

## **CREATING AND PROMOTING DOMESTIC DRUG MANUFACTURING CAPACITIES: LEGAL AND ECONOMIC FEASIBILITY ASSESSMENT<sup>1</sup>**

### **Objectives and outline of the note**

Access to drugs in developing countries is expected to worsen after 2005 when all WTO members – except LDCs – has to enforce the TRIPS agreement. This note addresses the role of promoting local production in improving the access to drugs in developing countries. The note was specifically expected to explore:

- medium and long-term strategies for the creation and improvement of domestic manufacturing capacities
- current policies and the legal environment, in general, for pharmaceutical production
- the feasibility of expanding existing manufacturing units or setting up new ones, as well as the possible instruments such as subsidies, investment regulation and government procurement policies, incentives by developed countries to improve technology transfer or provide technical assistance, as well as South-South technology transfer

Some case studies should illustrate the analysis

The first section describes the expected impact of the 2005 deadline. Section 2 analyses the complexities of the pharmaceutical production process. Section 3 reviews the feasibility of several strategies. Section 4 describes two country case studies: Bangladesh and Colombia. The paper ends with some reflections and potential topics for the debate.

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## Section 1

### The 2005 effect

It has been generally acknowledged that the price of new pharmaceuticals will go up after 2005 in most developing countries, when product patents are introduced in all WTO countries with the exception of LDC<sup>2</sup>.

The first, short term effect is related to the mailbox system, that required WTO members that delayed the granting of pharmaceutical patents until 2005 by taking advantage of the transitional arrangements, to accept patent submissions and to grant these products patent protection from the date of filing. Mailbox applications had to be examined in 2004 and eventually granted on 2005. As the examination of the patent submissions on the mailbox by the country patent offices might take some time, a certain delay of the 2005 effect beyond January 1, 2005 might be expected. It is moreover not clear which requested patents will be actually granted.

The second effect relates to products whose patents are submitted after 2005. This effect will be noticed much later, when the corresponding products enter the markets.

The negative impact for developing countries is likely to include not only a price increase of the products under exclusive marketing rights, but also a reallocation of production from South to North. These effects have already taken place in some countries and will probably be more relevant for small countries that rely mostly on imports of new technologies. The impact of the 2005 effect will vary from country to country and from drug to drug. Welfare losses will be higher for products with a low elasticity of demand – due, for instance to the relevance of the drug and to the lack of substitutive - and in countries that consume large quantities of the product.

It is however difficult to assess and quantify these negative effects. The main reason is the lack of precise information on patents - in spite of some initiatives by WIPO, OMPI and MSF - and on the products on the mailbox. Although no official figures are available, some estimates put the figure over 3,000 patents in 1998 for India, probably the main international provider of generic drugs. Balasubramanian<sup>3</sup> looked at the priority dates of 17 ARV and two other drugs (Glivec and Singulair) and found that six of these products might be subject to patent in India after January 1, 2005 (Atazanavir, Nevirapine, Kaletra, Combivir, Trizivir, and Singulair)

In spite of the apparent high risk of discontinuation of the present flows of exports from India, China and other provider countries and the negative impact on patients health and domestic formulation companies that such an event might pose, no studies seem to have been done, nor alternative plans seem to be in place in order to ensure the continuity of treatment at affordable prices to people in

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<sup>2</sup> Carlos M. Correa, "Health and intellectual property rights" *Bulletin of the World Health Organisation*, 2001, 79 (5).  
Carsten Fink, "How Stronger Patent Protection in India Might Affect the Behaviour of Transnational Pharmaceutical Industries", *World Bank Working Paper*, (2000) at <http://econ.worldbank.org/docs/1106.pdf>. Julio Nogues, 'Social Costs and Benefits of Introducing Patent Protection for Pharmaceutical Drugs in Developing Countries', *International Journal of Technology Management*, Vol. 10, No. 1/3 (1993). A. Otten, "The GATT/TRIPS Agreement and health care in India", *National Medical Journal of India*, 1995, 8(1), 1-3.

<sup>3</sup> <http://lists.essential.org/pipermail/ip-health/2003-September/005222.html>

need. The main mechanism provided by the TRIPS – issuing compulsory licenses – is practically an unused tool for most developing countries. Price control, a second tool to moderate the likely price increases derived from the new monopolistic situations, has been removed from the toolkit of many developing countries following the advice and pressures they received from international agencies for increasing deregulation and free market mechanisms.

The high costs of imported drugs and the fear of discontinuation of the supply from their traditional suppliers after 2005 seem to have encouraged many countries to set up their own production facilities, for instance:

Namibia announced on June 2003 that a local company would soon start producing ARV<sup>4</sup>  
Kenia announced on September 2003 that it would be the second country in Africa to produce ARVs<sup>5</sup>  
Varichem Pharmaceuticals, a Zimbabwean pharmaceutical company based in Harare announced on June 2004 that it had started manufacturing generic anti-retroviral drugs and is producing nine types of ARVs to be sold in Zimbabwe for the millions of HIV and AIDS sufferers in the southern African country and that it was probably the first generic company to produce ARVs in Africa<sup>6</sup>.  
On September 2, 2004 Zambia declared HIV/AIDS a national emergency "in an effort to begin manufacturing generic AIDS drugs"<sup>7</sup>. Although the declaration enables local firms to produce generic versions of patented drugs, no plans or news have been disclose regarding the willingness of local manufacturers to do so.

The efficiency and sustainability of a proliferation of drug manufacturing in many developing countries is, however, questionable. It is hard to assume that most developing countries might be successful in trying to solve the problems of access to new and technologically complex to produce pharmaceuticals, such as ARVs, by developing a domestic production. It is not only the issue of whether and how technology transfer can take place, but also the scarcity of appropriate human resources, energy, water supply, ancillary industries and, especially, the limited size of the market, which might make unprofitable a local industry restricted to the domestic market. Local production, in any case, is likely to be at best restricted to formulation and packaging processes, which have a limited added value.

Some kind of regional approach would probably facilitate the attainment of the required economies of scale. COMESA<sup>8</sup> Africa's major free trade bloc made up of 20 countries from Egypt to Madagascar applied to the World Trade Organisation in 2002 for the right to manufacture cheap antiretroviral drugs and to treat COMESA as one region so that drugs manufactured in one country can be sold in

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<sup>4</sup> <http://www.namibian.com.na/2003/june/national/03D7C6D117.html>

<sup>5</sup> <http://news.bbc.co.uk/1/hi/world/africa/3123008.stm>

<sup>6</sup> **Zimbabwe starts producing anti-AIDS drugs, *Agence France-Presse - June 8, 2004* HARARE.**  
<http://www.aegis.org/news/afp/2004/AF040628.html>

<sup>7</sup> Zambia to manufacture generic HIV/AIDS medicines. BRIDGES, ICTSD, 8 September 2004, 3.  
<http://www.ictsd.org/weekly/04-09-08/BRIDGESWeekly8-29.pdf>

<sup>8</sup> <http://lists.essential.org/pipermail/ip-health/2002-November/003725.html>

all member states without problems. This regional approach is likely to be more sustainable than other aimed at supplying single national markets.

**Section 2**  
**The complexity of drug production processes**

When considering the feasibility of policies implying domestic pharmaceutical production and technology transfer it is important to take into account the varying complexity and technological requirements of the different types and stages of the process of production of drugs and how the technological and productive capacity is distributed across countries. The reference study on that issue is still the relatively old one by Ballance et al.<sup>9</sup>

Production activities of the pharmaceutical industry can be divided into the following categories:

1. Chemical Synthesis - the manufacture of pharmaceutical products by chemical synthesis.
2. Fermentation - the production and separation of medicinal chemicals such as antibiotics and vitamins from micro organisms.
3. Extraction - the manufacture of botanical and biological products by the extraction of organic chemicals from vegetative materials or animal tissues.
4. Formulation and Packaging - the formulation of bulk pharmaceuticals into various dosage forms such as tablets, capsules, injectable solutions, ointments, etc., that can be taken by the patient.

Further, the various chemicals used in making pharmaceuticals may be categorized as follows: basic building blocks; intermediates and custom-made active ingredients, including active pharmaceutical ingredients (APIs) (See Figure 1).

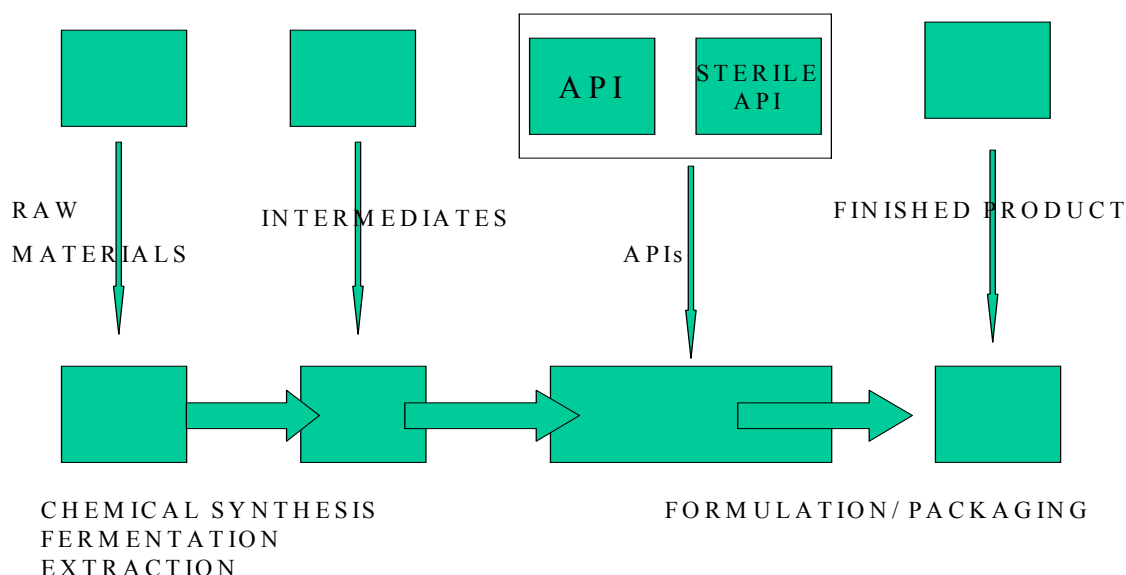


Figure 1: Schematic block diagram of a pharmaceutical manufacturing process (Source: Kaplan and Preker, 2004)

<sup>9</sup> Robert Ballance, Janos Pogany & Helmet Forstner The World's Pharmaceutical Industries: An International Perspective on Innovation, Competition and Policy, UNIDO, 1992.

A useful starting point for distributing countries according to the capacity to carry out the full range of activities is the typology devised by UNIDO<sup>10</sup> and applied by Ballance et al. is a useful starting point. They viewed production as being based on differences in source of the final product:

1. No manufacturing facilities and dependency on imported, finished medicines.
2. Packaging of already formulated medicines and small-scale local production of sterile or non-sterile formulations such as IV fluids.
3. Formulation of drugs in final dosage form and some production from imported intermediates.
4. Production from imported intermediates and manufacture of some intermediates from local materials.
5. Production of active substances and processing to produce the required pharmaceutical dosage forms.

Although some of the findings of the study by Ballance et al. might be outdated, the basic conclusion is still valid: the high technological capacity required for R+D and API production is concentrated in the industrialised world and in a few emerging countries (see table below).

*A typology of world's pharmaceutical industries*<sup>11</sup>

Stage of development of the pharmaceutical industry in the country	Number of countries		
	Total	Industrial	Developing
Sophisticated pharmaceutical industry with significant research base:	10	10	0
Pharmaceutical industry with some innovative capabilities: *)	17	12	5
Pharmaceutical industry with capability to produce both therapeutic ingredients & finished products:	14	6	8
Pharmaceutical industry formulating finished products only (from imported therapeutic ingredients):	89	2	87
Countries and states without a pharmaceutical industry:	60	1	59

\*) Each country in this group discovered and marketed at least one NCE between 1961-1996.  
 ADAPTED FROM BALLANCE ET AL (3):

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<sup>10</sup> UNIDO 1980, *Appropriate industrial technology for drugs and pharmaceuticals*, UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION, New York, NY, Monographs on Appropriate Industrial Technology, 10

<sup>11</sup> WHO and Bakti Husada, *The TRIPS agreement and pharmaceuticals*, Report of an ASEAN Workshop on the TRIPS agreement and its impact on pharmaceuticals, Jakarta, 2-4 May 2000

Few developing countries have the capacity to produce API. These include India, China, Thailand, Egypt, Brazil, México and Argentina, and to some extent, Yugoslavia and Turkey. In fact, one of the most remarkable recent trends in the international drug market is the emergence of India and China as generic manufacturers and major international suppliers of API and finished products. This trend was made possible by the lack of patent protection in these countries until 2005 and their capacity in reverse engineering, i.e. finding out the process to manufacture a certain API<sup>12</sup>.

One of the key elements of pharmaceutical production at present is the capacity to comply with quality standards, which tend to be driven up and harmonised at international level

### **Section 3**

#### **Strategies for improving access to drugs by creating and promoting domestic drug manufacturing capacities: the “make or buy” dilemma**

##### **The state of the art**

Two articles (Attridge and Preker, 2004; Kaplan and Laing, 2004)<sup>13</sup> and two World Bank meetings (available at B-SPAN, the World Bank's webcasting station for development)<sup>14</sup> have recently addressed the issue of the role of local production on the access to medicines in developing countries. These activities probably provided more questions than answers, but they nevertheless provided a "state of the art" review of the issues and of the apparent consensus on some of the solutions, as well as a future agenda for research. Many of their findings are later quoted and discussed in this note, but it is worthwhile transcribing here the summary conclusions of the two studies.

Attridge and Preker conclude that

*"Many of the issues we have addressed in this paper are not susceptible to formal academic analysis because, for the most part in Middle Income and LDC countries, relevant data sets are limited, of*

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<sup>12</sup> India and China have replaced Spain and Italy in that role. These two countries had to enforce product patent when they joined the EU.

<sup>13</sup> Attridge, C.J., Preker, A.S. Improving Access to medicines in Developing Countries, March 2004 . HNP Discussion Papers Series (in press)

Kaplan, W.A., Laing, R. (2004), "Is local production of pharmaceuticals a way to improve pharmaceutical access in developing and transnational countries? Setting a research agenda",

[http://dcc2.bucm.bu.edu/richardl/RPM+ Project/local\\_production.htm](http://dcc2.bucm.bu.edu/richardl/RPM+ Project/local_production.htm)

<sup>14</sup> Workshop on Improving Access to Drugs in Developing Countries, The World Bank, June 2, 2003, [http://www.worldbank.org/wbi/B-SPAN/sub\\_drugs\\_dev.htm](http://www.worldbank.org/wbi/B-SPAN/sub_drugs_dev.htm)

Meeting on The Role of Generics and Local Industry in Attaining the MDGs in Pharmaceuticals and Vaccines, The World Bank, June 24-25, 2003 [http://www.worldbank.org/wbi/B-SPAN/sub\\_generics\\_mdg.htm](http://www.worldbank.org/wbi/B-SPAN/sub_generics_mdg.htm)

*doubtful quality and compiled on different bases. Thus, whilst IMS, the leading international pharmaceutical market research audit company, has excellent long-term data on OECD countries, beyond that it tails off rapidly. In drawing conclusions, therefore, it is important to be clear that the evidence, information and opinions drawn up are not just empirical but, to a degree, subjective, judgements.*

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*We would suggest that, faced with a specific situation in an international agency or a private company, or in defining a national strategy, this analysis provides at least an insight into how ideas of 'make or buy' organisation boundary setting, writing and managing contracts and the fit between objectives-strategies and capabilities might be used to formulate a relevant and useful framework for high level consensus building and choice of strategies or policies.*

*Also that understanding the nature of the technologies, capabilities and resources needed to operate professionally and efficiently in the pharmaceutical sector, can greatly enhance the quality of decision making.*

*More specifically on the issue of public sector engagements, either internationally, in national policies or at the individual company level, it is critically important to understand likely future global scenarios for location of the most efficient, low cost production and the resulting patterns of international distribution or trade.*

*Finally, there may be as much merit in seeking to achieve best value from the worldwide industry in its many guises, to think not only in terms of regulation and control, but of incentives and capability building.*

Kaplan and Laing, in its turn, state that:

*"Based on the qualitatively and quantitatively limited datasets available to us, our preliminary conclusions are:*

- *In many parts of the world, there is no reason to produce medicines domestically since it makes little economic sense.*
- *In the local pharmaceutical-manufacturing sector, local production is often not reliable and, even if reliable, it does not necessarily mean that medicine prices are reduced for the end user.*
- *If many countries adopt local production, it may lead to less access to medicines, since there are no economies of scale in having a production facility in each country.*
- *It may be possible for small country markets to be co-ordinated or otherwise joined together to create economies of scale.*
- *Regarding state-controlled local production, the WHO considers state-owned owned production to be "ill advised". Profit margins on bulk generic drugs are low so that public production must be as efficient as private manufacturing if economies of scale are to be met.*
- *For many countries, technical expertise, raw materials, quality standards, and production and laboratory equipment need to be imported so that foreign exchange savings may be small or non-existent.*
- *Few developing countries have the capacity to produce active ingredients for pharmaceutical manufacture.*
- *We need much better and comprehensive data on types of local production, particularly purely domestic, production.*

- *Industrial investment to promote local manufacture of pharmaceuticals in most, but not all developing countries, could be better used to improve health infrastructure or stimulate the existing market but developing countries need to decide this for themselves and not have such decisions imposed upon them by developed countries.*
- *A research agenda should be created that is specifically designed to test assumptions about local production of pharmaceuticals. This agenda must be based on evidence and not just on post-hoc case studies. It should provide for creation of accurate 'baseline' information on variables needed to test these "local production" assumptions and sufficiently robust experimental designs (pre/post, time series with controls) to garner and test the evidence."*

The research agenda proposed by the authors for testing local production assumptions and beliefs against the evidence can be summarised in the following items:

*"1. Generating Good Data on Local Production:*

*2. Testing the long term effect of TRIPS on the Pharmaceutical Industry and on pharmaceutical access, quality and use*

*3. Testing the assumptions about local production*

- *Does local production save foreign exchange?*
- *Does local production create jobs?*
- *Does local production facilitate technology transfer?*
- *Does local production stimulate exports to neighbouring countries?*
- *Does local production lead to lower prices and/or improved access to pharmaceuticals?*

*4. Creating a predictive index of local production based on easily measurable markers"*

### **Industrial and health goals of the domestic production of drugs**

The question of whether the development of a domestic drug industry is an effective and **efficient way to improving the access to drugs** has been often raised in national and international debates as a consequence of the barriers of access raised by the generalisation of IPR and the resulting increase in the prices of new patent-protected drugs. Before the TRIPS most developing countries were able to import recently marketed drugs from countries that did not grant patent protection to pharmaceuticals. A domestic pharmaceutical industry based on the formulation and marketing of drugs could easily be established and compete with multinational innovator-industries on the domestic markets. This situation empowered governments to force multinational innovator companies to establish themselves in most countries, as a requisite to have their products registered, and to keep their prices relatively low, as a result of domestic competition, price regulation or both. With the harmonisation of IPR, the Balance of power has shifted towards patent holders and weakened both national regulators and domestic industries.

The support by governments or by international agencies for the development of a domestic drug industry can be justified on either industrial and health goals or both. This goals might however conflict with each other



In the past many countries tried **to develop local industries** with the aim of substituting imports, creating employment and becoming self-sufficient in the procurement of certain products. The incentives for an import-substitution approach are especially strong in the case of pharmaceuticals, which are often subsidised as input to publicly funded health systems.

The present globalisation trends points to a specialisation of countries in the production of goods and services where they have a comparative advantage. According to the traditional theory of comparative advantage, each country should specialise in the types of products where it has a comparative advantage and exchange them for goods that other countries produce with a higher relative efficiency. According to this theory, all countries - even countries that are less efficient in the production of any goods - will be left better off. Trade barriers will protect the domestic industry only at the expense of the consumers and the overall welfare of a country. Of course, a strict interpretation of this approach would condemn developing countries to the production and export of raw materials and labour intensive manufactures and would deny them the possibility of industrial and economic development.

On purely industrial development grounds, support for the development of a domestic industry can be justified as a transitory measure, assuming that after a period of protection the industry will become competitive and self-sustainable. However, countries trying to industrialise themselves must carefully consider which are the sectors more likely to quickly become competitive in the international market and pull economic development in the whole economy.

There might certainly be opportunities and certain niches of the pharmaceutical sector for developing and emerging countries to successfully establish a domestic industry; but pharmaceuticals might not always be the best option. Of course, this debate must take into account the different types of pharmaceutical production and the level of development and other characteristics of the countries concerned.<sup>15</sup>

### **Creation of domestic manufacturing capacities**

To develop a pharmaceutical industry a country requires not only a huge initial capital outlay, but it must else meet certain conditions, like “availability of special technologies, reliable supplies of high quality raw materials, dependable provision of top-quality water, electricity, gas and other utilities. It also needs sufficient human resources, such as experts in pharmaceutical development, quality assurance and regulatory processes”<sup>16</sup>

Kaplan and Laing suggest that, apart from India and China, developing countries with educational structures that might allow them to have the human resources from which they can draw the required expertise for pharmaceutical production are Philippines, Ukraine, Egypt, Russia and Poland.

More generally, they suggest that in order to become internationally competitive as a producer of pharmaceuticals, several of the following factors are crucial:

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<sup>15</sup> For instance, *Artemisa annua*, grown in Tanzania, is 10 to 15 times more potent than the varieties found in China and Thailand. Presently, the plant is exported to Europe where it is processed into antimalarial medicine and exported at US\$6-7 per dose, beyond reach of most people in the country. A feasibility study suggests that if produced locally it could be sold at a US\$2 per dose <http://www.afro.who.int/press/2003/pr2003042502.html>

<sup>16</sup> WHO. Executive Board. Manufacture of antiretrovirals in developing countries and challenges for the future. Report by the Secretariat. 114<sup>th</sup> Session, 29 April, 2004.

- GDP greater than about \$100 billion
- Population greater than about 100 million
- Sufficient numbers of the population enrolled in secondary and tertiary education
- Competitiveness index (UNIDO) greater than about 0.15
- A net positive pharmaceutical Balance of trade

### ***Promoting existing domestic drug manufacturing capacities***

Some developing and emerging countries do already have a well-established pharmaceutical industry usually restricted to the formulation phases of the production process. It is likely to be more feasible to base the development of a domestic industry on already existing companies than to create new industries. Some key issues for ensuring the continuity and growth of these companies include.

- The attainment of international quality standards, which can be identified with the compliance with GMP or attaining WHO prequalification. Complying with GMP might impose a substantial initial investment and recurrent costs to the companies: some might not be able to afford it and will close or be sold to other companies. However, those overcoming the challenge might become more competitive at the national and international level and be able increase production, sales and exports. Subsidies or soft loans might be offered to companies in order to help them make the necessary investments. Colombia might be a good case study of such a regulatory initiative (see below).
- Regulations derived from the international harmonisation of technical standards might as well impose additional costs and become market barriers to local producers. One clear example is the requirements for generics to prove therapeutic equivalence or interchangeability by means of bioequivalence studies, even if it is not strictly required from a technical point of view. The cost of bioequivalence studies can be easily borne by large generic manufacturers, but they might become prohibitive for small and medium size manufacturers. A study by FEDESARROLLO in Colombia estimated that the requirement of bioequivalence studies for antihypertensive and anti-inflammatory drugs would increase price of domestically manufactured products by a percentage between 46% and 61%<sup>17</sup>. The need for bioequivalence studies is in principle a technical issue, but the criteria vary from country to country.
- Ensuring the supply of raw materials (APIs). The supply of off patent APIs is not likely to be discontinued after 2005, but that of innovative drugs will probably experience major changes. Innovative drugs include those patented after 2005, as well as those that will obtain market exclusivity as a result of the TRIPS mailbox system. Some of these APIs might be the object of compulsory licensing, although it is far from clear how smoothly the system might work. For the other, domestic manufacturers will have to seek licensing agreements from the patent holders or wait until the patent expires. This will result in higher prices for new products during the period of

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<sup>17</sup> Based on an assumed cost of bioequivalence studies in the range of US\$15-30,000 if done in Colombia and of US\$30-80,000 if done abroad. Zuleta Jaramillo, L.A., Junca Salas, J.C. EFECTOS ECONOMICOS Y SOCIALES DE LA REGULACION SOBRE LA INDUSTRIA FARMACEUTICA COLOMBIANA: El Caso de los Estudios de Bioequivalencia y Biodisponibilidad, de los Secretos Empresariales y las Buenas Prácticas de Manufactura. FEDESARROLLO, Bogotá, Abril de 2001

market exclusivity. Of course, any type of TRIPS plus provisions will become an additional barrier to generic competition and will restrict the opportunities for the domestic industry.

### ***Technology transfer***

Although many agreements and declarations including the TRIPS<sup>18</sup> pay lip service to the goal of technology transfer, there are few incentives for the producers and proprietors of the technology to share or transfer it to developing countries and little is known on which are the best strategies to make it work and speed it up.

The supporters of the establishment of strong patent regimes in developing countries claim that by providing incentives for direct investment and licensing, this is one of the best ways of promoting technology transfer, but the evidence on that issue is far from conclusive. In fact, the experience of countries such as Japan, Switzerland and India seem to point to the opposite hypothesis, namely that a low level of patent protection has been a key factor in allowing a strong productive and R+D capacity to be developed in the pharmaceutical sector: In spite of its present advocacy for generalising strong patent protection, Japan introduced pharmaceutical product patents as late as in 1976 and Switzerland, in 1977.

Moreover, in order to become effective mechanisms for technology transfer, licensing agreements should include much more than the right to formulate and sell a given product in a country by purchasing the API or the finished product from the patent holder. Of course, from a commercial perspective, technology and know-how are valuable assets that confer a competitive advantage to their holders and there is no reason to expect that private companies will be willing to freely disseminate this knowledge and give up the associated market advantage. Some companies on humanitarian grounds have taken isolated initiatives related to specific products, usually drugs that do not have a relevant market in the more affluent markets. Kaplan and Laing report an announcement made by Eli Lilly, by which the company would participate in a PPP aimed at making transfers of technology to a China, India, South Africa and Russia in order to help them produce drugs to combat TB. But this is not likely to become a general solution, as R+D on these products and diseases (neglected diseases) is actually insignificant in relation to the public health needs measured, for instance, in terms of burden of disease, because of the lack of profitability and commercial incentives to invest in it. In that sense it might be worthwhile to support and learn from the experience of initiatives such as the IPTT, Initiative on Pharmaceutical Technology Transfer, a partnership created in December 2001, that aims at promoting its transfer to African countries on a non-profit basis<sup>19</sup>.

Regarding South-South technology transfer, there are a few reported initiatives – such as Thailand helping Ghana and Zimbabwe setting up factories to produce ARV, and a similar offer from Brazil to several African countries – but no evidence of success has been found so far in the literature review.

### ***Public production***

Public production of pharmaceuticals is usually discouraged as an appropriate strategy for developing industrial capacity and improving access to drugs. The cases of Lesotho and Indonesia support that

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<sup>18</sup> The TRIPS agreement explicitly states among its objectives “the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare”

<sup>19</sup> <http://www.accessmed-msf.org/documents/rio/giorgio%20Rosigno.ppt>

distrust. Public manufacturers seem to work for a while, but at the end they either become permanently dependent on public subsidies or have to be sold at a loss to the private sector. In the case of Indonesia, it is not clear how far the present financial problems of the public manufacturers reflects a failure of public management or is the result of a broader misguided policy: Whereas most drugs have unregulated prices, public manufacturers were forced to produce generics at low controlled prices.

There are nevertheless some success stories: Brazil has developed a key productive capacity in the public sector that allowed the country to make the threat of compulsory licensing credible and, as a consequence, gave it a strong negotiating capacity for obtaining low prices from patent holders. Moreover, the cost information available from public manufacturers, allows the regulator to have an appropriate empirical evidence for the purposes of price control.

Cuba is a more unusual case. "Cuba's pharmaceutical production capacity is backed by strong government support. In 1993, it was estimated that 1150 biologic and diagnostic products, as well as 30 non-prescription drugs and 132 generic products, were manufactured in Cuba. The growth of the local pharmaceutical industry, which by the mid-1990s was bringing Cuba some 100 million dollars a year in export earnings, has not only covered domestic demand for medicines, but has also led to the development of products that compete on the international market. Cuba is the only country in the world, for example, that has come up with an effective vaccine against meningitis B. The vaccine is administered free of charge to all children in Cuba, and sold to countries like Argentina, Brazil, Colombia and Mexico. With low, stable prices, China provides around 40 percent of the raw materials used by Cuba's pharmaceutical industry, although the distances involved mean transportation of the products often takes a month and a half or even longer. At present, nearly 80 percent of finished pharmaceutical products employed in Cuba are locally made"<sup>20</sup>.

#### ***Other tools to support foreign investment and domestic production***

Countries have traditionally supported domestic industry by means of high tariffs and other regulatory barriers. They have also used a broad range of fiscal and regulatory tools in order to encourage foreign manufacturers to invest in the country, for instance, tax exemptions and speeding up regulatory procedures (for instance, reducing the delay in the registration of new drugs). However, and leaving aside the questionable efficacy and efficiency of these strategies, protectionist policies are becoming increasingly difficult to apply under the present international trade trends.

### **Section 4**

#### **Case studies**

##### **The case of Bangladesh**

Before 1982 Bangladesh was heavily dependent on imports of raw materials and finished products. The local production was dominated by eight MNC that produced 75% of the value of production. The national Drug Policy enacted in 1982 created a restricted national formulary of essential drugs and banned 1666 products assumed to be useless or even harmful. Local manufacturing of formulary drugs and restrictions to imports of drugs locally produced were also enacted. Essential drug production rose from 30% to 80% of total production in value between 1981 and 1990. The market share of national companies rose from 35 to 60 percent and by 1991 the top three firms in sales were

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<sup>20</sup> Grogg, P. 2001. HEALTH-CUBA: Nearly 80 Percent of Medicines Produced Locally, InterPress Service, March 19, 2001, available at <http://www.aegis.com/news/ips/2001/IP010312.html>. Quoted by Kaplan and Laing, 2004

locally owned. Critics, however, argue that the NDP reduced foreign investment and the availability in the country of new valuable drugs.<sup>21</sup>

Bangladesh seems to have recently become a possible model or reference for developing countries that try to set up pharmaceutical production. Companies not only from India and other emerging countries, but also MNC seem to plan establishing production plants in the country, not only for formulation, but also for the production of APIs. The most topical and very important advantage of the country as far as the pharmaceutical sector is concerned is its LDS status under the TRIPS. Based on the Doha declaration, Bangladesh will be able to produce drugs until 2016, which are still under patent protection. A recent article describes the apparent success and high expectations of Bangladesh regarding the development of pharmaceutical production:

*Bangladesh, a nation currently having more than a couple of hundred manufacturing facilities with huge potential in pharmaceutical formulations, is heading on a new path of industry economics for self-reliance. Aiming at minimising the import dependency on basic drugs, the country's prime concern is about building up of own capability in the manufacturing of active pharmaceutical ingredients (APIs), base materials and other allied industry inputs.*

*With around 200 formulation plants, which include even state-of-art facilities having approval for regulated markets, the country has only two API manufacturing facilities at present. The Bangladesh pharmaceutical industry, with serious absence of bulk drug as well as engineering and other allied sector to supplement its huge requirement, depends on the imports from India, China, UK and few other European countries heavily.*

*However, the combined capacity of the industry for the pharma formulation is huge and a number of companies have recently got approval from UNICEF as its global as well as local supplier of pharma products.*

*Besides, out of the total domestic requirement of medicines almost 95 per cent is met by the local manufacturing and the country also exports formulations to 27 countries around the world.*

*According to industry sources, the formulation industry in Bangladesh currently grows at the rate of 22 per cent. With this estimate, the expected business in year 2005 is 50,000 million Tk. Today, Bangladesh is dealing with USA, India, China, Taiwan, Hong Kong, European Union, Singapore, Malaysia, Pakistan, Sri Lanka, Thailand, Burma, Bhutan, Nepal, Yemen, Mauritius, Vietnam, Kampuchea, Laos, Mexico, Columbia, Ecuador, Kuraso Russia, Uzbekistan, Tazakistan, Kenya, Tunisia, Maldives, etc. as well as with the least developing countries where there is hardly any industry for the production of pharma formulations.*

*Though the country has all the potential to become a major global source of APIs and will also be able to produce drugs, which are still under patent protection, as the TRIPS Council meet at Doha has declared the least developed country (LDC) status to remain without patent regime till 2016, it needs active participation and contribution from local as well as foreign companies to build upon the capability.*

*However, the trend now seems to be favourable to the country as the domestic pharma industry as*

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<sup>21</sup> Bangladesh pharmaceutical policy and politics, Reich, M.R. 1994. Health Policy and Planning 9(2): 135 and Chetley, A. 1993. The future of the Bangladesh national drug policy. Essential Drug Monitor 15:10-11. Quoted in Management Science in Health, Managing Drug Supply.

*well as the companies from neighbouring countries like India, China and even MNCs have queued up to put in investments on this front as every stakeholder will benefit of vast potential that Bangladesh can offer.*

*The local entrepreneurs are capable and willing to invest and collaborate with suitable foreign partners in order to develop the existing API manufacturing facilities. However, since there is strict quality awareness and the prevailing competition among the foreign supplier especially from China, the industry is still not sure about the viability of setting up own facilities for bulk and other allied products as the imports may prove economical. But the serious question concerns the industry is the reliability.*

*India, as a close business partner to the country, has been transacting with it since long and still continues to be the major trade partner in the areas of bulk drugs, pharma machinery and other allied sectors. The total pharma exports of India to Bangladesh have been increasing steadily over the years. During 1999-2000, India exported drugs to Bangladesh to the tune of Rs 934.1 million. It grew to Rs 1361.6 million in 2000-2001 and showing a further growth in current year as the first six months' exports have touched Rs 1262 million.*

*The bulk drug majors from India namely Dr Reddy's Laboratory, Sun Pharmaceuticals, Ranbaxy, Aurabindo and many others are already in advance stages of setting up bulk drug manufacturing facilities in Bangladesh, besides a large number of companies including JB Chemicals and Pharmaceuticals, Glenmark, Ajanta Pharma, Fabricare, Zydus Cadila, Cadila Pharma are trading with the country in bulk drugs in big volumes.*

*Presently top pharma companies in Bangladesh are also in the process of getting into bulk drug production with collaborative technology, technology transfers and joint venture basis. The large-scale players in the Bangladesh pharmaceutical industry currently include Square Pharma, Beximco<sup>22</sup>, Alma, Apson Chemicals, FEI, Araneta, General Pharma, Hudson Pharma and SKF among others. The MNCs that have a major presence in the country's pharma sector are Aventis, Pfizer, Novartis and Astra Zeneca.<sup>23</sup>*

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<sup>22</sup> Beximco Pharmaceuticals Ltd (BPL), the leading pharmaceutical manufacturing company in Bangladesh, is currently setting up a new formulations plant conforming to US FDA standards to meet the growing demand both at home and abroad. With this plant nearing completion, the company is getting ready to export its products to the US and the European markets.

For nearly two decades, BPL's products have been the trend-setters in the country's pharmaceutical industry. The company, which started operations in 1980 with products made under license of Bayer AG Germany; followed with the products made under license of Upjohn Inc. In 1983 BPL launched Aristovite-B, its much-acclaimed Vitamin B Complex tablet.

At present, the company holds around 16 per cent share in the domestic market, which is estimated at \$308 million. According to source in the company, while Pharmaceutical companies in many developed countries have lost their luster, the business is still highly attractive in Bangladesh.

BPL is at present an industry leader in the country as many of its products are brand leaders in their respective fields. The company produces pharmaceutical specialities of uncompromising quality. Its comprehensive range of about 80 formulations, cover all major therapeutic groups. BPL's products come in tablet, capsule, powder, liquid, cream, suppository and inhaler forms.

Beximco Pharma to export formulations to US, Europe. PHARMABIZ, Thursday, November 21, 2002 Dhaka

<sup>23</sup> C H Unnikrishnan, New pharmanomics to bridge dosage abundance with API scarcity. PHARMABIZ, Thursday, November 21, 2002 08:00 IST

The case of Bangladesh raises a paradoxical issue, namely that, thanks to the especial treatment LDCs got in Doha regarding patent enforcement, they may be in a better position to attract national foreign investment in the pharmaceutical sector, than other more industrially advanced developing countries. Of course, without the previous enforcement of its protectionist industrial policy it is unlikely that Bangladesh could have been able to take advantage of the 2016 patent exemption. This outcome might not be optimal from the point of view of global efficiency - companies are locating in Bangladesh partly as a result of a regulatory agreement, rather than a truly productive efficiency - but it can be seen as positive from the point of view of international equity, as the 2016 patent exemption might benefit LDCs not only in terms of its primary purpose - improved access to drugs - but also in terms of industrial development.

### **A second case study: the implementation of GMP in Colombia**

The introduction of GMP following the guidelines of the WHO Report 32 started in Colombia with a 1993 Decree that foresaw their enforcement within one year. The measure was initially not welcome by most national companies, which viewed it as an achievement of MNC. At that time about thirty MNC had a market share of 90% in Colombia and was starting a process of closing plants in the country and turning to imports from the headquarters. The national industry was able to lobby for several extensions of the adjustment period, which ended in 2000. About 10 companies - half of them of medium size - are supposed to have closed as a consequence of the introduction of GMP. Compliance with often GMP required large investments that companies were not able or willing to undertake. It is worth mentioning that companies did not receive any grants or soft loans in order to help them face the required investment. According to a study by FEDESARROLLO quoted above<sup>24</sup>, 10 companies that answered a survey on the costs of the investment made in order to comply with the GMP reported a total expenditure of US\$28 million, about one sixth of the annual turnover of the 10 companies.

In spite of their initial reluctance, the present view of the companies that managed to survive is that the introduction of GMP had a beneficial long term effect, as it made the national industry more competitive in relation to MNC (which market share decreased to 65% in 2003) and opened them new markets for export to neighbour countries, especially those that were not able to implement GMP, such as Venezuela and Equator. At present, some companies consider exporting even to the US and other developed markets<sup>25</sup>.

Available figures show indeed a dramatic increase of pharmaceutical exports from Colombia, from 27.1 to 248.5 million US\$ between 1991 and 2002 (see Annex 1) of which roughly 50% go to countries from the Andean Community. It is however difficult to assess how far this success can be accounted to the introduction of GMP.

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<sup>24</sup> Zuleta Jaramillo, L.A., Junca Salas, J.C. EFECTOS ECONOMICOS Y SOCIALES DE LA REGULACION SOBRE LA INDUSTRIA FARMACEUTICA COLOMBIANA: El Caso de los Estudios de Bioequivalencia y Biodisponibilidad, de los Secretos Empresariales y las Buenas Prácticas de Manufactura. FEDESARROLLO, Bogotá, Abril de 2001

<sup>25</sup> Personal communication from Mr Alberto Bravo, Executive president of ASINFAR, the Colombian Manufacturers Association that represents 36 national companies

### **Final reflections and potential topics for the debate**

The problem of high and rising prices of new drugs in the present global world, that limit their affordability to low income and disadvantaged populations is an issue of IPR and exclusive marketing rights, rather than of high manufacturing costs. It is therefore not clear how promoting or subsidising local production might help to bring the prices substantially down. This is not to say that developing and emerging countries should not try to set up and develop a domestic pharmaceutical industry to produce a substantial range of drugs of good quality at internationally competitive prices for internal consumption and for export.

In order to address the IPR-related element of high and rising prices of new drugs, other strategies are required, such as measures to promote competitive international markets and to limit or counterbalance the monopoly power and potential abuses derived from the present IPR system by means of a mix of pro-competitive interventions, regulation or by building monopsonies (e.g. pooled procurement) with a purchasing and negotiation power similar to the monopolistic power of the suppliers.

A combination of compulsory licensing, pro-competitive interventions (generic policies) and price control are probably the best way for developing countries to both improving the access of new drugs to low income populations and to promote local production. Subsidies to private production or state production should not be totally discarded, but should be seen as risky strategies restricted to special cases and situations.

Multicountry approaches are, whenever possible, desirable: the success of the "Brazilian model" is the result of political commitment and appropriate policies. But smaller countries are not likely to succeed if they try to follow the same strategies on their own. Moreover, multicountry strategies reduce the problems of intimidation and direct confrontation that might inhibit single developing countries to hold strong positions when negotiating with the US, EU or MNC.

In the long run, strategies involving the separation of the innovation (R+D) and the manufacturing markets might be the best alternative to the present system, as it would enhance world-wide competition and work at the benefit of consumers of all countries irrespective of income and industrial development and would also offer fair opportunities for efficient domestic production.



Annex 1. Pharmaceutical exports in Colombia

EXPORTACIONES SECTOR  
FARMACEUTICO

AÑO	VALOR US\$
1991	27.085.235
1992	27.199.523
1993	38.001.384
1994	37.185.293
1995	72.355.229
1996	103.554.408
1997	116.080.189
1998	125.401.627
1999	161.787.701
2000	178.054.567
2001	257.817.077
2002	248.542.858

Fuente: PROEXPORT