that which is addressed to learning-by-doing and knowledge and research-based industries such as the pharmaceuticals industry,[4] from which it is clear that, where policy encourages it, there are large information spillovers from multinational R&D companies to the production of brand and generic products in less developed countries. In other words, the interaction effects of collaboration across phases of production, researchers and countries, along with the lure of new markets and pressures for cost reduction felt both by the industry (patent-expiry laws) and developing countries (health needs), result in a self-sustaining growth process made possible by the revolution in computer-based technologies.

The paper is divided into four parts. Part I describes the place of developing (including emerging) countries in the pharmaceuticals market, including both the product and process development in innovation and production. Part II shows how learning effects are fostered by characteristics of the technology and process management in pharmaceuticals, heightening the importance of collaboration between researchers and between firms of all kinds and sizes; part III focuses on the learning process at the local level with examples from the countries particularly benefiting from pharmaceuticals development. Part IV is a conclusion.

I PHARMACEUTICALS: PRODUCTION AND GLOBAL MARKETS

Industrial Concentration

At first glance, it would seem that the production and sales of R&D based pharmaceuticals (brand products) could hardly be a focus for development conceptualisation. As Table 1, below, shows, drug production and sales are geographically concentrated in the advanced western economies, where there is a high level of per capita income and technological development.

[4] See particularly Gambardella 1995 and Pisano 1996; and also the considerable literature on the geography and economics of innovation.

Table 1
Leading 10 Global Pharmaceutical Markets Projected Pharmaceutical Sales and Growth Rates Through 2005

	Annual Sales 2000 (US$ Billions)	*Projected Annual Sales 2005 (US$ Billions)*	*Projected Compound Annual Growth Rate 2000–2005 %*	*Projected 10-Country Market Share 2005 %*
Australia	3	5	9.3	1.1
Belgium	2	3	5.6	0.7
Canada	6	10	10.7	2.4
France	16	22	6	5
Germany	17	24	7.5	5.6
Italy	11	16	8.2	3.6
Japan	58	66	2.3	15.1
Spain	6	10	9.9	2.3
UK	11	16	8.3	3.7
US	150	263	11.8	60.5
TOTAL	281	434	9.1	100

Notes: Sales cover direct and indirect pharmaceutical channel purchases from pharmaceutical wholesalers and manufacturers in 10 key international markets. Figures include prescription and certain over-the-counter data, and represent manufacturer prices

Source: IMS HEALTH Pharma-Prognosis International, 2001–2005

Of these countries, the US has a particularly large share in the R&D based industry. According to IMS data, 57% of sales of new medicines marketed since 1995 are generated on the US market, compared with 25% on the European market, 5% in Japan and only 13% for the rest of the world. In biotechnology, U.S. firms have a lead in patenting their innovations. Of the 150 genetic engineering health-care patents issued by the U.S. Patent and Trademark Office in 1995, U.S. applicants received 122. U.S. spending on drugs per capita ranks highest, close to that of France (Phrma 2001). The leading pharmaceutical markets as identified by IMS are all located in developed countries. Japan after the US is the world's second largest market for pharmaceuticals.

The geographical concentration is due to the technological intensity of process and product development of pharmaceuticals and the relatively higher prices of such drugs, affordable only in the advanced economies. The high and growing fixed costs of the R&D based side of the industry and increasing sophistication of its products are reflected in the growing average years required in the production process. In the early 1990s, it typically took 10 years and $100 million in R&D to take a new drug from the laboratory to the marketing phase (UNIDO 1995, p. 188). DiMasi (1998) estimated in 1997 that the average cost of innovation in 1997 was $312 million and the average production time was 12-13 years, to turn a newly synthesized active substance into a marketable medicinal product. [5] In aggregate numbers, in 2001, research-based

[5] Research Report cited in Phrma (2001).

pharmaceutical companies will invest $30.5 billion in R&D. This represents an 18.7 percent increase over expenditures in 2000 and more than triple the investment in 1990. As a per cent of sales, in the research-based industry, allocations to R&D increased from 11.4 percent in 1970 to 17.4 percent in 1999, and for 2001, the estimate is 18.5 percent (Phrma 2001) Based on corporate tax data pharmaceutical manufacturers invest a higher percentage of sales revenue in R&D than virtually any other U.S. industry, including high-tech industries such as electronics, aerospace, computers, and automobiles, well beyond industries, such as the oil and gas sector, which devotes at most 0.7 percent of turnover to R&D.

Part of the high cost is due to the extent of regulations in the drug industry, which is subject in developed countries to strict controls and rules to ensure that the products are safe and that they have the advertised effect; entire divisions in government health departments manage the regulatory process, which can consist of thousands of tests.[6] Large amounts of data, drawn on laboratory experiments on the basic chemicals for reaction changes (indicating toxicity or therapeutic action), trials on animals to monitor the effect of the product, and clinical trials on patients when the drug has been declared non-toxic.[7] Only when these stages of the process are completed, can the drug be licensed so that doctors can prescribe it, or, for those drugs not requiring a prescription, pharmacists can stock the product so that the public can purchase it.[8] This process typically accounts for about 17 per cent of total sales, a very high cost, compared to those of other companies (UNIDO 1995). Also, in most European countries and in Japan, the government is the largest purchaser of drugs, so that governments can negotiate directly or indirectly to control prices of pharmaceutical products. With differing kinds of controls, the general effect is to lower the profit margin, keeping the cost of drug development high.

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[6] Competitive market forces are constrained in most parts of the world. In most European countries and Japan, the government is the largest purchaser of pharmaceuticals and negotiates directly to control the prices of drugs. The methods of price-control systems differ, but price controls everywhere tend to undermine the innovation and vitality of the European and Japanese pharmaceutical industries.

[7] Government intervention practiced outside the U.S. includes (1) delisting, which disallows reimbursement for products, over-the-counter products that otherwise could be prescribed and reimbursed, or which forces switching of prescription drugs to over-the-counter status; and (2) local performance requirements to stimulate private investment in own markets, requiring companies to manufacture products locally, conduct R&D locally, co-market or co-develop products with a local partner, and/or license their products to a local manufacturer (Phrma 2001).

[8] The development and testing of drugs, conducted primarily by pharmaceutical companies in company and university laboratories, includes clinical trials, dosage testing, and research to determine information that should be included in product labelling. Human clinical trials take up roughly one/third of the R&D budget in the US: the first, second and third phase trials, required for drug approval, account for 29.1 percent, and an additional 11.7 percent is allocated to trials, which occur after a product has been approved by the FDA. In addition, 8.3 percent of R&D is for process-development and quality-control functions required to meet stringent manufacturing standards. Companies allocate approximately 36 percent of R&D expenditures to preclinical functions. Ten percent is spent on synthesizing and extracting compounds for evaluation; 14.2 percent is for biological screening and pharmacological testing, in which thousands of compounds are evaluated for every one that continues in the development process; 4.5 percent is for continued testing in the areas of toxicology and safety; and 7.3 percent is spent for dosage formulation and stability testing. Only 3 out of 10 drugs introduced after 1980 had higher than cost of R and D returns (Phrma 2001).

Within the industry, through the mid-1990s, the industry was not highly concentrated at the firm level, with only the three largest firms having more than a 4 per cent share of the world market and none with 20 per cent of any major national market (Tarabusi and Vickery 1997, p. 71). To be sure, intense competition has led to mergers. Ballance, Pogány and Forstner (1992), in their typology of pharmaceuticals producers, emphasise that the multinationals are large, integrated corporations engaged in all three stages of production (research, manufacture and distribution), with a high priority on product development, generating the new molecular entities (NMEs) upon which their R&D is based. Table 2, below, lists the top ten companies by sales:

Table 2

Top 10 Pharmaceutical Companies by Sales in 1999

Company	*Rank*	*1999 Proforma*
		Sales (US$ billion)
Glaxo Smithkline	1	22.2
Pfizer (Warner-Lambert)	2	20.2
Merck	3	15.5
AstraZeneca	4	14.8
Aventis	5	13.1
Bristol-Myers Squibb	6	12
Novartis	7	11.6
Roche	8	11
J&J	9	10.7
Lilly	10	9.3
Pharmacia	10	9.3

Source: Philing (2000), p.92.

There is substantial continuity in the market share of these firms over the past two decades, as Table 3, below, demonstrates:

Table 3

Top Ten Pharmaceutical Companies, by Revenues in 1980 and 1990.

	Position in 1990	*Position in 1980*
Merck	1	4
Bristol-Myers Squibb	2	8
Glaxo	3	Not in 1st 10
Smith Kline/Beecham	4	10
Hoescht	5	1
Ciba-Geigy	6	3
Johnson & Johnson	7	Not in 1st 10
American Home Products	8	6
Sandoz	9	7
Eli Lily	10	Not in 1st 10

Source: quoted in Beesley, 1997, Table 23.3, p.460.

However, there are also other kinds of firms, innovative companies and reproductive firms. Innovative companies are modest in size, but they have sufficient capacity to produce patent-expired drugs and can discover and develop NMEs as well as export significant quantities. There are also reproductive firms, small, family owned enterprises or publicly owned companies of medium size, which grow by accessing the technological knowledge developed by the larger forms and manufacture products sold under brand names or low-cost generics.

All of these kinds of companies can be found in many countries. The large companies have begun to disperse their activities around the world, and new firms of all kinds appear, those which are niche producers and other specialists, known for research or marketing strength or for the particular drugs that they produce (Ballance et al 1992, p. 2). The industry is not a global one in the same way that textiles, food processing, clothing or steel is, but it is achieving greater size rapidly, with many of the developing countries achieving and holding on to roughly 1 per cent of the export market share, despite the growing dominance of the US and European producers (IMS). In Ballance, Pogány and Forstner (1992, pp. 8-9), many of the larger Latin American and Central and East European countries have substantial innovative capabilities and many of the smaller and less developed countries produce finished products. Establishing a strong base after the World War II, by the early 1990s, the drug industry had reached at least $100 million in nearly 60 countries (p. 22).

On a global level, a distinguishing feature of pharmaceuticals is the great variety of products, with about 20,000 different drugs in large markets like the US or Japan, but more than 10,000 in both the leading developing countries, like Brazil, Mexico, Algeria and the Republic of Korea, and in the smaller developing countries (Balance et al. 1992, p. 4).

The rapid growth of pharmaceuticals after World War II is due mainly to on-patent drugs, only sold on prescription with high profit margins but high fixed costs. Other kinds of drugs include off-patent generic or multi-source drugs are also sold by prescription under their original patented brand name or generic names, which have low profit margins; there are also over-the-counter OTC drugs, which have high advertising and low

R&D costs and can be either generic or brand. Following the passage of the Waxman-Hatch Act in 1984, there was a large increase in the sales of generic drugs in pharmaceutical markets. The Drug Price Competition and Patent Term Restoration Act of 1984, called the Waxman-Hatch Act, made easier the entry into the market by lowering testing requirements. The law created the Abbreviated New Drug Application (ANDA), where a generic product was required to be only "bioequivalent" to an innovator drug for approval when the patent expired (Phrma 2001). It is also important that the patents of many widely sold drugs expired in the mid-1980s. The competitive dynamics of drugs markets has been transformed (Tarabusi and Vickery 1997).

The share of generics differs widely between countries. Overall, in the late 1980s, they were roughly 14 per cent of all drugs, with on-patent being per cent and OTCs, 16; by the early 1990s, in the US market, they made up about 20 per cent, although only 6 per cent in Europe (Tarabusi and Vickery 1997, pp. 70-72). The share of drugs sold by prescription in pharmacies that were comprised of generics roughly doubled in the 1980s from 18.5 per cent at the end of 1984 to 47 per cent in 2000 (Frank and Salkever 1995), and the large number of innovator products due to lose patent protection over the next 10 years will foster even greater expansion of generics.

For example, in the Brazilian market, both generic and brand products are hampered by a centralised distribution system and the requirement that all medicines be licensed by the Ministry of Health. In 1996, original and licensed brands had a market share of about 58 per cent, whereas generics had about 42 per cent. However, a law easing generic production in 1999[9] and OTC (over-the-counter) markets, since medicines cannot be sold in supermarkets, assisted production of generics in Brazil. In other developing countries, for example, Nigeria, there is a rising share of so-called imitations, low quality drugs often representing a danger to health.[10] These are beyond the focus of this paper.

Trade Competitiveness

However, global trading conditions are not differentiated on the basis of whether a product is on or off-patent, and there are currently no specific additional barriers to trade for patented-pharmaceuticals products, but markets in developed and developing countries are often separated to a certain extent by differences in standards.

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[9] The Generic Law in January 1999 allows a 40-45% reduction of pharmaceutical prices, in view of the income constraint on drug purchases, and provides incentives for manufacturers of generic drugs. The legislation makes it mandatory for the generic name to be included on all product packs (at least half of the size of the brand name) and requires that under the governmental system all prescriptions be written by their generic name and that generic drugs be used in all purchasing proposals and contracts. Industry sources estimate that the market for these products should increase 40% over the next two years.

[10] Saxenian (1994), p.9: "As a rule, drugs newly developed by innovative companies are patented and sold by them under their own brand name at prices sufficient to recuperate research costs and finance further innovation. When patents expire, the same drugs may be marketed by other firms, which will often sell them under 'generic' (non-proprietary) names at a lower price since they need make no allowance for research expenses. Until recently, most companies specialised either in research based innovative products or in generics. Since the late 1980s, the distinction has become blurred, with many firms engaging directly or through subsidiaries in both types of activities. Since 1980, a large concentration trend has led to the take-over of most large western manufacturers of generic drugs by multinational research –based pharmaceutical companies."

Markets for patented-pharmaceutical products are located where a patent is registered. In other words if a patent is registered in a particular country the patent holder has the legitimate right to market that product exclusively in that country. This prerogative is incorporated in the TRIPS (the Trade Related Aspects of Intellectual Property) international agreement (1995), governing the rights of patent holders and minimum standards of intellectual property protection for WTO members.[11] However, the TRIPS agreement does not prevent governments from allowing the importation of goods from the cheapest legitimate international sources. In other words it does not restrict parallel trade.[12]

The IMS estimates the future growth of the pharmaceuticals industry between 1999 and 2003 from these developments. The fastest growing regions are Southeast Asia, including China at 11%, the Middle East by 10%, and North America by 9%. Forecasts of sales growth in seven key Latin American pharmaceutical markets (Mexico, Venezuela, Peru, Colombia, Brazil, Chile, Argentina) are estimated at a compound average rate of 7.8 percent constant dollar for the five years through 2005, as below, in Table 4,

[11] The TRIPS agreement was signed by 123 participating countries and became binding by 1996. The agreement permits developing countries to bring their intellectual property systems into compliance with the new standards by January 1, 2000,.with added provisions for an additional 5 years transition period in the areas of chemicals and pharmaceutical products. Least developed countries have until 2006. The pharmaceutical industry has a clear stake in TRIPS:

1. Companies risks losing sales and profits when consumers purchase counterfeit products (Lybecker 1999);
2. Companies face reputational effects of counterfeit products.

In the absence of IPRs, R&D and future investments decisions can be negatively affected, however, research on life-saving medicines is constrained by the poverty of consumers in developing countries; in general only a small proportion of R&D goes into searching effective drugs for tropical diseases (Phrma 2001).

[12] This is however at the heart of a heated debate: developing countries claimed parallel imports are clearly allowed under Article 6 and that it is essential to ensure prices are as low as possible. The EU, US and Switzerland warned that this could undermine "differential pricing" (companies selling at lower prices in poorer markets) if cheaper products flow into developed countries' markets.

Table 4

World Pharmaceutical Market Growth by Region 1999-2003

REGIONS	*CAGR%*
North America	8.60%
Europe	5.30%
Japan	-0.20%
Latin America	7.20%
S E Asia & China	11.10%
Eastern Europe	9.40%
Middle East	10.40%
Africa	3.20%
Indian Sub-Continent	7.90%
Australasia	9.20%
CIS	6.10%
Total World Market	6.60%

CAGR: Compound annual growth rate
Source: IMS HEALTH Global Services Forecasts

Sales in Mexico and Venezuela grew at a 5.6 percent compound average rate between 1995 and 2000. Total pharmaceutical sales in the seven Latin America countries featured in the IMS Health prognosis 2000-2005 are expected to exceed US$29.6 billion in 2005, up more than 45 percent from the $20.4 billion in sales recorded in 2000. Mexico is the most dynamic pharmaceutical market in Latin America, with 13 percent annual growth forecast through 2005. IMS expect sales in Mexico to reach $11 billion annually by 2005, when it will account for more than 37 percent of total Latin American sales and supplant Brazil as the region's top market. IMS HEALTH forecasts robust 11 percent annual growth in Venezuela, which is expected to account for an estimated $2.5 billion in annual pharmaceutical sales and 8.4 percent of the total Latin America market by 2005. Brazil, which has seen its market share decline from 44 percent in 1995 to 33 percent last year due to economic conditions there coupled with the strong performance of Mexico and Venezuela, is forecast to grow 5 percent annually during this period. Solid growth opportunities are reflected in projected sales growth rates for Peru and Colombia of 7 percent and 6 percent, respectively. Both Chile and Argentina are forecast to grow 4 percent annually through 2005. Argentina is projected to have a 15.3 percent regional market share in 2005, down from the country's 18.4 percent market share in the 1995-2000 period due to economic conditions there, as shown below in Table 5,

Table 5

Projected Latin America Pharmaceutical Sales and Growth Rates Through 2005

	Projected Annual Sales 2005 (US$B)	*Projected C A G R 2000-2005 (%)*	*Projected Regional Market Share 2005 (%)*
Mexico	11	13	37.4
Venezuela	2.5	11	8.4
Peru	0.5	7	1.8
Colombia	1.7	6	5.8
Brazil	8.4	5	28.4
Chile	0.9	4	2.9
Argentina	4.5	4	15.3
Total	29.6	7.8	100

CAGR: Compound Annual Growth Rate
Source: IMS HEALTH Pharma-Prognosis Latin America, 2001-2005

To summarise the locational implications for growth in pharmaceuticals, the 1990s proved a decade of solid advances for the least developed as well as most developing countries, by contrast with the 1980s. Annual average growth rate of real per capita GDP in developing countries from 1990-1997 was 3.1 per cent, outpacing that of developed market economies at 2.3 per cent (UNCTAD 1999, p. 1777). . During the 1960s, MVA (Manufacturing Value Added) in developing countries grew by an average of 7.6 per cent, in the 1970s, by 7.2 per cent, but in the 1980s, by only 3.7 per cent. In the development process, in the 1980s, structural imbalances, promoted by internal policy and market distortions, domestic market weakness, lack of competitiveness both on the export market and domestically as well as a series of external shocks led across the developing world to de-industrialisation, a fall in income and employment and growth of external debt (UNIDO 1995, p. 35). Yet over time, the share of developing countries in global MVA rose from 8.6 per cent in the 1960s to 20.9 per cent in 1994. To be sure, a small number of developing countries actually accounted for the lion's share of manufactured exports, concentrated in East and South-East Asia and in Latin America.

Industrial Competitiveness

By contrast with older models based on price and cost factors in export markets, industrial competitiveness is based now on the export potential for high technology products. This kind of competitiveness does not depend on labour costs, which have greatly reduced in their component of value-added in manufacturing. The critical component is quality standards. In the past, in developing countries, competitiveness was restricted to a narrow range of non-traded goods. Contemporary developing countries now must compete in a world where high technology has become an important basis for competitiveness. Product life cycles are short, sometimes no longer than three years, and the demand for commodity exports is falling. In other words, the developing world must

adapt to the requirements in global trade for high technology products, and in view of the universalised standards and collaborative global research in drugs, this is a particularly accessible, almost automatically transferred aspect of the technologies that are now so widely shared.

Moreover, the diversity that is rewarded in pharmaceuticals exports in the 1990s provides new opportunities globally for adaptive learning in export markets. Where countries have taken advantage of the demand for diversity, there is tangible growth of output as well as export earnings. The literature notes the benefit of taking advantage of natural endowments to boost non-traditional exports of all kinds, with examples of the garments industry in Bangladesh, and fish processing in East Africa, or, the expansion of tourism, the most important service export of developing countries (LDC 1999, pp. 100-107). Many of the developing countries have university structures where the classical education of experts in chemicals provides a basis for the growth of expertise in pharmaceuticals, and thus competitiveness in the production of high valued products.

The area of exports affected is, broadly, fine chemicals. In 1991, 44 per cent of the application areas for fine chemicals was pharmaceuticals (ID 1995, p. 187). The drugs industry tends to produce its own fine chemicals; the largest drugs companies are also dominant in fine chemicals production. The growing interest in substituting cheap generic drugs for their branded equivalents after medicines are off-patent will not only make certain common analgaesics and heart medicines more available at lower cost but also require in substantial volume the production of fine chemicals in the shape of specific intermediates used in the final product (ID 1995, p. 188).

The production of generic drugs based on off-patent products requires little investment in R&D, and generic industries are far more competitive than the R&D based industry (Barro and Sala-i-Martin, 1995). For developing countries, the technical part of the process can lie in imitation, or development of known technologies that are widely available in scientific digital data bases or from networked science (Caselli and Coleman, 2001). Although it is well known that imitation can be of advantage in development, as in Japan and East Asia, the empirical research that would be required for further generalisation has not been done (Coe, Helpman and Hoffmaister, 1997). What is not well known is that in developing countries there is also some considerable advancement of R&D based pharmaceuticals and not only imitative production (Barba Navaretti and Carraro 1996). There is a relatively dynamic R&D activity in developing countries.

The advantage in terms of industrial competitiveness of expansion of pharmaceuticals in the developing world can be summarised from the obvious relevance to pharmaceuticals of the key ingredients in modern technology:

1) computer-aided design (CAD) and manufacturing (CAM) to generate firm flexibility in response to changing design requirements and production tasks;
2) information and communications technologies for finance and accounting, personnel and marketing with solid benefits for efficiency;
3) quality management to aid firms in gaining contracts with developed countries; biotechnology, with implications for health and waste management and the substitution of engineered for more expensive natural products (ID 1993/1994, p. 240).

II THE LEARNING FRAMEWORK: TECHNOLOGICAL DIFFUSION

Technological Diffusion and Information Spillovers

On its own, analysis of the digital divide by degree of Internet penetration may fail to turn up some important trends in global technological research. Emerging from the spread of computer technologies in business and research is a central force in economic growth, the linkages between computers—and the Internet—and R&D networks and other sectors of economic activity. Historically, information technology developed as an intensive R&D investment for defence-related applications in advanced economies. In the past few decades, R&D in CIT has focused more on high-speed information networks for civilian R&D usage to contribute to developing global communications and computing infrastructure for business and the public sector.[13] The knowledge spillovers leading to organisation learning occur through formal and informal channels of communications, and there are many mechanisms of knowledge diffusion. Especially significant in the biotechnology and pharmaceutical areas, where innovation and cost-savings depend upon updated information, formal mechanisms are licensing, technology partnerships, strategic alliances, and acquisitions; informal channels are the mobility of scientists and engineers, who participate in international trade or communicate at conferences and social meetings (Deeds, Decarolis and Coombs 2000).

The governments of advanced economies now provide national information infrastructures (highways, societies, etc.) linked to global networks, allowing the transmission of large quantities of information at low cost, including integrated data, video, text and voice traffic. It is well understood that open access to these super-highways (including interconnections and interoperability), competition, and universal service, combined with new relaxed trade policies regarding computers, stiffening of IPRs and the development of de-facto standards has led to the spread of high-technology industries, including pharmaceuticals, across the developing world (OECD 1997). Collaborative agreements, including with minority participations, have sharply risen over the period 1964-1992 in both the computer industry and in pharmaceuticals, and the two industries with complementarities and interdependencies, provide a new arena from which to assess the impact of information technology in development.

Technology transfer in pharmaceuticals, that is, the development implication of technology transfer, has generally been viewed from the perspective of innovation and R&D-based industrial development. Rapid development of new products is viewed as the main determinant of the success of entrepreneurial firms in advanced countries, and it is certainly a demonstration of local learning in the developing world.

However, although quality control spread the results of R&D research throughout the world by the 1995 TRIPS agreement, in the developing world, rarely are resources available for integrated development of all phases of process and production in pharmaceuticals. Depending upon the kind of IP property regime and health policies in developing countries, the domestic production may move in a more or less research-oriented direction, and in all likelihood, will specialise in imitative production of generic

[13] For models of learning in the management of industrial development and the impact of computers and networking, see Cohen and Levinthal (1990); and the Web page of the Austin 1999 Third International Conference on Technology Policy and Innovation, August 30-September 2, 1999;

drugs. It is important to underscore, however, that even this evidence of technology transfer via digitalised resources and management- rather than scientific learning will improve the efficiency of drug supplies in developing countries and thus benefit both the doctor and the patient and development itself, as Wartensieben (1983) observed:

> Any reduction of outright losses and/or extra costs incurred in a poorly operated system would immediately make more resources available both for health in general and for drug procurement in particular, whether domestically or by way of imports. In the long run, strengthening the pharmaceutical sector in developing countries at increasing levels of employment, productivity and income connected with the industrial and technological capacity opens up promising new dimensions for both public and private commercial intercountry cooperation, independently of whether drug supplies in developing countries follow more or less centralised organizational schemes (p. 170).

Knowledge yet to be acquired can nevertheless be guaranteed through opportunities opened up by the Internet, changing the way local industries acquire new skills and information. The innovative potential is enhanced in local firms in the developing world by interactive process inherent in Internet and computing technology that transform heuristic activities. The Internet will no doubt be the source of benefits as yet undetermined (Litan and Rivlin, 2001). There are some studies, however, that make the attempt to estimate the impact. In support of the larger point implicit here, regarding the entire sweep of Internet-related benefits for drug production and consumption, Danzon and Furekawa (2001), for example, estimate the saving effect of the Internet on the medical industry and they reached the figure of $20 billion savings from improvements in the processing of health-insurance claims.

Local Learning Mechanisms

Learning achievement as an economic good is not easily measured. Most measures are of capacity, and they are thus indirect. Inputs are measured in years of schooling, outputs by various measures of innovation, including the composition of exports and R&D (university research and patents) (Barba Navaretti and Tarr, 2000). Because knowledge is a public good, with the use of it non-rivalrous (Arrow, 1962), it is also generally a non-excludable good, in that it is difficult to prevent unauthorised use. In the drug industry, patent protection has been the focus of a great deal of international and national policy discussion as virtually the only way to ensure the viability of the industry. In pharmaceuticals, however, patent laws can be difficult to enforce. That IPs are difficult to enforce is both a stimulus to production and a source of spillovers from advanced to less advanced countries, and it is also the cause of regulatory responses, which also affect the production and consumption costs of drugs.

The stock of knowledge has to be continually increased for productivity growth to be self-sustaining (Romer (1990)). Developing countries tend to 'imitate' imported technologies, at least initially, rather than develop their own research and development (R&D) based industry (Caselli et al 1996; Klenow and Rodrigues 1997; Hall and Jones

1999).[14] Although the best known mechanisms for information spillovers and technology transfer between developed and developing countries is Foreign Direct Investment through multinationals, which transfer staff, equipment and communications networks from the home firm to the locally based affiliate and learning in outward processing industries (Eichengreen and Kohl 1998), the stock of knowledge accumulates through all kinds of cross border acquisitions and mergers and collaborative alliances in R&D. Thus, although pharmaceuticals R&D remain highly centralised in the advanced countries, through risk and cost sharing, the joining of large firms with small biotechnological firms and the expansion of markets is productive for the large companies, which recuperate R&D expenditures, the small innovative firms with imported intermediary goods and the pharmaceutical service deliverers and generics producers in the developing world. Tarabusi and Vickery (1997, p. 71) explain how critical local services and production are in this process:

> International trade is not as important as in many other industries, reflecting the multi-country pattern of globalisation, high penetration of foreign firms, and the necessity to produce finished products in final markets. Intermediates make up a fairly high share of pharmaceutical trade (40 per cent), as international firms ship active ingredients for formulation in final markets, but overall the ratio of imported to domestic sourcing is still lower than for many other industries, reflecting strategies and requirements to produce locally.

The incentives for international collaboration and learning are powerful at both ends: the shorter product-life cycles, cost-containment pressures, and the need for diverse research skills and knowledge dictate cost sharing. Multinationals form strategic alliances, whose number grew from 121 in 1986 to 712 in 1998.[15] Collaboration at the international level involves small and large companies, biotech firms, university research centers, and contract research organizations. Strategic alliances allow companies to bring products to market more rapidly and to market drugs more effectively and quickly, after licensing but before patent expiry. For example, to gain venture capital, experience in dealing with regulations or reputation, a small biotech firm may form a strategic alliance with a larger pharmaceutical company to develop a drug, while yet other specialised firms advertises and markets in an ever expanding global community, underscoring intra-sectoral spillovers from the networked knowledge groups (Phrma 2001).

Within industries and across entire economies, the contribution of knowledge-based production, or research-based innovation, enhances local activity.[16] The gradual

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[14] WT0 (2001): " Dictionaries tend to define a "generic" as a product – particularly a drug – that does not have a trademark. For example, "paracetamol" is a chemical ingredient that is found in many brand name painkillers and if often sold as a (generic) medicine in its own right, without a brand name. This is generic from a trademark point of view."

[15] See Deeds and Hill (1996).della Valle and Gambardella (1993); Nightingale (1999); Grabowski and Vernon (1990).

[16] In the environment of new and revolutionary discoveries relevant to health, there are incentives for take-up and application that spillover from scientists to consumers, who powerfully affect the spread of knowledge. From 71 interviews conducted with representatives of the media, specialist medical societies, consumer special interest groups, the Australian Red Cross Blood Service (ARCBS), government, private health insurers, technology manufacturers, prominent clinicians in the area and a sample of clinicians drawn from hospitals with variable use of blood-saving technologies, Treloar et al.(2001) identified the

expansion of pharmaceuticals production from the 1930s to the 1950s began with highly specialized, integrated manufacturing firms, based less on research conducted outside the firm and more on corporate R&D organizations. But there are now pressures, because of the diversity required for continual innovation, for off-shoots of these parent companies to spread in new urban markets across the developing world, and thus learning effects are increasingly rapid as the industry becomes increasingly diversified and localised.

To be sure, the capacity for learning and using transferred technology or information depends upon local regulations and the elasticity of domestic demand for new drugs. In pharmaceutical markets the two kinds of competitive structures, one, branded substitutes, which typically have unique chemical compounds as well as patent protection, and the other, generic versions of new and existing products, have entirely different pricing and demand conditions. For branded competitors, initially, the differentiated products face inelastic demand due to the power of physicians to influence choice of product and the impact of patent protection. Once a firm registers a patent for a new product, it has the exclusive right to market the product anywhere. Due to the small number of firms in the industry, an R&D-based firm thus exercises power over the production of specific products and prices as a monopoly supplier only until the point of expiry of patent. Patent expiry promises future returns, and IPRs do not contain the spread of information about products, including their composition and testing, whatever the regulatory regime.

With increasing competition after the expiry of patents, demand is more elastic and opportunity for developing countries is large. For off-patent brand and generic drugs, then, the competition is entirely price-based. In the year of an expiration of a patent, for example, a branded drug sales may fall up to 20 per cent with the price remaining high or even increasing, and the product life cycle may actually shortly come to an end. This will have particular effect on development, in that it yields a surge in opportunities for new entrants with generic products, even as the profit margins shrink (Caves et al 1991; Lu and Comanor 1998, p. 110). With the patent expirations of the 1980s and the fact that two of the highest selling brand drugs will expire in 2002, generics markets will maintain a powerful expansionary momentum.

Government pricing policy can have dampening or encouraging effect on this process especially in the developing world, where it can be determinant in capacity for technology transfer. Capacity is influenced by tariffs and taxes and procurement policy including competitive tendering and bulk purchase opportunities. Policy is crucial also in the developed world, as in the US, where constraints on market growth include the reform of Medicare, which may subject 40% of the US prescription drugs market to government price controls.

Sources of Innovation

Of the three institutional levels identified as sources of innovation in pharmaceuticals, the national, the network, and the individual or firm, interactions at all levels show that

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source of technical advances. The main influence on the decrease in the use of allogeneic blood transfusion in the past decade, for example, was 'enthusiasts', i.e., consumers (doctors or others), who became involved in educating, negotiating resourcing and maintaining the use of a technology (Treloar et al. 2001).

innovation is dependent upon cooperative efforts and the capacity for communications among researchers of different countries and research environments (Galambos and Sturchio 1997). From their research on Mulford, Sharp & Dohme and Merck, Galambos and Sturchio (1997) show, that in the development of serum antitoxins and vaccines, although these firms were highly competitive, the scientists collaborated with government researchers and officials, with university scientists and at times with other pharmaceutical firms. The firms that were successful innovators maintained close links between industry, academe and the government.

The use by firms of IT implies an educated workforce. Where labour is not technologically oriented or educated, skills must be imported and human capital maintained. Education and training are important not only for production but also for IT and Internet to secure a strong demand base.[17] On one hand, in the developing world, systems of education are not adequately funded to produce a large highly skilled work force; on the other hand, the knowledge and skills required in the development of new drugs, at least until very recently, could be found in the classical preparation of chemists, which is part of research education across the developing world. To be sure, where, as in high income countries, public expenditure on education is higher (5.4% of GDP in 1997), numbers of skilled chemists is larger; in middle income countries spending reached 4.8% of GDP, but in low income countries, it averaged only 3.3%.[18] India ranks even lower than Sub Saharan Africa in level of government expenditures on education, marginally higher in this category than other Asian countries, and although this has not stopped the country from becoming a major domestic producer of pharmaceuticals, it may have a bearing, along with the lack of patent protection, on the relatively low level of R&D investment as a per cent of sales.[19]

Technological diffusion depends not only on education but also free transmission of information across countries. Although the Internet promotes transmission of information, the degree to which it can achieve its full potential is indicated in the penetration rates, below, in Table 6,

[17] See Quah (2000). .

[18] The World Development Report (2001), Table 6, p.285.

[19] However, Acharya (1999) points out that the approximately 1.5 per cent of sales invested in R&D by Indian companies, although much lower than the average of 15.8 per cent by multinationals globally, is, for developing countries, is well above the norm (p. 88).

Table 6

Internet Penetration in 1999

Regions and Countries	*Internet Hosts (per 10000 persons)*	*Personal Computers (per 1000 persons)*
Advanced countries:		
United States	1479.8	510.5
Developing Countries:	4.2	16.6
Argentina	27.8	49.2
Brazil	18.5	36.3
Colombia	7.5	33.7
Guatemala	1.3	9.9
India	0.2	3.3
Russian Federation	13.1	37.4
South Africa	33.4	54.7
Thailand	4.6	22.7
Uganda	0.1	2.5

Source: *World Development Indicators Database*

Innovation and Regulation

Apart from the extent of penetration, Internet can be limited in its impact by regulation, affecting specific industries such as pharmaceuticals.[20] It is hard to distinguish whether bottlenecks occur as a result of regulation of the Internet and/or of the specific industry. For example, where intellectual property rights (IPR) are used to protect a firm such as Microsoft and deter small software firms from entering the market, they have a decisive impact on local software production even if the Internet as a whole falls under broader international agreements.

However, poor enforcement of such regulations is suggestive that the effects on Internet capacity may be limited (Granville, Leonard and Manning 2000). It has not been empirically demonstrated that such regulation can slow down learning and technology transfer effects. Indeed, policy conclusions would be very different if regulation were understood to be unenforceable.[21]

[20] Patents issues are summarised in Stiglitz (1999), p.315: "drug companies can, and have an incentive to, act like discriminating monopolists, charging higher prices where the consumer surplus is higher or where they can extract more of the consumer surplus. Some European countries have policies that offset these monopolistic powers: given the large role of government in health care, they can effectively exercise their monopolistic powers. Thus it is conceivable (and there are anecdotes supporting this possibility) that consumers in less developed countries could be charged higher prices for drugs than consumers in far richer countries. (In doing so, the consumers in less developed countries are in effect paying the fixed cost of research; consumers in more developed countries are partial free riders.)"

[21] Regulation is currently of enormous concern in US, EU and Asian policy (Spar 1999). Different stances have been taken. The American position asserts the greater importance of the commercial aspect over the public goods aspect of the Internet (The Framework for Global Electronic Commerce,1997). US policy is that governments should "adopt a non-regulatory, market oriented approach to electronic commerce" and

Similarly, property rights laws, however strong, may not have overall effect.[22] Kremer (1996) points to cases where 'strong' IPR protection can lead to duplication of research. Also Heller and Eisenberg (1998) argue that rather than encouraging research, strong IPR protection can lead to overlapping patent claims in the hand of different owners, increasing the transaction costs of research downstream. The high transaction costs and complex obstacles to an inventor mean less or slower new research. In addition, there are moral arguments favouring a laxer IPR regime in pharmaceuticals. Pricing people out of the market for consumer products in pharmaceuticals, so as to produce an incentive for innovation, may price them out of the market for life-saving drugs.

One test of the impact of regulations on the search for drug treatments is in the area of tropical diseases, a problem particularly in some of the world's least developed countries. Lanjouw and Cockburn (1999) find, that although it is probably early to judge if TRIPS (1995) resulted in an increase in research results on malaria, research directed towards other tropical diseases has indeed increased. In 'Tackling the Diseases of World Poverty" (Annex 3, 2001, p.27), however, the complexity is added that although IPR protection might provide the right incentives for increased R&D in the area of tropical diseases, along with other kinds, the difficulty of the research and/or the lack of a market for high-priced treatments will always remain critical in research decisions. Anecdotal evidence from an Indian pharmaceutical company (CIPLA) suggests that once India has become fully TRIPS-compliant on patent protection, the pharmaceuticals industry will surely become more R&D based. Ironically, this will divert their research toward developed world diseases, such as heart disease and obesity, where there is a guaranteed and profitable market, away from more urgent research on anti-infectives. Only around 10 percent of global pharmaceutical R&D activity actually targets the so-called "diseases of poverty". The challenge of the research, the uncertain prospects of success and the long timescale required for developing effective new products combines with the absence of effective markets in discouraging such innovative research where it is especially needed.

"refrain from imposing new and unnecessary regulation, bureaucratic procedures, or taxes or tariffs on commercial activities that take place via the Internet (White House, 1997). The EU supports the US position, but not absolutely. In 1997, the Ministerial Declaration at Global Information Networks declared that "the expansion of Global Information Networks must essentially be market-led and left to private initiative … private enterprise should drive the expansion of electronic commerce in Europe", and the European Commission has imposed no restraints on the content of online communications. However, Germany prohibited posting or transmission of offensive material, and the EU moved to regulate the protection of privacy against undue scrutiny of individual personal communications. A directive of October 1998 laid forth stringent rules on the collection and use of personal data on the Internet and other computer systems. More dramatically, the directive also threatened to block the transfer of personal information to countries that lack 'adequate' protection of privacy. The US government quickly launched discussions and as of mid-1998 the two sides were working on their differences (check if resolved and when). The Asian model is more prone to emphasise government initiatives and to channel the use of the Internet.

[22] Stiglitz (1999), pp.314-315: "The stance sometimes taken by producers of knowledge, that we need "strong" intellectual property rights, masks this underlying debate. Strong, in this context, becomes equivalent to "good", with the implication that the "stronger" the better. But […] stronger, in the sense of "tighter" protection, could not only have large distributive consequences (between, say, developed countries and less developed countries) but also large efficiency consequences, with the pace of innovation actually impeded and living standards in less developed countries diminished."

The Internet and Local Learning

All activities in pharmaceutical production are knowledge intensive. The development of new products, the conduct of clinical trials, and the side-effects appearing only with up-scaling and mass introduction show the need for knowledge-intensive processes. Knowledge comes from inside and outside firm, is continually gathered, processed and communicated throughout the product life cycle. Marketing a product sifts, filters, accumulates and distributes the knowledge necessary to market a product world wide. Marketing provides the background knowledge to carry out marketing in each country such as training on the product features; clinical tests information; prescription strategies.

The Internet in the pharmaceutical industry is used internally for communication from headquarters to the locally based firm, for marketing policy, which involves: a template of advice, for knowledge and training materials to the affiliates and externally, for communication with lobbies, pressure groups, and doctors. The multifaceted and interoperable Internet is used to provide the information about results of drug therapies more effectively and rapidly than is distributed by scientific journals. The extent to which this mode of communication can be contained by regulation, imposed by firms which are threatened by the public nature of Internet knowledge, is yet to be researched.

More technically, the Internet can be referred to as a self-organising cognitive filter for facilitating technology transfer, or knowledge transfer for technological (technical and administrative) learning and unlearning (Carayannis 1999). In pharmaceuticals, it is required for the constant need for feedback and new learning, or the expansion of the capacity to learn. Quoting the Bristol Myers-Squibb Executive VP for R and D, in an interview on August 10, 1993, Carayannis (1999), illustrated process communications:

> several review and decision making loops that are 'activated' on several different levels within our company and at varying frequencies (depending on the strategic import of the decisions being made), and that rely on feedback from our most recent experiences with both internal and external events….No major drug addition or pruning takes place unless R and D has come up with either a significant breakthrough or serious contra-indications resulting from a drug's laboratory or clinical trials….

Perhaps even more than in other modern, technologically-driven industries, in pharmaceuticals, the organisational culture of the firm is focused on learning.

Gambardella (1995) explains why this is so and how it developed. There was a shift in the 1980s from a largely empirical industrial research process (based on trial and error of many compounds) to more systematic means of searching for data with the aid of computerised research technologies. Gambardella's work, focused on "the technology of technological change", describes what has been made possible by the "impressive progress in computational capabilities and instrumentation" which reduce lags between scientific discoveries and industrial applications (p. 2):

> Using X-ray crystallography, nuclear magnetic resonance, the scanning electron microscope, laser, and other new magnetic- or optical-based techniques, they can "look" at the arrangement of atoms and molecules in exceptionally small clusters (De Solla Price, 1984; Lederman, 1984; Rosenberg, 1992). This is important, as

> the geometry of atoms and molecules governs the properties of matter (CSE&LPP, 1983; Baker, 1986; PSI&TA, 1986). Also, using advanced instrumentation techniques—like ion implantation or, more recently, synchroton radiation—they can intervene at atomic and sub-atomic levels to obtain selected alterations of matter, and hence control specific properties of materials like strength or conductivity (PSI&TA, 1986 [23] ; Steinmueller, 1987; David, Mowery, and Steinmuller, 1992).

Most important, from the perspective of local learning, he underscores that advances in computer power (both hardware and software) make possible efficient simulations of experiments, which yield both time and cost advantages over the actual physical experiments (p. 3). In the pharmaceutical industry, molecular biology and genetic engineering, together with new possibilities of computerized drug modelling and instrumentation, allow scientists with classical fundamental knowledge to use the most advanced modelling methods and technologies. With the assistance of computers, computational chemists can rely on basic theories of quantum chemistry about the density of electrons and the position of atoms to discover protein structures without actual evidence; computers can provide three-dimensional images of the solution of protein models for the understanding of the intricacies of molecular shapes (Gambardella 1995, pp. 36-37). Given the importance of professional training, firms tend to hire scientists with university backgrounds, who have reputational incentives to publish their research, and this leads to a more open kind of research that firms may initially want. This leads inevitably to knowledge spillovers through science networks.

There is another major point production incentive, made by Gambardella, which can be extended, by implication, to developing countries, whereas the original context is advanced urban economies. The point is that the absorption of external information is, itself, an incentive for the local development of R&D. In-house R&D is useful not only because of profits in appropriating and utilising one's own research outcomes but also—for which there is ample empirical evidence—to comprehend and evaluate external information and research findings available by digital communication. He cites Cohen and Levinthal (1989) on the two "faces" of R&D, one to produce innovation and the other to absorb technological information obtained from others. The implication is that a service, such as the Internet, which facilitates the speed and ease of absorption of external information influences both the conditions of research (technological opportunities and appropriability possibilities) and the incentives for investment in R&D (Gambardella 1995, pp. 5-6).

III LOCAL LEARNING: SOME EVIDENCE FROM PHARMACEUTICALS INDICATORS

In the early 1980s, when the drug question became a vital part of issues related to public health in the developing world, ways were sought to reduce the cost of imported drugs while finding avenues to increase the production of pharmaceuticals in the developing world (Patel 1983, p. 165). There is a substantial literature attesting to the tendency of manufacturing performance to improve with cumulative production experience,[24] and the

[23] Panel on Scientific Interfaces and Technological Applications (see Gambardella 1995, p. 179).
[24] Pisano (1996); Stobaugh and Townsend (1975), Adler and Clark (1991)

evidence is overwhelming that learning-by-doing is required in productivity improvement. This part rephrases to cumulative experience argument to say that learning-and-doing is a self-sustaining process that leads naturally not only to imitative and generic production in pharmaceuticals but to innovation, for which incentives build up.

The following focus on India, Brazil and China provides an example of three patterns, where policies followed different routes and learning in the pharmaceuticals industry took different forms, but it is not clear that the long-term consequences differ. The spread of the industry globally, due to incentives for R&D and appropriability of profits as well as new opportunities in the remarkable computerisation of drug design and networking of researchers, has its own dynamic, and this is affecting the development implications of the pharmaceutical industry.

Naturally, the regulatory regime in separate countries and the degree of patent protection has had some influence on the degree to which large companies invest and develop collaborations in particular emerging markets, despite the attraction of new markets and low-cost skilled labour. The critical issue is: How much influence? Pharmaceuticals is fairly unique in this regard because of the enormous fixed costs and time horizon required for R&D based production. Thus opportunities for learning, or for developing R&E capacity, differ entirely by local regime characteristics.

The introduction of patent protection, for example, had striking effect in the Italian industry. Strong patent protection, beginning in 1978, led to the quadrupling of investment in local pharmaceutical R&D. Also, Canada, where patent protection was recently under pressure from the WTO, strengthened, experienced dramatic growth in R&D investment from 2.7 percent of pharmaceutical sales in 1979 to 15.7 percent by 1997, according to the Pharmaceutical Manufacturers Association of Canada (PMAC). Canada still fails to provide an effective period of exclusivity for the commercially valuable and confidential clinical test data generated for marketing approval of pharmaceutical products, but legal reforms brought its generic products into compliance after a ruling by a WTO panel that their manufacture prior to patent expiration violated the TRIPS Agreement.

Of the larger emerging markets, Korea and Mexico introduced strong patent protection in the early 1990s and experienced significant increases in R&D; Brazil enacted strong intellectual property protection for pharmaceuticals in May 1996, and since then, it has become a major recipient of multinational investment and domestic development (Phrma 2001).

Some key emerging market countries, however, lack strong patent protection, and these are far more numerous. India adopted a patent law in 1970, but disallowed product patents and permitted only seven years of process patent protection from the data of filing or five years from the date of sealing (by comparison with 16-20 years from the date of filing in Europe and 17 years from the date of granting in the US (Acharya 1999, pp. 87-88). It is in conflict with the TRIPS Agreement, whose patent term is 20 years from the time of filing and a period of exclusivity for the confidential and commercially valuable clinical data generated in the course of research and development of pharmaceutical products (Phrma 2001). Argentina too implemented only very weak product-patent protection and only in 2000, through a new industrial-property law that does not meet many TRIPS standards, and is faced with a case before the WTO. Egypt recognized its TRIPS requirements in the areas of exclusive marketing rights and data exclusivity, but

also approved marketing applications for illegal copies of the patented products of foreign companies and generally has failed to meet minimum international standards for protection of intellectual property for pharmaceutical products. Hungary has never had effective data protection and remains in violation of TRIPS requirements, acknowledging its obligations, but failing to meet them. Israel disregarded intellectual property protection of pharmaceutical products by curtailing the effective patent term, limiting exclusive rights for patent holders, and allowing parallel importation. In Taiwan, the 1993 patent law failed to provide a WTO-consistent 20-year term for all patents, curtailing patent terms by five years for applications filed before 1994. China's "administrative protective" regime for pharmaceutical products, part of its pending TRIPS obligations, are unenforceable and widespread counterfeiting of pharmaceutical products poses a serious public-health threat.

The above brief descriptions are suggestive about implications for local learning, which are explored in greater detail below for three different regimes, that of Brazil, where strong patent law protects innovators, and that of India and China, where the regimes provide considerably weaker protection.

India

Pharmaceuticals development in India has taken place behind a wall of protection and regulation with the design of providing low cost health care and encouraging innovation in the industry. As industry literature observes, a result has been low levels of R&D, by comparison with the industry in advanced countries (but not by comparison with other developing countries).

In India, there is de facto minimal patent protection, and, in addition, a cap on royalties from bulk sales at 4 per cent of the sales price, by contrast with the 30-45 per cent maximum imposed in Europe of that era, has produced a significant industrial range of large and small firms and substantial domestic production. With the benefit of extensive protection, India became a net exporter beginning in 1979 and is now the fourth largest exporter of bulk pharmaceutical products worldwide, although it conducts only 0.001 percent of global pharmaceutical research. It acquired a high level of technological capacity. Larger firms attained success in imitating products and processes patented, and small service-oriented firms multiplied and acquired experience in exports.

Brazil

The Brazilian economy is the most industrialised in Latin America, in 1998, the 8th largest GDP in the world and the 6th biggest market for pharmaceutical products, representing 3% of the total sales worldwide. Much like India, pharmaceuticals grew up in a protective environment. The non-patentability of pharmaceutical products initially was designed to promote public health, but it became a means of protecting local industry. Until 1992, prices were allowed to increase only at a rate below inflation. After 1992, the regime loosened to a state characterised by the World Health Organization as "monitored freedom", with voluntary price controls arranged between government and the pharmaceutical industry. The market for generic products is growing in Brazil, especially

after the Generics Law of January 1999, resulting in a 40-45% reduction of pharmaceutical prices. There has been a policy trend favouring the manufacturers of generic drugs: the generic name is required on all product packs; prescriptions must be written by generic name; and generic drugs must be used in all purchasing proposals and contracts.

Brazil has thus dealt simultaneously with the development and IPR issues. One of the problematic areas of the pharmaceutical sector in Brazil, for example, is the lack of access of at least 40 per cent of the population to needed pharmaceutical drugs. The generic drug program is designed to avoid the unfortunate trade-off between the promotion of innovation and of public health. The following data, in Table 7, below, show that the impact of the new patent laws has not shrunk domestic production or damaged exports.

Table 7

Statistical Data (US$ billions)

	1997	*1998*	*1999** (est.)	*2000** (est.)
Total Market Size	12.7	10.3	11	11.5
Local Production	11.6	9.5	10	10.3
Imports	1.2	1	1.3	1.5
Exports	0.1	0.2	0.3	0.3
Imports from the U.S.	0.2	0.2	0.2	0.2

Sources: SECEX - Brazilian Government Statistics and ABIFARMA-Brazilian Association of Pharmaceutical Industries
Average Exchange Rate in 1998: R$ 1.00 = US$ 1.15

China

China is also a large producer, generating almost 40% of South East Asian sales. The incentives for government intervention are the same as elsewhere in the developing world, the urgent price/cost problem: pharmaceuticals account for an estimated 60% of all health care-related costs in China (the figures for the United States and Germany are 8% and 12% respectively). More than 50 per cent of this cost is directly related to expensive foreign produced drugs (Quinn 1998). The Chinese government has instituted reforms including price caps, and strict marketing and advertisement laws, and it has reorganised the state-owned enterprises system to create larger companies more capable of R&D and competition with foreign companies. Low in standards and selling primarily generic drugs, these companies nevertheless some competitive strength in that they benefit from the lack of enforcement of China's IPRs. China's support of patents generally conforms to TRIPS requirements. However, registration of foreign produced drugs takes roughly

two years, while domestic drugs are not subject to the same approval process. For all of these reasons, sales of foreign produced drugs have stagnated.

What is driving the continued resilience of investment in this market, despite stagnating sales, is suggestive of the particular features of attractive features of pharmaceutical markets in the developing world. First, China, important for the size of its market and growing affluence of the populace, also has a policy of controlling unethical marketing practices, which improves the business environment. Although entry of new firms is exceedingly difficult, this, itself, is an encouragement for existing firms to remain:

> Most foreign multinationals use former health care professionals (doctors, pharmacists) to market their products by directly approaching hospitals, pharmacies, and whole sellers/consumer distribution companies. Importers go through one of the established agents licensed to operate in this sector. Most of the world's largest pharmaceutical producers have an established presence in China and claim that this investment leads to better relationships within the bureaucracy surrounding the sale of pharmaceuticals in China (Quinn 1998).

Also, sales are held up by hospitals, which, funded by drug sales, have an incentive to sell Western-produced products. The opening of the OTC market has been another force encouraging foreign investment to continue.

In summary, the experience of only three countries suggests that, despite the disadvantages of protectionist laws and weakly enforced patent laws, particular countries can provide an environment where the production of pharmaceuticals and sales of foreign brand products are attractive to multinationals. Even at low levels of investment, however, developing countries and emerging markets, as in transition countries, have benefited from policies favouring the pharmaceuticals sector that are now widespread and somewhat to the detriment of foreign investment. There is sufficient knowledge spillover from the multinationals, for the reasons outlined above, for both interest and profit to be generated across the developing world, as the Table 8, below shows:

TABLE 8 *Net Trade, Selected Countries (Emerging Markets, Developing Countries), 1993-1998*

Origin/destination	1993: Net Trade Balance	1994: Net Trade Balance	1995: Net Trade Balance	1996: Net Trade Balance	1997: Net Trade Balance	1998: Net Trade Balance	Average annual rate of growth of trade balance, 1993-1998
				Value (1000 US$)			
World	7,566,953	8,674,908	10,081,710	11,030,102	13,668,828	15,437,626	6
G7	-187,859	19,985	-44,421	-866,959	-49,849	1,229,336	
OPEC	1,486,285	1,524,884	1,688,629	1,449,999	1,699,039	1,869,929	2
CIS	404,728	490,024	533,323	711,302	996,586	770,952	6
MERCOSUR	339,126	488,056	591,735	722,771	892,312	932,644	9
ASEAN	495,030	571,140	703,632	793,521	923,520	711,108	3
OECD total	844,171	1,174,013	1,092,732	1,457,839	3,224,459	4,747,448	15
NAFTA	29,558	371,213	623,767	22,803	929,691	2,304,111	38
Korea	122,843	156,887	165,915	191,692	194,454	167,624	3
Czech Republic	123,171	215,756	283,036	340,884	373,378	422,724	11
Hungary	176,155	226,379	267,519	265,625	299,976	357,614	6
Poland	347,202	396,109	540,044	638,014	772,842	895,334	8
Turkey	193,556	192,089	309,726	363,286	469,492	562,515	9
Russian Federation	257,404	376,305	378,738	557,751	746,442	566,910	7
Slovak Republic	24,937	45,967	82,857	101,533	118,609	128,420	14
Slovenia	47,926	57,149	72,897	78,481	87,328	109,669	7
Other Former Yugoslavia	28,719	53,365	85,497	95,523	97,268	120,988	12
Baltic States	15,099	29,794	60,949	95,745	137,186	165,072	21
Algeria	320,097	448,353	451,020	229,930	348,297	458,631	3
Egypt	120,759	145,072	178,732	182,587	215,266	262,919	7
South Africa	198,411	250,789	303,798	331,915	403,419	409,444	6
Columbia	53,036	79,111	94,354	102,083	117,505	137,988	8
Brazil	166,024	282,795	371,109	478,135	589,428	562,431	11
Argentina	146,133	176,743	184,908	209,431	245,940	298,420	6
Saudi Arabia	527,964	467,584	467,102	497,565	539,271	571,490	1
India	42,286	63,553	50,460	66,422	110,534	135,828	10
Singapore	101,563	116,209	131,502	172,835	199,194	174,388	5
China	-70,453	-112,180	-119,555	-28,126	-79,282	-148,601	-6
Chinese Taipei	163,950	183,395	203,998	245,926	267,425	292,542	5

IV CONCLUSION: HYPERLEARNING, GROWTH AND DIVERSITY

The innovative potential is enhanced in local firms in the developing world by interactive process inherent in Internet and computing technology that transform heuristic activities. This phenomenon across a range of high technology industries is called hyperlearning (Carayannis 1999). The direction of the effects is clear, if exact outcomes cannot be predicted (Litan and Rivlin, 2001). Authors such as Danzon and Furekawa (2001) estimate the savings brought about by the Internet, for example, on the medical industry in the range of $20 billion due, alone, to improvements in the processing of health-insurance claims.

In a recent paper, the limited direct effect on the populace due to barriers in the spread of internet observed by Granville, Manning and Leonard (2000) is not contradicted: the effects observed here are long-term, gradual and industry-related, but they are powerful. The remarkable impact of computerized calculations and three-dimensional imaging upon the diffusion of technology in pharmaceuticals, the development of a culture of learning across the pharmaceuticals industry, the emergence of small innovative and service-oriented firms that help break up the fixed costs for large firms, and the classical nature of the original training of professionals are all clear indicators that pharmaceuticals has a large role to play in development through technological diffusion.

Collaboration and cost-reduction have important benefits across the spectrum of development objectives. Many multinationals now have generic divisions or close ties with generic companies. In turn, generic companies in the U.S. and a number of European countries have often actively sought arrangements with multinationals to take advantage of distribution capabilities and to ensure a place in managed care systems. Indeed, the trend by some majors to move into benefits management opens up the prospect of more alliances as the need to provide a full range of inexpensive products grows. Through the WTO, TRIPs is playing a role to provide greater security to IPRs in WTO countries, and providing such regulations can be enforced, this step may help spread R&D further into developing regions, especially in Latin America and Asia where it has a firm foothold. For ten years, US, Europe, and Japan have coordinated an International Conference on Harmonization (ICH) to modify and harmonise requirements for drug development and approval. In 1997, the United States and the European Union negotiated a pharmaceutical Mutual Recognition Agreement (MRA) with the intent of eliminating regulatory barriers and promoting trade between the two regions. Once the MRA is fully implemented, the regions will recognize each other's inspections of manufacturing facilities for human drugs and biologics in their respective regions. This sort of collaboration will speed up the clinical and administrative phases of drug development and reduce costs, which are a barrier to entry into this lucrative field.

Collaboration has the benefit of enlarging the role for every phase in the complex of steps between process development and marketing and every kind of firm in the marketing of brand and generic products. Another factor promoting the spread of the industry in the 1980s, despite its early negative impact on innovation in developing countries, was the encouragement of the generic sector. An example can be seen from

Canadian data, where prior to 1993, compulsory licensing of brand– name pharmaceuticals allowed generic producers to copy and sell drugs still under patent in return for a royalty fee, generally set at 4 percent of sales. At the provincial level, government encouraged substitution toward lower–priced drugs, usually generics. In 1996, the generic sector accounted for 39.8 percent of the total number of prescriptions filled in Canada and 17.4 percent of their value.

This paper has argued that there is a synergy between the particular characteristics of pharmaceuticals production, process development and marketing strategies, and the needs of the developing world which, enabled by the Internet, makes a very fruitful collaboration that enhances possibilities and likelihood ofincreased domestic production. This has obvious benefits for health, where countries take measures to control costs, and although such measures are a barrier to investment, again, the conditions of emerging markets are such as to maintain foreign interest and investment. With this beginning, trade liberalization and TRIPS requirements for the WTO will not suppress domestic production, in part because of the countervailing forces enabling and encouraging information spillovers from multinationals and cooperation with domestic entrepreneurs.

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