Local Production of Pharmaceuticals and Related Technology Transfer in Developing Countries

A series of case studies by the UNCTAD Secretariat

Intellectual Property and Trade
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UNITED NATIONS

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Abbreviations

AIDS	acquired immunodeficiency syndrome
AIM	Alternative Investment Market
API	active pharmaceutical ingredient
ARV	antiretroviral
ASEAN	Association of South-East Asian Nations
cGMP	current good manufacturing practices
CIF	cost, insurance and freight
COMESA	Common Market for Eastern and Southern Africa
CRO	contract research organization
DFID	[UK] Department for International Development
DSU	Dispute Settlement Understanding
EAC	East African Community
EMEA	European Medicines Agency
EU	European Union
FDA	Food and Drug Administration
FDI	foreign direct investment
FTA	free trade agreement
GCC	Gulf Cooperation Council
GDP	gross domestic product
GIZ	Gesellschaft für Internationale Zusammenarbeit
GMP	good manufacturing practices
GSPA-PHI	Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property
HDI	Human Development Index
HIV	human immunodeficiency virus
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICSID	International Centre for Settlement of Investment Disputes
ICT	information and communication technologies

IFC	International Finance Corporation
ICTSD	International Centre for Trade and Sustainable Development
IFPMA	International Federation of Pharmaceutical Manufacturers Association
INN	international nonproprietary name
IPRC	International Pharmaceutical Research Centre
KfW	Kreditanstalt für Wiederaufbau
LDC	least developed country
LIBOR	London interbank offered rate
MDG	Millennium Development Goal
MENA	Middle East/North Africa
MHRA	United Kingdom Medicines and Healthcare Products Regulatory Agency
NCE	new chemical entity
NDDS	new drug delivery system
NGO	nongovernmental organization
NIH	United States National Institutes of Health
OECD	Organisation for Economic Co-operation and Development
OTC	over-the-counter
PAHO	Pan American Health Organization
PCT	Patent Cooperation Treaty
PIC/S	Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme
PPP	purchasing power parity
R&D	research and development
SCI	Science Citation Index
STA	scientific and technological activities
TB	tuberculosis
TRIPS	Agreement on Trade-Related Aspects of Intellectual Property Rights
UN	United Nations

UNCTAD	United Nations Conference on Trade and Development
UNICEF	United Nations Children's Fund
UNIDO	United Nations Industrial Development Organization
USAID	United States Agency for International Development
USPTO	United States Patent and Trademark Office
VAT	value-added tax
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

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Note

UNCTAD serves as the lead entity within the United Nations Secretariat for matters related to foreign direct investment, as well as on matters related to technology transfer. UNCTAD's work is carried out through intergovernmental deliberations, research and analyses, technical assistance activities, seminars, workshops and conferences.

The countries for the case studies cover firms from Argentina, Bangladesh, Colombia, Ethiopia, Indonesia, Jordan, Thailand and Uganda. These countries were agreed with project partners WHO and ICTSD. Efforts were made to cover countries that are not widely researched in the literature concerning pharmaceutical production in developing countries and related technology transfer.

The term "country" as used in this publication refers, as appropriate, to territories or areas. The designations employed and the presentation of the material do not imply the expression of any opinion whatsoever on the part of the United Nations concerning the legal status of any country, territory, city or area, or of authorities, or concerning the delimitation of its frontiers or boundaries. In addition, the designations of country groups are intended solely for statistical or analytical convenience and do not necessarily express a judgment about the stage of development reached by a particular country or area in the development process. Reference to a company, public or private centres and national programmes and their activities should not be construed as an endorsement by UNCTAD of those institutions or their activities.

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Preface

As stakeholders in the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI) adopted by the World Health Assembly in 2008,[1] the United Nations Conference on Trade and Development (UNCTAD), the World Health Organization (WHO) and the International Centre for Trade and Sustainable Development (ICTSD) are collaborating on a project funded by the European Union (EU) to identify the main challenges and obstacles to local production in developing countries, with particular reference to technology transfer issues, and providing evidence-based recommendations on their feasibility and sustainability. As part of its contribution to this project, UNCTAD was responsible for undertaking this series of case studies designed to examine the transfer of technology and local production of pharmaceuticals in different regions, highlighting different characteristics such as firm structure, the means by which local producers obtained and developed the technological capacity to produce medicines, and the types of product handled, among others.

The case studies complement other activities of WHO and ICTSD under this project, which include a stakeholder analysis, regional dialogues and a trends survey, with a view to identifying perceived obstacles to acquiring and developing technology, enabling local production and identifying means to overcoming these obstacles.

This series of case studies also complements UNCTAD's ongoing work in the areas of technology transfer, investment and local pharmaceutical production. The case studies make an important contribution to a 2005 recommendation by UNCTAD's Commission on Investment, Technology and Related Financial Issues that:

> UNCTAD should, within its work programme on investment, technology transfer and intellectual property, assess ways in which developing countries can develop their domestic productive capability in the supply of essential drugs in cooperation with pharmaceutical companies.[2]

By giving concrete examples of successful technology transfer initiatives in the area of pharmaceutical production, the case studies provide a number of important lessons for policy-makers and other stakeholders in both developing and developed countries on issues of investment, science, technology and innovation, and intellectual property rights.

Dr. Supachai Panitchpakdi
Secretary-General of UNCTAD

1 World Health Assembly Resolution WHA61.21. Geneva, World Health Organization, 2008.

2 Para. 9(c) of the 2005 Agreed Recommendations. See http://www.unctad.org/en/docs/c2l22_en.pdf.

Overview:
The local production of pharmaceuticals and related technology transfer: An overview of eight country case studies

This series of case studies on local pharmaceutical production and related technology transfer in Argentina, Bangladesh, Colombia, Ethiopia, Indonesia, Jordan, Thailand and Uganda was undertaken by the Intellectual Property Unit in UNCTAD's Division on Investment and Enterprise, Investment Capacity-Building Branch.

1. Introduction

Local production of pharmaceuticals and vaccines has been a subject of intense discussion in international, regional and national forums since the 1970s.[1] A variety of interests – economic, legal and political economy oriented – have been responsible for varied, often contradictory, perspectives on what constitutes local production and whether or not it should be fostered. The past decade has seen a stronger emphasis on issues of local production, technology transfer and access to medicines. The need to harmonize some perceptions on the topic led to critical international developments on the topic. Most significantly, WHO Resolution WHA 61.21 on a Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI), adopted in 2008, outlines a new focus on local production as a means of contributing to the overall goals of promoting innovation, building capacity and improving access.[2]

Against this backdrop, WHO and the European Union (EU) conceptualized and launched a project on local production and technology transfer entitled Improving Access to Medicines in Developing Countries through Technology Transfer Related to Medical Products and Local Production. The agreed objective was to identify the main challenges and obstacles to local production of pharmaceuticals, vaccines and diagnostics relevant to public health needs of developing countries, and related transfer of technology, and to provide evidence-based recommendations based on their feasibility and sustainability. The underlying premise was to delve deep into this highly complex interface of technology transfer and local production in developing countries, with a view to understanding the conditions under which such local production and related transfer of technology could lead to improved access.

1 The subject of local production appeared in WHO as part of the Report of the International Conference on Primary Health Care (Para. 93), and in Resolution WHA 31.32 (1978).

2 Element 3 of GSPA-PHI, on building and improving innovative capacity, highlights key areas for investment including capacities related to science and technology, local production of pharmaceuticals, clinical trials, regulation, intellectual property and traditional medicines. Element 4 of GSPA-PHI, on transfer of technology, emphasizes north–south and south–south development cooperation, partnerships and networks to build and improve transfer of technology related to health innovation.

This compendium of country-based case studies on local production focuses on bringing to light newer, lesser-known and lesser-researched cases of successful local production and related technology transfer in the field. Chosen with a view to shed light on the ways and means in which countries and firms build capacity in a newer range of developing countries and least developed countries (LDCs), the case studies enhance our understanding of how complex firm-level, country-specific and international political economy-oriented factors interact towards building capacity in pharmaceutical enterprises in countries.

2. Selection of countries and firms

A survey of emerging trends and data on local production emerging in the field indicates that the global landscape of medical products manufacturing industry is changing. Although India, China and Brazil have been and continue to be significant producers and suppliers of cheaper medicines that presently serve the needs of their local markets and much of the developing world, the pharmaceutical sectors in these countries are transforming. New empirical work shows that as firms expand and compete in the global economy, their product portfolios are becoming more geared towards the more stringently regulated markets in industrialized countries.[3] Mergers and acquisitions of firms in these countries with global pharmaceutical firms,[4] and other international political economy factors, such as India's free trade agreement with the EU, are all crucial in determining the future potential of generics drug production in these countries. Such changing market dynamics are not only evident in the case of pharmaceutical products but also equally relevant for vaccines and diagnostics. As companies in these countries transform, other options are required to ensure a steady supply of essential medicines, vaccines and diagnostics to poor populations in developing countries and LDCs.

Newer firms and sectors in a newer range of developing countries and LDCs are showing some potential to move up the technological ladder to capture some of these production spaces and cater to greater access to medicines. However, capacity in these countries is diverse and anathema to generalizations. It is against this backdrop that the eight case studies were chosen under Phase 1 of the project specifically to capture these variations, ranging from simple inputs along the value chain (hard gelatin capsules in Ethiopia), to over-the-counter drugs in Colombia, to a wide range of generic drugs in Bangladesh and Indonesia, to more complex formulations such as antiretrovirals (ARVs) in Uganda, and to more advanced research and innovation in countries such as Argentina and Jordan. A case study method substantiated by semi-structured questionnaires that were used to elicit firm-level data was chosen as the appropriate methodology for this exercise, given the need to improve our understanding of how local firms produce and innovate in this sector, and

3 Chaudhuri (2007) and Gehl Sampath (2008) note this in the context of India, while Vidotti et al. (2008) present data of products being introduced in Brazil to make the same point.

4 The past 3 years have seen mergers between seven large local Indian companies with multinational companies. See Government of India, discussion paper on compulsory Licensing, 24 August 2010, on file with author.

what factors impede or facilitate the transfer and absorption of technology at the firm level. Within this approach, although the individual firm was the focus of the analysis, country-specific factors, such as the national framework for science, technology and innovation, intellectual property laws, the investment climate, and the ability of firms in the country to absorb and use technologies for production and innovation, were all analysed from the perspective of the individual firm.

The selection of countries and firms presented reflects the variety of means by which technological capacity has been transferred to developing countries and LDCs that undertake to manufacture pharmaceutical products. When choosing the firms for the case studies, due regard was given to these countries' specific situations and geographical considerations, without prejudice to any one model of industrial development, health-care system or related policies. Four key models of technology transfer for local pharmaceutical manufacture guided our choices, based not only on the literature on technology transfer but also on the plethora of evidence available on how countries have fostered the emergence of the pharmaceutical sector in the south. Although firms and sectors mostly emerge in an environment that cannot easily be categorized into a specific model (for example, south–south transfer can be complemented by north–south transfer, or both of these models of technology transfer are often most successful in an environment where the state is actively engaged in building local production capacity), the firms were chosen to represent each one of the four models, in order to understand the dynamics of technology transfer and local production more closely.

2.1 South–south transfer of technology related to local production of pharmaceuticals

This model examines cases where a developing country firm has opted to transfer technology to manufacture finished pharmaceutical products in an LDC. Many of the countries that fit into this model seek to take advantage of the fact that they are not obliged to offer patent protection on pharmaceutical products as required by the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) until 2016, and therefore would be able to offer a base for manufacturing generic versions of drugs that are patent-protected in certain non-LDC countries. As LDCs, however, they nonetheless face numerous constraints in establishing viable local production facilities that meet quality standards. As part of this category, case studies were undertaken in Bangladesh, Ethiopia and Uganda.

Bangladesh, through the assistance of Indian and other foreign producers, has established itself as a major manufacturer and exporter of pharmaceutical formulations and is on its way to take advantage of its LDC status to manufacture active pharmaceutical ingredients (APIs) for, inter alia, antibiotics, among other drugs. Bangladesh provides a good illustration of how firms in an LDC have been able to thrive in this complex sector by concentrating their businesses on key inputs along the pharmaceutical production process.

Ethiopia presents an example of an LDC where an active effort is made by the government to strategically target foreign investment in the pharmaceutical industry, and where local firms are producing medicaments including antimalarials and intravenous infusions, and related pharmaceutical products such as hard gelatin capsules. The latter are produced under a Chinese–Ethiopian joint venture, Sino-Ethiop Associate (Africa) Private Limited Company. Sino-Ethiop recently received international good manufacturing practice (GMP) certification for its hard gelatin capsules; it exports to African and Middle Eastern countries, and sells its capsules in the local market. Ethiopia in general and Sino-Ethiop in particular have benefited from a German Government initiative, Bundesministerium für wirtschaftliche Zusammenarbeit und Entwicklung (BMZ)/Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) to encourage the local production of pharmaceutical products. The BMZ/GIZ initiative provides factory-level support to firms to help ensure viable and sustainable pharmaceutical production.

Uganda presents an archetypical example of an LDC where the government has actively supported a specific deal with a major developing country manufacturer to establish a joint venture in the country that would produce high-quality, low-cost ARVs and antimalarials for the east Africa region. Quality Chemicals Industries Limited is a joint venture between India generic manufacturer Cipla and Ugandan local firm Quality Chemicals Limited. The Quality Chemicals joint venture provides a very interesting case of how technology and related tacit know-how have been transferred to support sustainable local production of ARVs and antimalarial medicines, and shows the set of incentives offered to encourage Cipla to choose Uganda and the local firm with which it partnered. The Quality Chemicals joint venture received a significant amount of technology transfer from Cipla as part of the deal.

2.2 North–south transfer of technology related to local production of pharmaceuticals

This case study examines examples where a large research and development (R&D)-based pharmaceutical firm in a developed country has established factory facilities to manufacture pharmaceutical products in a developing country. Such firms typically produce a portfolio of medicaments covering a number of products, the patent for which is held by their parent company, through licences that include the terms for technology transfer. The dynamics and drivers of the foreign investment by these firms in developing countries can be compared and contrasted with the dynamics and drivers of the foreign investment of the developing country generic manufacturers that decided to locate manufacturing facilities abroad.

A case study following this pattern was undertaken in Indonesia, a country representing this model from the point of view of parent companies based in developed countries such as those in western Europe, the United States of America and Japan. Several Japanese R&D-based pharmaceutical firms established factories in Indonesia in the 1970s. These include PT Takeda Indonesia (Takeda), PT Eisai Indonesia (Eisai), PT Tanabe Indonesia (Mitsubishi

Tanabe Pharmaceuticals), PT Otsuka Indonesia (Otsuka) and PT Meiji Indonesia (Meiji). These companies generally produce for the domestic market or export to other Asian countries, including other Members of the Association of South-East Asian Nations (ASEAN). The operating environment for local production, in so far as foreign R&D-based firms are concerned, could be considered unique and worth examining, because in late 2008 the Ministry of Health introduced regulations requiring drug companies to establish production facilities in Indonesia as a condition for obtaining marketing approval for their products in that country, subject to specific conditions.

2.3 State-supported creation of domestic technological capacities related to production of pharmaceuticals

Under this model, local pharmaceutical production is directly supported by the government, usually through allocation of state budget or subsidy to a state-owned enterprise with its own R&D facilities. The Government Pharmaceutical Organization of Thailand has strong R&D capabilities in a number of areas (including ARVs and vaccines) and out-licenses its technology; it has not, to date, exported any of its products.

Direct government support of local production illustrates strong strategic interests in all countries that have historically done so, a main one of which has been the promotion of access to medicines, often followed closely by industrial policy concerns. In the area of vaccines, the Thai Government has in recent years begun to place increasing focus on domestic vaccine development and production. Driven by concerns about timely vaccine access in the wake of the avian influenza outbreaks and the H1N1 pandemic influenza situation, as well as the higher prices of newer vaccines such as that for human papilloma virus (HPV), the stated policy objective is to strengthen the country's preparedness against vaccine-preventable diseases and reduce spending on imported vaccines. As stated by the then Public Health Minister, Witthaya Kaewparadai, "[V]accine development is a national agenda ... [its] direction ... in the long term must be addressed by the Government... If we could develop vaccines by ourselves, that would mean standing on our own feet and no longer depending on other countries for imported vaccine" (Sarnsamak, 2009).

2.4 Creation by the local private sector of domestic technological capacities related to production of pharmaceuticals

In some developing countries, local pharmaceutical manufacturers have established themselves without much state support or foreign investment from large multinational R&D-based firms or large transnational generic manufacturers. These enterprises often start out by manufacturing off-patent drugs and scale up by obtaining licences to manufacture other products or otherwise partnering with large, international R&D-based manufacturers. Argentina, Colombia and Jordan were chosen as the countries for case studies under this category.

Argentina has a very significant pharmaceutical market.[5] In Argentina, immigrant businesspeople from Europe in the first half of the twentieth century founded the first wave of small family-run pharmaceutical firms that still play a significant role today, such as Roemmers, Bago, Roux Ocefa, Andromaco, Gador, Casasco, Baliarda, Beta, Temis Lostalo and Phoenix. The case study examines one such company, ELEA. In contrast, most multinational companies arrived in Argentina during the 1950s, when the country's authorities stimulated foreign investments to industrialize Argentina. Local subsidiaries of foreign R&D-based pharmaceuticals such as Pfizer, Abbott, Glaxo Welcome, SmithKline Beecham, Bayer, Boehringer Ingelheim, Aventis, Novartis, Merck, Sharp & Dohme, AstraZeneca, Schering Plough, Wyeth and Bristol-Myers Squibb bought local factories to establish their operations, although it appears that some of these factories have been bought back by local firms. In the past few decades, both local and multinational companies have thus competed with each other for their share of the market. None of the foreign subsidiaries appears, however, to have displaced Argentine firms such as Roemmers, Bago or ELEA in terms of total market share.

In Colombia, many pharmaceutical firms acquired initial technological capacity in pharmaceutical production through licensing agreements with multinational pharmaceutical companies. Locals firms used this initial expertise to develop other avenues of technological learning after the termination of most of the licensing agreements with multinational companies. Domestic firms now source know-how and technology from foreign suppliers of APIs, consultants and former employees of multinational firms. Some firms, such as Tecnoquímicas, which is the subject of the case study on Colombia, benefit from a well-developed cooperation network with Colombian universities and research centres. API and equipment suppliers also provide advice on plant design, processes and formulations.

Jordan is increasingly becoming a major site for production of pharmaceuticals in the Middle East and North Africa region. Jordan's local pharmaceutical companies produce locally and dominate the local market for branded generics. The case study for Jordan examines one such company, Jordan Pharmaceutical Manufacturing Co., PLC. This market coexists with a market for on-patent, imported drugs from the large international R&D-based pharmaceutical companies, which distribute in Jordan through local companies but do not manufacture in the country.[6]

3. Key results and their wider applicability

The case studies and the data generated therein complement the other outputs of the project in Phase 1. Their key results are classified into three

5 For example, in 2009, sales in the Argentine pharmaceutical market totalled US$ 3.846 billion. See WHO et al. (2011).

6 Several other countries, such as Brazil, China and India, are often cited as examples of countries that have been able to develop significant capacity to produce medicines (including ARVs and vaccines) through this particular model. These countries were not chosen in this case because of the extensive attention they have already received by academics, policy advocates and investment agencies.

main categories, namely those on local production, on the role of transfer of technology in making local production possible, and on the impact of local production and related technology transfer on access to medicines. The results generated, as supported through other literature on the topic, not only show that there are other countries on the global horizon with an expanding ability to locally produce pharmaceuticals and diagnostics, but also point our attention to the fact that channelling these expanding capabilities to promote the case of access to medicines in the developing world calls for greater policy coherence between industrial policy and public health.

3.1 Local production is feasible in developing countries and least developed countries

Case studies in Argentina, Bangladesh, Indonesia and Jordan show clearly that a second tier of countries such as these are well poised to take on the role of supplying cheaper medical products to poor people across the developing world. Firms in these countries have attained the economies of scale required to produce drugs competitively and will expand over the next decade. For example:

- The Argentina case study shows that local firms control over 60% of the total market, providing stiff competition to foreign firms in the country. Some firms have attained a level of sophistication and technical capacity that contributes to greater access to medicines through development of new medicines and vaccines locally. The new focus by ELEA on anticancer and influenza vaccines represents a first step in longer-term efforts to establish the firm's capacity in this important area.
- Similarly, in Bangladesh, Beximco Pharmaceuticals Limited and Square Pharmaceuticals Ltd are among the largest pharmaceutical companies in terms of capital and market share. Both companies produce and supply to more than 30% of the total local market and are fast expanding into export markets.
- PT Eisai Indonesia is the subsidiary of Eisai Co., Ltd., a major Japanese R&D-based pharmaceutical firm, and its activities are representative of the general expanding trend in the market, where local manufactures now control and supply to over 70% of the local market. This is a large step ahead from the early 1990s, when multinationals held a dominant share of the market.

The case studies, supported through other literature, also show that there are other countries on the horizon where, although there is no extensive capacity to produce, the firms are growing and expanding their production activities. In these countries, the case studies show that firms tend to often focus on niche products and markets, such as in Ethiopia, where the firm produced hard gelatin capsules, and in Uganda, where the firm focused exclusively on drugs for human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) and malaria.

3.2 Technology transfer has been an important factor in making production feasible and competitive

Access to technology has played a critical role in local production. Of the countries studied, those that demonstrated the most advanced levels of production had absorptive capacity (human skills and scientific infrastructure) that was strengthened consistently through technology transfer throughout their growth and expansion.

The two companies that are the subject of the case study on Bangladesh have their roots in private-sector initiatives of Bangladeshi entrepreneurs who built their capacity at an early stage through technical collaboration and licensing arrangements with multinational pharmaceutical companies. In the case of Indonesia, in the 40 years of existence of the firm PT Eisai, technology transfer from parent to subsidiary company has occurred through detailed manuals, recipes, training and ongoing communication by the subsidiary with the parent. The result has been a state-of-the-art facility. The Jordan Pharmaceutical Manufacturing Company, established in 1978, built its technological capacity initially from multinational corporations and used Jordanians with technical and managerial expertise acquired abroad. Subsequently, it tapped a highly educated workforce with good manufacturing and technical experiences. It now produces 184 products. In countries where local production has been a more recent phenomenon, such as Uganda and Ethiopia, technology transfer has been critical.

Technology transfer continues to support the firms to expand into new product categories for both local consumption and exports in the following ways:

- Expanding export markets and product portfolios: For example, the Argentine company ELEA is currently negotiating an R&D and technology transfer agreement with Novartis for developing a vaccine against influenza, and has in place agreements with domestic universities and an R&D centre in Cuba for the development of anticancer vaccines.
- Meeting quality standards needed for export markets: For instance, in the case of Uganda, Cipla is supplying the technological know-how required to obtain WHO prequalification for the ARVs being manufactured.
- Technology transfer for API production helps to increase the competitiveness of local production initiatives for drugs. The cases of Bangladesh, Uganda, Argentina and Jordan all demonstrate this to various degrees.

However, the project outputs thus far also show, in the case of both pharmaceuticals and vaccines, that these trends in technology transfer may be changing in two important ways. First, sectors and firms that had relatively successful experiences in technology transfer that led to the establishment of production capacity are witnessing a gradual decline in such collaborations, as the cases of Argentina, Colombia and Bangladesh show. A second and related result is that the demand for technology and related know-how varied largely between those countries that are currently well equipped to produce medical products and countries that are currently lagging behind. This raises issues of what constitutes successful technology transfer, how to best articulate its

components, and what an enabling technology transfer environment may look like in this sector.

3.3 Local production may promotes access to medicines

The case studies show that there are at least four ways in which local production occurs in developing and least developed countries and how it impacts on access to medicines.

First, local production may increase price-based competition in the market, contributing to ensuring lower prices of drugs and greater affordability. In a number of case studies, the firms are engaged in the production of generic equivalents of originator pharmaceuticals patented elsewhere. While some foreign generic producers, especially those from India and China, still offer the lowest prices worldwide, the present case studies illustrate that a mere comparison of prices charged by local generic producers and foreign generic suppliers frames the picture incorrectly. Foreign generic suppliers in their quest for new markets often benefit from some form of cooperation with established local producers, opening up interesting business opportunities that would not exist to the same extent without the involvement of local firms. This often concerns local distribution networks, but also other factors. In Uganda, for example, an Indian investor is benefiting from generous government support for the provision of technology transfer to the local partner company. In Ethiopia, a Chinese investor is taking advantage of the proximity of local production sites to African markets. In Latin America, foreign generic producers play a more limited role, due to the comparable strength of the local industry, with well-established distribution networks and university partnerships in pharmaceutical and vaccines R&D, and due to language and other cultural barriers. Indian and Chinese companies are nevertheless an important source of active pharmaceutical ingredients purchased and formulated by Latin American firms, thereby combining the strengths of the foreign suppliers (i.e. competitive prices of key ingredients) and local manufacturers (i.e. established distribution networks and familiarity with local needs and conditions).

Second, local production may in the future fill an important gap for developing country needs in case Indian generic companies continue to shift their focus to developed country markets and needs. With improved production and R&D capacities, Indian firms have started targeting more affluent markets and their specific disease patterns. Local producers in less advanced developing countries and in LDCs do not have comparable capacity and therefore continue focusing on incremental innovations in generics of existing drugs. Firms in all the case studies catered to specific developing country health needs by producing drugs that were needed in local contexts. This included antibiotics, anti-infectives, vaccines, drugs to treat malaria and ARVs. Firms in Bangladesh, Argentina, Indonesia and Uganda were producing ARVs and antimalarials. Firms in Bangladesh were beginning to venture into vaccines for rabies, typhoid, tetanus and polio, whereas Indonesian firms were specifically engaged in producing vaccines and heat-resistant ARVs. The firms in Jordan

and Argentina were rapidly expanding into product categories (including diagnostics), which resulted in incremental adaptations and improvements to existing products.

Third, local firms in more advanced developing countries are not limited to incremental innovation, but also produce new products that meet both local and international needs. Firms in developing countries that supply such products profit from the large demand and associated economies of scale. Examples of such cases and promising initiatives include the current undertaking by the Argentine firm ELEA of phase III clinical trials on anticancer vaccines and ELEA's cooperation with Novartis on the envisaged local production in Argentina of influenza vaccines. Among the companies included in the case studies, several firms are producing such new drugs. The Bangladesh firm Beximco, for example, is engaged in production of chlorofluorocarbon (CFC) inhalers, which it also supplies to global procurement agencies.

Fourth, efficient and widespread distribution networks and pharmaceutical supply chains controlled by many local companies by definition enhance access by developing country populations, especially in rural areas. But the existence of distribution networks and pharmaceutical supply chains is also a starting point for the development of formulation capabilities in countries and expansion into other niche areas. For instance, Quality Chemicals, a Ugandan firm producing ARVs, was a distributor for Cipla's medicinal products and has extensive distribution networks in rural Uganda. Similarly, most local companies were adept at using context-relevant strengths for distributing their products and in creating newer modes of distribution for their medicinal products. Historical narratives of the pharmaceutical sector show that most pharmaceutical firms in developing countries, including those in Bangladesh, Kenya and India, are all offshoots of distribution companies to a certain extent.

In addition to the relevance of local production to access to medicines, it is obvious that local production may make important contributions to a country's industrial development, including the creation of jobs in highly relevant areas of technology.

4. Concluding remarks

In sum, the results of the case studies show that the conditions under which technology transfer results in strengthening local production, and the ways and means in which this promotes greater access to medicines, are highly complex. While helping to bring out the relevance of these parameters, these important results on local production and access to medicines lead us to push the boundaries of our understanding. Although access to medicines is being enhanced through local production, the project and its results suggest that a coherent framework that links local production to greater access from the onset within countries is urgently called for to harness the full potential of local production capacities. Improvement in access to medicines in the context of local production should not be incidental but should be an explicit goal.

The results of the case studies show that such an institutional and policy framework includes (but may not be restricted to):

- a systematic assessment of national and regional public health needs with reference to local production of medical products with a view to generating information on the market viability and public health considerations;
- the ability of countries to create a threshold of absorptive capacity (in terms of availability of human skills to engage in production, management and marketing, and relevant scientific and physical infrastructure);
- a favourable policy framework that promotes domestic and foreign investment into production of medicaments and technology transfer;
- a rational intellectual property rights regime that explores flexibilities; and
- policies and mechanisms to promote access to locally produced medicines.

References

Chaudhuri S. *Is product patent protection necessary in developing countries for innovation? R&D by the Indian pharmaceutical companies after TRIPS*. Working paper no. 614. Calcutta, Indian Institute of Management, 2007.

Gehl Sampath P. *India's product patent compliance: Emerging strategies for global and local access to medicines.* London, Department for International Development, 2008.

Sarnsamak P. Push to revive Thailand's vaccine industry. *The Nation,* 14 August 2009 (http://www.nationmultimedia.com/2009/08/14/national/national_30109761.php).

Vidotti CCF et al. New drugs in Brazil: Do they meet Brazilian public health needs? *Revista Panamericana de Salud Publica*, 2008, 24:36–45.

Case study 1

Argentina

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Abbreviations

ACTH	corticotropin
ANMAT	Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (Drugs, Food and Medical Devices National Administration)
ANPCyT	Agencia Nacional de Promoción Científica y Tecnológica (Scientific and Technological Promotion National Agency)
CILFA	Cámara Industrial de Laboratorios Farmacéuticos Argentinos
ELEA	Laboratorio Elea S.A.C.I.F. y A.
FONARSEC	Fondo Sectorial Argentino (Argentine Sectoral Fund)
FONCYT	Fondo para la Investigación Científica y Tecnológica (Scientific and Technological Research Fund)
FONTAR	Fondo Tecnológico Argentino (Argentine Technology Fund)
GAD	glutamic acid decarboxylase
G-CSF	human granulocyte-colony stimulating factor, recombinant
GYM	GyM S.A. (originally Golosinas y Medicamentos)
hCG	human chorionic gonadotrophin
hMG	human menopausal gonadotrophin
HTS	Harmonized Tariff System (Mercosur)
INDEC	Instituto Nacional de Estadística y Censos (Statistics and Census National Institute)
INPI	Instituto Nacional de la Propiedad Industrial (Industrial Property National Institute)
LHRH	luteinizing hormone-releasing hormone
MCN	Nomenclatura Común del Mercosur (Mercosur Common Nomenclature)
MINCyT	Ministerio de Ciencia y Tecnología (Science and Technology Ministry)
PIC/S	Pharmaceutical Inspection Convention and the Pharmaceutical Co-operation Scheme
PMSG	serum gonadotrophin
SPPS	solid-phase peptide synthesis
TRH	thyrotrophin-releasing hormone
UBA	University of Buenos Aires
UNQ	Quilmes National University

1. Background and methodology

This case study was designed to investigate the high prevalence of domestic pharmaceutical companies in Argentina, the source of their technology, the factors behind their sustainability, and the issues that local companies currently face. Specifically, this case study examines the technological innovation strategy of a large Argentine pharmaceutical company through its research and development (R&D) efforts; the transfer of technology from multinational R&D-based firms to local firms in Argentina; and strategic alliances with public universities and R&D institutions, including South–South cooperation.

UNCTAD thanks Laboratorio Elea S.A.C.I.F. y A. (ELEA) for agreeing to be the subject firm for this case study.

A case study research methodology was used in this study. Data were collected from academic literature and policy documents and through open-ended, face-to-face interviews with individuals in Argentina. Interviewees were identified through purposive sampling. For the preparation of this case study, 18 people from various sectors of the pharmaceutical industry were interviewed, including 10 pharmaceutical experts (affiliated with Laboratorios Beta, Roemmers, Raffo, ELEA, Cámara Industrial de Laboratorios Farmacéuticos Argentinos (CILFA), Gador, Tecnofarma and Chemo); 5 government representatives (from Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (Drugs, Food and Medical Devices National Administration; ANMAT), Ministerio de Ciencia, Tecnología e Innovación Productiva (Science and Technology Ministry; MINCyT), and Instituto Nacional de la Propiedad Industrial (National Industrial Property Institute; INPI); 2 university representatives (from the Pharmacy and Biochemistry School of the University of Buenos Aires and Quilmes National University; UNQ); and 1 representative of Fundación Mundo Sano, a nongovernmental organization (NGO).[1]

In addition, a semi-structured questionnaire designed to capture the dynamics of firm-level activities related to production and technology transfer was administered to the above-listed firms, the results of which are included in the case study where relevant.[2]

This case study defines innovation as any new product, process or organizational change that is new to the enterprise, context and country in question. The innovation need not be novel to the world at large (UNCTAD, 2007). In keeping with the scope of the project, technology transfer is defined as all components of technology, both codified (such as blueprints, hardware, machine parts and plant technologies) and tacit (such as know-how and skills), that are essential to enhance the capacity of the organizations in the recipient country to produce pharmaceutical products.[3]

1 See Annex: Interviewed individuals and institutions.

2 See Annex: Field questionnaire.

3 A uniform definition of technology transfer was used for all components of the project, including the trends survey, the regional dialogues and the stakeholder analysis.

2. Description of the firm, structure and range of products

ELEA is an Argentine laboratory located in the city of Buenos Aires. It was founded in 1939 under the name Argentine Endocrine Laboratory. In 1973, the company converted to a public limited corporation and changed its name to ELEA. The shares of ELEA have been held by the Gold, Sielecki and Sigman families since the 1990s; none of the ELEA shares are publicly traded. These three families possess extensive experience in the pharmaceutical sector, including more than 60 years of management experience gained after founding other laboratories.[4]

In 2003, ELEA merged with GyM S.A. (GYM), another laboratory controlled by the same shareholders. GYM had served as the Warner Lambert Company's (Warner Lambert)[5] licensee for the complete Parke Davis line of products in Argentina since 1989. After the merger, ELEA assumed the role of Warner Lambert's licensee, a role it continues to fill. ELEA also possesses licences to commercialize products made by Chiron Corporation (vaccines) and Novo Nordisk (hormone therapy), and a promotion agreement with Novartis for its line of transdermal patches in hormone therapy.

In 2003, ELEA's sales ranked seventh out of all domestic and multinational laboratories operating in Argentina. By 2009, ELEA held 3.8% of the market and reported sales of US$ 145.5 million. ELEA also improved its ranking two spots and moved up to the fifth position, behind Roemmers, Bagó, Bayer and IVAX.[6] Compared with other domestic laboratories, ELEA ranked third.

ELEA's main market is the domestic one. In 2009, ELEA exported US$ 4.6 million of pharmaceutical drugs, which represents only 0.6% of Argentina's total exports of finished pharmaceutical products. But ELEA exports its products to diverse destinations, including Azerbaijan, Bolivia, Brazil, Chile, Colombia, Dominican Republic, Ecuador, Guatemala, Lebanon, Mexico, Panama, Peru, Spain, Switzerland, United Arab Emirates, Uruguay, Turkey, Turkmenistan and Vietnam.

ELEA operates one manufacturing facility in the city of Buenos Aires. This plant produces solid, semi-solid and liquid formulations, but it specializes in liquid solutions. It is one of the most sophisticated pharmaceutical facilities in Latin America. The facility has the capacity to annually produce 50 million tablets, 50 million capsules, 109 tons of semi-solids (29 million suppositories and 1.2

4 The Gold family founded and managed Chemotécnica Syntial. In 1997, the then GD Searle (now Pfizer) purchased Chemotécnica Syntial's pharmaceutical division. The Sielecki family founded and managed Laboratorio Phoenix, which the family sold to GlaxoSmithKline in June 2010 (see http://www.gsk.com/media/pressreleases/2010/2010_pressrelease_10053.htm).

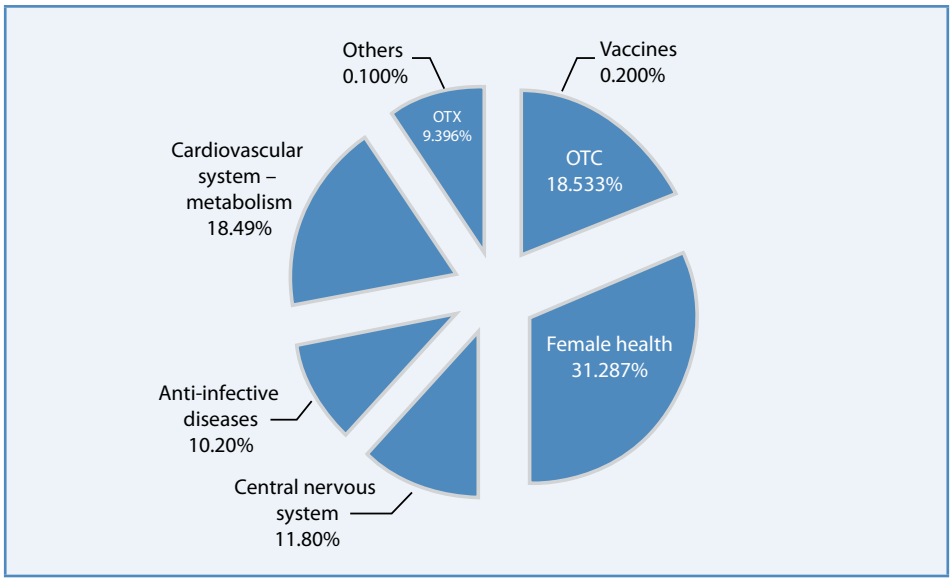
5 Pfizer acquired Warner-Lambert Company in 2000. Thus, ELEA's licensor is Pfizer (see http://www.pfizer.com/about/history/pfizer_warner_lambert.jsp).

6 ELEA is ranked first in the sale of statins (11.1% of the market share), bisphosphonate bone calcium regulators (28.5%), antiepileptics (20%), laxatives (21.6%), antihistamines (18.8 %), antacids (86.4%), and antipruritics (80.9%). Furthermore, ELEA is second in sales of hormone replacement therapy (21.3%) and hormonal contraceptives (22.2%). Source: ELEA.

million ointments), 800 m^3 of solutions, and packaging for 16 million units. A Uruguayan company related to ELEA also operates a second plant in Uruguay for the production of specific hormonal and contraceptive medications.

ELEA's current portfolio is very diverse: it consists of 120 products and is available in 286 different presentations. The drugs cover a wide range of therapeutic areas, such as (i) a female health line, with a focus on osteoporosis, contraceptives and hormone replacement therapy; (ii) a cardiovascular line, consisting mainly of lipid-reducing agents, antihypertensives, potassium-sparing products, antiplatelet therapies and oral antidiabetic therapies; (iii) a neuroscience and psychiatric line, including antiepileptic, antidepressant and antipsychotic products; (iv) vaccines, including antimeningococcal polysaccharide (B+C) vaccines and hepatitis B vaccines; (v) an anti-infective and medical clinic line, including antibiotics and antivirals, anti-inflammatories, analgesics, antacids, antihistamines and antihaemorrhoidal products; (vi) antiretroviral medications for human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS);[7] and (vii) over-the-counter products, such as laxatives, dermatological products, pregnancy tests and antacids. The composition of sales by product line is shown in Figure 1.

***Figure 1** Breakdown of ELEA's sales*



Source: ELEA.

Hugo Sigman, an Argentine businessman and one of ELEA's shareholders, is also a partner of the Chemo Group. Chemo Group is a company located in Madrid, Spain that owns and operates chemical plants for the manufacture of active pharmaceutical ingredients (APIs) in Spain, Italy and China. This relationship has afforded ELEA access to high-quality information related to new therapeutics and generics, and provided a reliable source for the supply of raw materials and technical assistance.

7 Antiretroviral medications for HIV/AIDS include lamivudine, efavirenz, tenofovir and abacavir.

ELEA distributes its pharmaceutical products through Disprofarma S.A. Disprofarma was founded in 1978 and provides overall logistics in the sale and distribution of pharmaceutical products throughout Argentina, including storage, sale, invoicing, distribution and collection of payments. Disprofarma has 40% of the market share in this area and is the largest pharmaceutical distributor in Argentina.

Some of ELEA's shareholders are also shareholders of the group that controls Disprofarma, affording ELEA a level of vertical integration that allows the company to focus on its core business and become increasingly more efficient. Other laboratories, domestic and multinational, have also followed this model, vertically integrating with other companies in the supply chain that specialize in the distribution of pharmaceutical products.

3. ELEA's technological capacity

ELEA's facilities are designed to manufacture a wide range of products, from solids to semi-solids to liquids.[8] ELEA's facilities comply with good manufacturing practices (GMPs) mandated by the Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (Drugs, Food and Medical Devices National Administration; ANMAT) and the company has made continuous improvements to its infrastructure over the past 20 years. In the past 5 years, ELEA has invested heavily in new capital equipment, production systems, and information and communication technologies (ICT). ELEA's production lies between 71% and 90% of its total capacity, a volume that permits efficient operation of the plants.

ELEA operates highly advanced production machinery. Local industry supplied ELEA with 47.3% of its production machinery and related components. Concerning production inputs, ELEA acquired 26.8% domestically. ELEA purchased 12.6% of APIs and bulk drugs domestically in 2009. The percentage of raw materials imported by ELEA is consistent with the rest of the Argentine pharmaceutical industry and demonstrates a high dependency on imported inputs. Like many other domestic manufacturers (see Section 4), ELEA does not produce APIs but formulates them into finished products and then distributes these finished products.

ELEA employs 817 individuals, of which 10.3% are skilled workers, such as chemists and engineers. Research and development (R&D) staff comprise 1% of the company's workforce. According to company officials, ELEA's technical staff are very highly qualified.

ELEA's strategic alliances and ability to reverse-engineer many products serve as the company's main sources of technology. Furthermore, ELEA obtains significant amounts of technology from the following sources, listed in order of importance: managers and skilled employees, equipment and component

8 The following information is based on the field interview with ELEA.

suppliers, universities and public research institutes, government agencies, and technical assistance providers.

ELEA's current technological capacity principally comes from three different areas: know-how generated over time by the company's R&D unit, particularly with regard to hormonal and biological products; knowledge transferred to the company vis-à-vis its licensing agreement with the Warner Lambert Company; and strategic alliances with universities and public research centres in Argentina and Cuba. Additionally, the company is currently negotiating with Novartis the transfer of technology for the manufacture of vaccines. This agreement is expected to greatly increase ELEA's technological capacity in this area.

3.1 In-house research and development

The first source of technical capacity is the know-how that ELEA's R&D unit has generated over time. Since its founding in 1939 as the Argentine Endocrine Laboratory, the company has been deeply involved in endocrinology, particularly in protein and steroidal hormones. The company has been a pioneer in the Argentine market, manufacturing human chorionic gonadotrophin (hCG) and corticotropin (ACTH) when these products began to appear on the international market. In the 1940s, the company built a facility for performing tests on mice and other laboratory animals, which was used for product development and quality control tests. This facility, which uses numerous species of animals, was a major supplier of test results to the most important R&D facilities in the country.

The company's experience with extractive methods, purification and biological control positioned it as the world's main producer of serum gonadotrophin (PMSG). Later, the company produced human menopausal gonadotrophin (hMG). In the 1970s, ELEA worked closely with the Argentine national regulatory authority to develop and establish the First National Standard for hCG, PMSG and hMG. Also in the 1970s, the company began to synthesize neurohormones, such as the thyrotrophin-releasing hormone (TRH) and the luteinizing hormone-releasing hormone (LHRH), by means of solid-phase peptide synthesis (SPPS).

The company possessed significant know-how regarding the handling of proteins, characterized by the strong correlation between structural integrity and biological activity; this know-how provided a strong foundation for the company's entry into the biotechnology arena. Amongst its completed projects, ELEA boasts the development and manufacture of a diagnostic kit for the early detection of diabetes mellitus and other autoimmune diseases by means of the autoimmune recombinant protein glutamic acid decarboxylase (GAD); the production of the human recombinant tyrosine phosphatase (ICA512) and its application to the early diagnosis of diabetes mellitus; the production of human granulocyte-colony stimulating factor, recombinant (G-CSF); and the development of the reverse-transcription polymerase chain reaction (RT-PCR) kit for tyrosinase as a tumour indicator for melanoma.

Additionally, in the area of R&D, ELEA has developed important technical capacities in galenic formulation and in new associations, presentations and processes. One example of ELEA's improved technical capacity is the development of an antitussive drug whose API is *Hedera helix* extract. ELEA developed this medicine and currently produces it for Merck, which markets the drug in Latin America under the trademark Arliv.

Based on the discoveries of its R&D department, ELEA has applied for 12 patents in Argentina. These applications relate to DNA molecules, new compositions, novel manufacturing processes and new formulations. The Argentine patent authority has so far granted 3 of the 12 requested patents.

ELEA also filed a patent application in the United States of America for an optimized DNA molecule sequence that encodes the IA-21C antigen, RNA molecules, expression vectors, transformed cells, the method for preparing the IA-21C antigen, the polypeptide of the human IA-21C antigen, and an in vitro procedure and kit for the diagnosis of autoimmune diabetes. The United States Patent and Trademark Office (USPTO) granted patent number 7 339 040 to ELEA for this invention. In addition, ELEA filed a patent application in Argentina, Mexico, Uruguay, Colombia, Chile, Brazil, Sweden and the European Patent Office, claiming a solid pharmaceutical composition for the oral administration of ibandronaic acid.[9]

3.2 Licensing agreement with Warner Lambert/Pfizer

The second source of ELEA's technical capacity is the know-how transferred under its licensing agreement from Warner Lambert to GYM, and subsequently to ELEA after its merger with GYM. In 1989, Warner Lambert withdrew from Argentina and granted an exclusive licence for the entire line of Parke Davis[10] products to GYM. At the time of the licence grant, the products in the Parke Davis line were already fully developed; therefore, only a specific amount of technology was transferred to the Argentine company. However, in addition to the licence to produce the Parke Davis line, Warner Lambert also transferred to GYM its Argentine industrial plant and technical personnel. This, in and of itself, represented the acquisition of significant and valuable know-how.

Two points must be highlighted with respect to ELEA's relationship with Warner Lambert/Pfizer. First, Warner Lambert inspected GYM to ensure the latter was GMP-compliant and had quality controls in place. The standards imposed by Warner Lambert played an important role in the improvement of GYM's practices and the development of the company's technical expertise. Second, at GYM, and later at ELEA, the R&D departments continued to conduct innovative research on the licensed products obtained from Warner Lambert in an attempt to expand the product line through new presentations, associations and improved processes.

9 Information based on the field interview with ELEA.

10 The licences include, among others, the following medicines: Agarol (a laxative), Anusol (an antihaemorrhoid treatment), Benadryl (an anti-allergy treatment), Caladryl (a skin product), Chloromycetin (eye drops), Lipitor (a blood cholesterol medicine) and Mylanta (a treatment for stomach ache).

Currently, ELEA continues to be the licensee for the Parke Davis line in Argentina. According to the transfer of technology agreement filed with the Instituto Nacional de la Propiedad Industrial (Industrial Property National Institute; INPI), ELEA is not obligated to purchase the licensed products' active ingredients from the licensor. Thus, ELEA can acquire these inputs at a lower price on the international or local market. However, ELEA does pay a royalty of 7% of net sales on the Parke Davis product line.

The most important medicine included in the licensing arrangement between Warner Lambert and ELEA is the blockbuster drug Lipitor (atorvastatin calcium). This is a statin that blocks the enzyme in the liver that the body uses to produce cholesterol. However, Lipitor is the only drug under the licence that ELEA does not formulate; instead, it purchases the drug in bulk from Pfizer, divides the drug into smaller packages, and distributes it throughout Argentina.[11]

3.3 Strategic alliance for development with Argentine universities

The third source of ELEA's technical capacity is the strategic alliance to develop new molecules that the company has formed with the University of Buenos Aires (UBA) and Quilmes National University (UNQ), both in Argentina, and Polo Científico del Oeste de La Habana (Havana's Western Scientific Pole) in Cuba.

ELEA and its strategic partners are focused on the discovery and development of anticancer therapeutic vaccines based on the generation of an immune system response against gangliosides expressed on the surface membranes of cancerous cells. This alliance has resulted in the development of three therapeutic oncological vaccines, as detailed below.

The vaccine that is in the most advanced stage of development is the racotumomab molecule. The racotumomab molecule is an anti-idiotypic monoclonal antibody that recognizes the P3 antibody and reacts against *N*-glycoliled gangliosides present on the surface of breast cancer, lung cancer and melanoma cell membranes. The vaccine preparation consists of the monoclonal antibody 1E10, administered with aluminium hydroxide.

In 2008, ELEA and its partners commenced a phase III multicentre international clinical trial of racotumomab as a vaccine for non-small-cell lung cancer. The phase III trials are taking place in Argentina, Brazil, Cuba, India, Malaysia, Singapore and Uruguay, with approximately 760 patients. The rights to this new vaccine belong to ELEA, Chemo Group and the Centre of Molecular Immunology, holding a 20%, 40% and 40% interest, respectively. To finance the phase III trials, the product has been licensed and pre-sold in 17 countries, including Malaysia, Indonesia, Singapore, Taiwan Province of China, the Republic of Korea, India and many Latin American countries.

11 Lipitor was never patented in Argentina. When the molecule was invented, Argentine Patent Law No. 111 prohibited the patenting of pharmaceutical products.

Two other molecular vaccines currently under development are directed against the *N*-acetil GM3 and the *N*-glycolyl GM3 gangliosides. Both vaccines are based on the non-covalent conjugation of two different antigens (*N*-acetil GM3 and *N*-glycolyl GM3) and a very small size proteoliposome (VSSP) carrier, a small protein obtained from the external membrane of the *Neisseria meningitidis* bacterium, and administered in conjunction with a nonspecific immune response booster (Montanide ISA 51).

The *N*-acetil GM3/VSSP is being tested in people infected with HIV as a potential way to restore immunological status in order to delay antiretroviral therapy. Currently, this vaccine is undergoing phase II clinical trials. The *N*-glycolyl GM3/VSSP vaccine is in phase III clinical trials for metastatic breast cancer and adjuvant breast cancer.

Finally, ELEA and UNQ have been working on the development of desmopressin, a vasopressin peptide analogue with anti-tumour activity that will be used as a perioperative drug in breast cancer and other solid tumours during cancer surgery and in association with conventional chemotherapy. A research group at UNQ created this molecule and later patented it in the United States.[12] The product is authorized for veterinary use in Argentina and is marketed by Biogénesis-Bagó.[13] ELEA is currently exploring the possibility of testing the uses of the molecule in treatments for humans.

The Argentine Government has provided funding for all these projects through the Fondo Tecnológico Argentino (Argentine Technology Fund; FONTAR) and the Fondo para la Investigación Científica y Tecnológica (Scientific and Technological Research Fund; FONCYT) programmes, which are administrated by the Agencia Nacional de Promoción Científica y Tecnológica (Scientific and Technological Promotion National Agency; ANPCyT)[14]. In 2008 alone the Argentine Government's financial support for the development of racotumomab through the Strategic Areas Programme totalled US$ 2.1 million.

3.4 Participation in the Sinergium Biotech Consortium

A fourth source of innovative technical capacity is the planned construction of a vaccine production facility using Novartis technology. ELEA, along with Novartis and Biogénesis-Bagó, are participants in the Sinergium Biotech Consortium ("Sinergium"). In November 2009, Sinergium submitted a proposal to build a factory that would produce influenza vaccines, including vaccines for the H1N1 virus. Then, in December of 2009, the Argentine Government declared this project to be beneficial to the public interest. After conducting a call for proposals, the Argentine Government selected the Sinergium project in February 2010.

12 US Patent No. 6 693 082.

13 Biogénesis-Bagó is a veterinary products laboratory that specializes in the manufacture of the foot and mouth disease vaccine. The Sigman and Gold families, both ELEA shareholders, are also shareholders of Biogénesis-Bagó, along with the Bagó family.

14 See Section 5.8.

The Argentine Government committed to purchase all of the vaccines needed for its influenza and H1N1 virus vaccination programme from Sinergium at the price set by the Pan American Health Organization (PAHO) Revolving Fund for Vaccine Procurement for the next 10 years. In 2010, the Argentine Government bought US$ 105 million of vaccines from Sinergium.

In exchange, Sinergium is obligated to build an industrial plant within 5 years that will fulfil the Argentine need for vaccines. It is estimated that the project will require an investment of US$ 50 million and will create 400 jobs. Until the plant is fully operational, Sinergium is required to fulfil the Argentine Government's needs by importing the necessary vaccines.

In order to give Sinergium the capability to produce vaccines, Novartis will transfer the technology of incubating the hybrid virus[15] in chicken eggs to the Argentine consortium. ELEA, Biogénesis-Bagó and Novartis are currently negotiating the conditions under which the transfer of technology will occur, including details such as plant design, engineering processes and price.

4. The pharmaceutical market in Argentina

Argentina has a population of 40 091 359 (INDEC, 2010). With a human development index (HDI) of 0.866, Argentina is ranked forty-ninth out of the 182 countries included and is considered to be a country with high human development (UNDP, 2009). Female life expectancy is 79.10 years and male life expectancy is 71.60 years (Ministerio de Salud & PAHO, 2009). Argentina's urban population equals roughly 89.5% of the total population. Approximately 19.2% of Argentine households live below the poverty line and, of these, 6.3% are considered poverty-stricken (INDEC, 2006). In 2007, the infant mortality rate was 13.3 deaths per 1000 live births (Ministerio de Salud & PAHO, 2009). Argentina has 321 doctors, 38 nurses and 11 midwives per every 100 000 inhabitants (Ministerio de Salud & PAHO, 2009).

The principal infectious diseases found in Argentina are Chagas disease, HIV/AIDS and tuberculosis. The tuberculosis morbidity rate is 27.1 cases per 100 000 inhabitants and the mortality rate is 1.76 deaths per 100 000 inhabitants. In 2007, roughly 80.4% of tuberculosis cases were detected and cured by directly observed therapy (DOT). The mortality rate for HIV/AIDS is 3.6 deaths per 100 000 inhabitants and the incidence rate is 39 per 1 000 000 inhabitants (Ministerio de Salud & PAHO, 2009).

The Argentine pharmaceutical industry consists of approximately 250 laboratories, of which 37 are state-owned (national, provincial or municipal) and the remainder are owned by private enterprises. Argentina is home to 110 industrial plants, 93 of which belong to Argentine businesses and 17 of which belong to foreign-owned laboratories. The Argentine pharmaceutical industry produces approximately 2000 pharmaceutical products with different APIs, or combinations thereof, which make up more than 10 500 products with

15 A hybrid virus is a mix of a standard laboratory virus strain and, for instance, the H1N1 virus.

commercial names and comprise roughly 23 000 different presentations (De la Puente et al., 2009).

In 2009, sales in the Argentine pharmaceutical market totalled US$ 3.846 billion.[16] Prescription drugs account for 90% of the market and over-the-counter sales comprise the remaining 10%. The pharmaceutical industry represents 5% of industrial gross domestic product (GDP). The pharmaceutical industry directly employs 27 000 people and indirectly employs another 100 000 people.[17]

Argentine laboratories control approximately 58.5% of the domestic market and foreign-owned laboratories control the remaining 41.5%. Four of the six largest laboratories located in Argentina – Roemmers (first), Bagó (second), ELEA (fifth), and Gador (sixth) – are domestic companies. As in other countries, the pharmaceutical industry is very highly concentrated, with the 15 largest laboratories accounting for 55% of the market; of these 15 laboratories, 9 are domestic companies.

Historically, there has been a strong market presence on the part of domestically owned laboratories. In 1963, Argentine laboratories controlled 50.7% of the market and by 1971 this percentage had increased to 51.6% (Katz, 1973). This upward trend continued throughout the 1980s, and by 1994 Argentine laboratories controlled 61% of the local pharmaceutical market.

In the 1990s, the pharmaceutical sector experimented with certain structural transformations, including the elimination of price controls, the reduction of tariff protection, the elimination of the prohibition against patents for pharmaceutical products, and the modification of the regulatory regime for the industry (Panadeiros, 2002).[18] At the same time, foreign laboratories acquired several domestic laboratories or specific product lines from domestic laboratories. Furthermore, foreign laboratories ceased to license products to Argentine laboratories and, instead, began to sell the products directly to the market. This led to a decrease in the market share of Argentine companies, which fell to 49.1% in 2000, the lowest level since 1962 (Panadeiros, 2002).

The devaluation of the Argentine peso in 2002 and the subsequent economic crisis constricted the local pharmaceutical market. From 2001 to 2002, the market slipped from US$ 3.659 billion to US$ 1.309 billion.[19] Despite the changes initiated in the 1990s and the depth of the 2002 crisis, Argentine laboratories adapted to the new circumstances and recouped their leadership positions in the market in subsequent years. At the beginning of the twenty-first century, Argentine laboratories began to buy manufacturing plants and

16 Source: IMS Health Argentina.

17 Source: CILFA.

18 2000 was the only year in which foreign-owned laboratories had higher levels of participation in the market than local laboratories.

19 Source: IMS Health Argentina.

production lines from the multinational laboratories.[20] In 2009, the market regained the value it possessed in 2000, totalling US$ 3.846 billion and, as described above, the market participation of Argentine firms reached 58.5%.[21]

The structure of the Argentine pharmaceutical industry has been the subject of numerous studies over the past 40 years (e.g. Katz, 1973, 1974, 1987; Katz & Burachik, 1992). Until the mid-1990s, the success of the national industry was thought to be the result of three main factors: (i) the prohibition of patents for pharmaceutical products, (ii) the approval regime for medications, and (iii) the high level of tariff protections afforded to the local industry (Santoro, 2000).

As a result of these three factors, domestic firms based their strategies on the rapid rate of introduction of new products to the market and the supply of raw materials to the international market. The cost to import raw materials was far below the transfer price that multinational subsidiaries usually paid, while the sale price for drugs was slightly less than the prices offered by the multinational laboratories. This price differential was used on many occasions to produce a backward vertical integration into production of APIs, to realize more aggressive marketing schemes (e.g. increased commercialization costs per unit), and to assist in many aspects of company development, ranging from production to pharmaceutical development (Santoro, 2000).

Local companies have undertaken new product launches at a high rate, and also launched products with new combinations of APIs. Argentine companies have based their model on the sale of branded generic drugs and the intense promotion of their products. This approach results in many branded generics having the same characteristics as the innovative products available in the international market. Consequently, the Argentine generics laboratories obtained market power through trademarks and promotion (De la Puente et al., 2009). On the other hand, multinational firms have based their strategies on the payment of transfer prices for the importation of finished products and materials, fewer new product launches per year, and a strong tendency to concentrate on drugs comprised of only one API (Santoro, 2000).

The Argentine pharmaceutical market relies very heavily on imported raw materials. Throughout the 1990s only approximately 25% of the raw materials used by the national drug manufacturing industry were of local origin, a proportion that has decreased over the past several years due to the transformations that the industry undertook during the 1990s (De la Puente et al., 2009). According to the Argentina Instituto Nacional de Estadística y Censos (Statistics and Census National Institute; INDEC), only 15.20% of inputs were domestic in origin in 2009.[22] These data reflect the elevated dependence

20 In 2002, Argentine laboratory Roemmers bought a Roche plant, Casasco bought a plant from Janssen Cilag, and Phoenix purchased a plant from Novartis. In 2004, LKM acquired a Schering AG plant, while HLB Pharma bought an Aventis plant. In 2005, Craveri purchased Valeant Pharmaceuticals Argentine plant. In 2006, Roemmers acquired Bristol-Myers Squibb's domestic production site and Richmond purchased a facility from Altana Pharma (CILFA, 2006, p. 25).

21 Source: IMS Health Argentina.

22 Conclusion of the author based on 2009 quarterly reports from INDEC (2009a).

on imported APIs that confronts the pharmaceutical sector (De la Puente et al., 2009). According to the interviews conducted for this case study, Argentine companies do not have the scale of production that Indian and Chinese firms possess, and so the Argentine companies cannot compete with the lower prices offered by Indian and Chinese companies. This – rather than a lack of technical expertise – is the principal impediment to increased development in the domestic pharmachemical industry.

In 2009, Argentine imports and exports of APIs, excipients, and finished and semi-finished products totalled US$ 1.424 billion and US$ 735.30 million, respectively. Of these totals, APIs and excipients comprised roughly US$ 297.88 million of imports and US$ 95.13 million of exports. The importation of finished and semi-finished pharmaceutical products totalled US$ 1.126 billion, while the exportation of finished and semi-finished products constituted US$ 640 million (Table 1). The export of pharmaceutical products represents 1.34% of Argentina's total exports, while the import of pharmaceutical products makes up 3.67% of the country's total imports.[23]

***Table 1** Finished and semi-finished pharmaceutical products, APIs and excipients imports/exports 2009*

	Imports 2009		Exports 2009	
	Value CIF (US$)	Variation 2009/2002	Value FOB (US$)	Variation 2009/2002
Finished and semi-finished pharmaceutical products	1 126 196 387	206.9%	640 159 199	142.25%
APIs and excipients	297 880 045	82.06%	95 138 990	142.00%
Total	1 424 076 432		735 298 189	

CIF, cost, insurance and freight; FOB, free on board.
Source: INDEC.

Table 2 demonstrates the composition of API and excipient imports. According to the data, 92.88% of API and excipient imports to Argentina come from 12 countries. China and India are the two largest providers of APIs and excipients to the Argentine market, providing imports totalling 27.46% and 12.61%, respectively. Since 2002, Argentina has experienced a spectacular growth in imports from China and India: imports from China increased by 598.37%, and imports from India increased by 184.71%. Brazil and Taiwan Province of China also greatly increased their share of imports to the Argentine market.

23 INDEC uses the Nomenclatura Común del Mercosur (Mercosur Common Nomenclature; MCN) to classify exports and imports in the pharmaceutical industry. Finished and semi-finished pharmaceutical products are included in MCN Chapter 30, and, as explained therein, INDEC computes pharmaceutical industry exports/imports under the headings 3002, 3003 and 3004. APIs and excipients are found in MCN Chapter 29. INDEC employs the United Nations' Standard Industrial Classification of All Economic Activities (ISIS) to determine pharmachemical imports and exports in Chapter 29 (CIIU Codes 2423 or 2100).

Table 2 APIs and excipients imports

Country	US$ (CIF)	Percentage of total imports (%)	Growth 2002/2009
China	81 783 528	27.46	598.37%
India	37 556 260	12.61	184.71%
Germany	35 832 465	12.03	52.54%
United States	29 654 376	9.96	7.61%
Italy	20 044 452	6.73	65.04%
Spain	15 285 484	5.13	21.87%
Brazil	13 114 758	4.40	109.85%
Switzerland	11 226 803	3.77	0.95%
Mexico	8 589 550	2.88	–11.92%
France	8 521 894	2.86	70.73%
Taiwan Province of China	8 431 107	2.83	2568.11%
United Kingdom	6 623 356	2.22	44.93%
Total		92.88	

CIF, cost, insurance and freight.
Source: INDEC.

The main destinations for the export of Argentine-produced APIs and excipients are Germany (46.71%) and the Netherlands (13.01%). Table 3 provides information on export destinations and the amount of APIs and excipients exported to those destinations. The principal APIs exported from Argentina are menotropin, polypeptide hormones and heterocyclic compounds (CILFA, 2007).

Table 3 APIs and excipients exports

Country	US$ (FOB)	Percentage of total exports (%)	Growth 2002/2009
Germany	46 719 239	49.11	142.56%
Netherlands	12 379 434	13.01	2571.60%
Spain	5 645 549	5.93	625.85%
Chile	4 301 971	4.52	232.34%
France	3 625 735	3.81	256.77%
Australia	1 627 235	1.71	1552.27%
Brazil	1 567 342	1.65	–8.28%
Venezuela	1 210 471	1.27	331535.88%
Mexico	1 143 475	1.20	–53.64%
Japan	1 039 873	1.09	27.67%
Egypt	1 009 786	1.06	n/a
Uruguay	1 009 264	1.06	32.38%
Total		85.43	

FOB, free on board; n/a, not applicable.
Source: INDEC.

Imports of finished and semi-finished pharmaceutical products to Argentina totalled US$ 1.126 billion in 2009. According to the data in Table 4, 56% of

finished and semi-finished products were imported from five countries. These five principal exporters to the Argentine market include the United States (18.22%), Switzerland (13.04%), Germany (11.29%), France (7.18%) and Brazil (6.32%). Multinational laboratories purchased 85% of these imports to supply the internal market (CILFA, 2006).

***Table 4** Finished pharmaceutical products imports*

Country	US$ (CIF)	Percentage of imports (%)	Growth 2002/2009
United States	220 137 226	18.22	221.07%
Switzerland	157 514 821	13.04	379.51%
Germany	136 418 855	11.29	247.47%
France	86 767 591	7.18	195.27%
Brazil	76 374 918	6.32	55.43%
Ireland	57 934 762	4.80	366.05%
Italy	56 391 969	4.67	231.37%
Denmark	45 219 310	3.74	858.13%
United Kingdom	42 677 871	3.53	15.71%
Japan	41 658 492	3.45	283.93%
Canada	27 079 689	2.24	939.63%
Spain	25 502 513	2.11	255.15%
Austria	21 558 650	1.78	176.17%
Netherlands	20 755 571	1.72	163.65%
Mexico	20 281 317	1.68	49.20%
Belgium	15 256 413	1.26	100.57%
China	13 313 341	1.10	1365.04%
Total		88.16	

CIF, cost, insurance and freight
Source: INDEC.

In the 6-year period from 2003 to 2009, the export of finished and semi-finished products increased by 240%, from US$ 266 million to US$ 640 million. In 2009, Argentina exported finished and semi-finished drugs to 114 countries, with Brazil (16.07%), Venezuela (11.11%) and Uruguay (9.31%) as the main destinations (Table 5). Even though there is diversification in the markets for Argentine pharmaceutical exports, exports tend to be highly concentrated in the Latin American markets and in particular in Mercosur.[24] Canada also represents a major destination for Argentine exports, and Canada has demonstrated very significant growth in this area over the past decade.

In 2000 the percentage of participation in exportation in relation to the total production of drugs was 10%. In 2010 sales to the external market totalled roughly 21% in relation to the total sales. Therefore, for every US$ 100 of pharmaceutical drugs manufactured in Argentina, US$ 21 are destined for the external market, of which US$ 3 go to Brazil.[25]

24 Mercosur is a regional trade agreement among Argentina, Brazil, Paraguay and Uruguay.

25 Source: Abeceb.com based on INDEC's reports.

***Table 5** Finished and semi-finished pharmaceutical products exports (2009)*

Country	US$ (FOB)	Percentage of exports (%)	Growth 2002/2009
Brazil	102 882 735	16.07	73.68%
Venezuela	71 121 321	11.11	194.87%
Uruguay	59 600 895	9.31	99.76%
Canada	55 314 354	8.64	39322.68%
Chile	39 934 768	6.24	33.24%
Colombia	33 452 599	5.23	197.77%
Mexico	28 526 660	4.46	52.84%
Paraguay	26 000 520	4.06	63.81%
Panama	25 209 712	3.94	306.44%
Peru	22 368 432	3.49	65.41%
France	20 837 771	3.26	1045447.99%
Ecuador	16 594 442	2.59	36.59%
Lebanon	14 178 873	2.21	2488.25%
Guatemala	11 987 039	1.87	50.38%
Bolivia	11 610 633	1.81	102.09%
Dominican Republic	10 232 795	1.60	261.00%
Thailand	9 654 259	1.51	270.72%
Latvia	7 358 745	1.15	24529048.90%
Total		88.15	

FOB, free on board.
Source: INDEC.

Even though local companies have greatly increased their investment in R&D over the past several years, the Argentine pharmaceutical industry has not yet achieved the capacity to develop new chemical entities (De la Puente et al., 2009). In this context, it seems that there has been a paradigm shift in the strategies of large Argentine laboratories, which consists of the formation of innovation networks with other national manufacturing industries and with the scientific-technological system. This shift is evidenced by the focus of R&D on biotechnology, mechanisms of controlled drug release, nanotechnology and vaccines, as well as on existing investigations related to different types of cancer (De la Puente et al., 2009).

5. The framework for local production and technology transfer in Argentina

5.1 Drug regulation

ANMAT is the regulatory authority for drugs, food and medical devices in Argentina.[26] PAHO named ANMAT a Level IV National Regulatory Authority for Reference Drugs, the highest level granted by PAHO, in December 2009.

ANMAT has participated in the Pharmaceutical Inspection Convention and the Pharmaceutical Co-operation Scheme (together, the PIC/S) since January 2008. ANMAT's participation in PIC/S facilitates the export of Argentine-manufactured drugs.

5.2 Marketing authorization

The Argentine drug manufacturing, importing, exporting and marketing regime is regulated by Law No. 16 463 of 1964, Presidential Decree No. 150 of 1992, and Law No. 24 766 of 1996. ANMAT grants marketing authorization. The marketing authorization regime for drugs manufactured in Argentina allows for two different scenarios: (i) whether the authorization concerns a drug not previously authorized in Argentina or in a country with a high level of health surveillance;[27] and (ii) whether the drug under consideration has received prior authorization in Argentina or in a country with a high level of health surveillance. ANMAT provides a specific process to obtain permission to market for each of these scenarios.

In the first scenario the drug in question has not received previous authorization in Argentina or in a country with a high level of health surveillance. In this case, ANMAT requires clinical trials that demonstrate the drug's safety and efficacy.

In the second scenario, the drug is similar to a reference drug that has been previously authorized in Argentina or in a country with a high level of health surveillance. In this case, the applicant can invoke pharmaceutical similarity and ANMAT will grant an exemption from the clinical trial requirement.[28]

Decree No. 150/92 states that the process to obtain marketing authorization by pharmaceutical similarity will take no more than 120 days, and ANMAT

26 ANMAT was created by Decree No. 1490/92 in August 1992. ANMAT is a decentralized agency of the Federal Government that depends, both technically and scientifically, on the Secretariat of Policies, Regulation, and Institutes and the Ministry of Health.

27 Decree No. 150/92, Annex 1. The following countries are considered countries with high levels of health surveillance: Austria, Belgium, Canada, Denmark, France, Germany, Israel, Italy, Japan, the Netherlands, Spain, Sweden, Switzerland, the United Kingdom, and the United States.

28 Law No. 24 766, Article 5; Decree 150/92, Article 3 (without limitation, those who solicit approval of a drug invoking pharmaceutical similarity must present certain information regarding the product (e.g. name, formula, drug form, pharmacological classification, and whether it is an over-the-counter or a prescription drug), technical information (e.g. methods of control, shelf-life, method of manufacturing in line with GMP, information on bioequivalence or bioavailability of the product in relation to similar products), and information on labelling and packaging.

has typically complied with this time limit. Marketing authorization for an approved drug or a drug imported from a country with a high level of health surveillance is granted automatically.

The Argentine regime does not grant exclusive rights to the undisclosed results of the clinical trials presented to ANMAT or the regulatory authority of another country (hereinafter, "pharmaceutical test data") by the applicant. The Argentine regime protects pharmaceutical test data presented to ANMAT only against unfair competition.[29] According to Article 4 of Law No. 24 766, approval by similarity (i.e. the submission of evidence of marketing in Argentina or a country with a high level of health surveillance) does not imply ANMAT's use of the pharmaceutical test data presented to obtain marketing authorization for the reference product, regardless of whether the pharmaceutical test data were presented in Argentina or another country.[30]

Another noteworthy aspect of the authorization process for drugs by similarity relates to bioequivalence trials. Even though comparative dissolution tests are generally required for solid pharmaceutical formulations – between the product for which approval is sought and a reference drug – ANMAT does not require bioequivalence tests in vivo for all drugs.

ANMAT Regulations No. 3185/1999 and 2814/2002 establish a process for bioequivalence trials, based on a two-variable model, which considers health risk on the one hand, and those drugs that require bioequivalence trials in Canada, Germany and the United States on the other hand (ANMAT, 2006a). The application of this model results in the categorization of APIs that require in vivo bioequivalence tests and a timetable for their gradual completion (ANMAT, 2006b).

Thus, drugs are classified into three categories: (i) drugs that do not require bioequivalence tests; (ii) drugs that require in vitro bioequivalence tests; and (iii) drugs that require in vitro and in vivo bioequivalence tests. Additionally, ANMAT Regulation No. 3311/2001 has mandated in vivo bioequivalence tests for antiretroviral drugs (ARVs) used in the treatment of infections caused by HIV.

ANMAT requires bioequivalence tests for 22 high-risk APIs.[31] Furthermore, ANMAT requires bioequivalence tests for the 27 APIs or API combinations used in the treatment of HIV;[32] 63 high-risk drugs and 110 ARVs have met the

29 Law 24 766, Article 11.

30 Law 24 766, Article 8, § 8.

31 The following drugs require bioequivalence tests: carbamazepine, lithium carbonate, ciclosporin, digoxin, divalproex sodium, ethosuximide, phenytoin, phenytoin sodium, isotretinoin, levodopa-benserazide, levodopa-carbidopa, oxcarbazepine, pyridostigmine, theophylline, magnesium valproate, verapamil, warfarin, everolimus, mycophenolate mofetil, mycophenolate sodium, sirolimus and tacrolimus (ANMAT, 2011a).

32 The ARVs in question are abacavir, amprenavir, atazanavir, darunavir, didanosine, efavirenz, emtracitabine, stavudine, etravirine, fosamprenavir, indinavir, lamivudine, lamivudine/zidovudine, abacavir/lamivudine/zidovudine, lamivudine/abacavir, maraviroc, nelfinavir, nevirapine, nevirapine/lamivudine/zidovudine, raltegravir, ritonavir, ritonavir/lopinavir, saquinavir, tipranavir, tenofovir disoproxil and zalcitabine (ANMAT, 2011b).

standard of this regulatory requirement. This requirement has also resulted in the suspension of marketing authorizations for 20 high-risk drugs and 118 ARVs that did not comply with or pass the bioequivalence tests.[33]

The practice of approving drugs by similarity and the requirement that bioequivalency tests be conducted only on high-risk drugs and ARVs has contributed to the preservation of a competitive pharmaceutical market in Argentina and favours new entrants and high levels of competition in the generic drug market. For example, in 2006, ANMAT granted 1610 marketing authorizations, of which approximately 89% were products approved by similarity; 10% were drugs imported from countries with high levels of health surveillance; and only 1% were drugs that underwent clinical trials to ensure their safety and efficacy.[34]

Multinational pharmaceutical companies and the United States Government have questioned the legal validity of the Argentine system of granting marketing authorization for drugs by similarity in both domestic and international fora. They have claimed that the Argentine system of similarity should be eliminated or modified. Their objections are based on concerns regarding the rights to pharmaceutical test data.

In the international forum, the United States Government initiated two separate consultations under the Understanding on Rules and Procedures Governing the Settlement of Disputes (Dispute Settlement Understanding; DSU) at the World Trade Organization (WTO) in 1999 and 2000.[35] In bringing its consultations, the United States alleged that Decree No. 150/92 and Law No. 24 766 were inconsistent with Article 39.3[36] of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement).[37]

On 22 June 2002, after nine rounds of negotiations, the United States and Argentina notified the WTO's Dispute Settlement Body that the two countries had reached a mutually agreed upon solution (WTO, 2002). The agreement stated that the disagreement over the meaning and applicability of Article 39.3 of the TRIPS Agreement would be resolved under the rules of DSU. Additionally it was agreed that both parties would continue the consultation process and jointly assess the progress of legislative reforms to the Argentine Patent Law; and, in light of this assessment, that the United States could decide to continue consultations or request the establishment of a dispute

33 Source: ANMAT.

34 Source: ANMAT.

35 WT/DS171/1. Geneva, World Trade Organization, 5 May 1999, and WT/DS196/1. Geneva, World Trade Organization, 6 June 2000.

36 Article 39.3: "Members, when requiring, as a condition of approving the marketing of pharmaceutical or of agricultural chemical products which utilize new chemical entities, the submission of undisclosed test or other data, the origination of which involves a considerable effort, shall protect such data against unfair commercial use. In addition, Members shall protect such data against disclosure, except where necessary to protect the public, or unless steps are taken to ensure that the data are protected against unfair commercial use."

37 The consultations also included other allegations of inconsistency between the TRIPS Agreement and the Argentine Patent Law No. 24 481.

settlement panel related to an alleged violation of Article 39.3 of the TRIPS Agreement (WTO, 2002).

Additionally, Argentina and the United States agreed "that should the Dispute Settlement Body adopt recommendations and rulings clarifying the content of the rights related to undisclosed test data submitted for marketing approval according to Article 39.3 of the TRIPS Agreement, and should Argentinean law be found to be inconsistent with Article 39.3 as clarified by the above-mentioned recommendations and rulings, Argentina agrees to submit to the National Congress within one year an amendment to Argentinean law, as necessary, to put its legislation in conformity with its obligations under Article 39.3 as clarified in such recommendations and rulings" (WTO, 2002). The United States has not requested to reopen the consultations or to establish a dispute settlement panel since the agreement reached in 2002.

In the domestic forum, multiple multinational pharmaceutical companies have challenged the constitutionality of the Argentine regime and its compatibility with the TRIPS Agreement. In 2005, alleging that the Argentine system is inconsistent with the TRIPS Agreement, G.D. Searle & Company, Novartis Pharma S.A., Schering-Plough Corporation and MSP Singapore (a joint venture between Schering-Plough Corporation and Merck & Co.) initiated 13 lawsuits challenging the constitutionality of Decree No. 150/92 and Law No. 24 766 in Argentine courts.[38]

Before the courts' hearings on the merits of the cases, the plaintiffs requested preliminary injunctions to suspend the marketing authorizations for several drugs. The Argentine Federal Appellate Court refused this request, stating that there was no likelihood of success on the merits. Of the 13 cases initiated in 2005, the Court of Appeals issued a final judgment rejecting the claim in 1 case; [39] the other 12 cases remain open on the merits.

In sum, there were two challenges brought against the validity of the Argentine system of drug marketing authorization, both alleging that Decree No. 150/92 and Law No. 24 766 are incompatible with Article 39.3 of the TRIPS Agreement. The first, brought by the United States in the WTO Dispute Settlement Body, was resolved through a mutually agreed upon solution between the two countries. The second, brought by several multinational pharmaceutical companies in the Argentine courts, has yet to be resolved, although the courts have dismissed requests for provisional measures.

38 In accordance with Article 75, Clause 22 of the Argentine Constitution and the holdings of the Corte Suprema de Justicia de la Nación (National Supreme Court of Justice) in the Unilever, Karl Thomae and Pfizer cases, the provisions of the TRIPS Agreement are superior to domestic laws and legislation; therefore, TRIPS' norms are operative and can be directly applied by a judge. National Supreme Court of Justice, cases Unilever c/ Instituto Nacional de la Propiedad Industrial s/ denegatoria de patente, decided on 24 October 2000; Dr Karl Thomae Gesellschaft mit beschränkter Haftung c/ Instituto Nacional de la Propiedad Industrial y otro s/ denegatoria de patente, decided on 13 February 2001; and Pfizer Inc. c/ Instituto Nacional de la Propiedad Industrial s/ denegatoria de patente, decided on 21 May 2002.

39 See Novartis Pharma AG v. Monte Verde SA, Buenos Aires Civil and Commercial Federal Court of Appeals, Panel 3, 1 February 2011, published in Revista Jurídica La Ley, 16 March 2011, p. 8. Novartis did not appeal to the Federal Supreme Court, and so the judgment is res judicata.

5.3 Clinical trials

There have been significant increases in both the establishment of regulations and the number of clinical trials undertaken in Argentina over the past 15 years. These developments have, in part, stemmed from ANMAT's publication of Regulation No. 5330 in 1997, which established a new regime for the conduct and approval of clinical trials.[40] As a result of this regulation, the number of clinical trials conducted in Argentina increased. In addition to the 157 studies to prove the bioequivalence of high-risk drugs or ARVs approved by reference from January 1994 to August 2007, ANMAT approved 1892 additional clinical trials and rejected approximately 100 protocols.[41]

In 2007, ANMAT published the *Guidelines of Good Practices for Clinical Research in Human Beings*.[42] Subsequently, the Ministry of Health created the Registry for Clinical Trials on Human Beings through the passage of Resolution No. 102 in 2009.

As in other countries, clinical trials in Argentina are classified into phases. The majority of clinical trials conducted in Argentina are phase III studies (59%). Phase II and phase IV studies constitute 19% and 18% of the clinical trials conducted in Argentina, respectively, while phase I studies total roughly 4%.[43] Data show that a variety of parties carry out clinical trials in Argentina; multinational laboratories sponsor approximately 60% of these studies, while contract research organizations, domestic laboratories and independent investigators account for 23%, 11% and 6% of the clinical trials conducted, respectively.[44]

ANMAT has not published statistical information on authorized clinical trials since September 2007. Statistics published by the United States National Institutes of Health (NIH) indicate that, as of the time of this report, 260 clinical trials are under way in Argentina.[45] From September 1999 to July 2010, according to NIH records, 1004 clinical trials were under way or completed in Argentina, representing a significant portion (36.38%) of the 2759 trials in all of South America.

Furthermore, Regulation No. 5330/97 dictated that ANMAT would begin to oversee ongoing clinical trials. Between 1997 and 2007, ANMAT conducted

40 The Argentine clinical study regime is in line with the International Declaration on Human Rights, which stemmed from the Nuremberg Trials of 1948, the Declaration of Helsinki, the WHO 2000 Operational Guidelines for Ethics Committees that Review Biomedical Research, the Council for International Organizations and Medical Sciences (CIOMS) Guidelines on Ethics of Clinical Trials, and the United Kingdom's Nuffield Council on Bioethics 2002 Ethics of Research Related to Healthcare in Developing Countries. See ANMAT Regulations No. 5330/1997 and 1490/2007.

41 Source: ANMAT.

42 ANMAT Regulation No. 1490/2007.

43 Source: ANMAT.

44 Source: ANMAT.

45 United States National Institutes of Health (see http://www.clinicaltrials.gov.ar). Of the 260 clinical studies open at the time of writing, 12 were in phase I, 59 in phase II, 150 in Phase III and 22 in phase IV.

418 inspections.[46] These inspections led to the adoption of voluntary measures by the entities undertaking the trials, as well as to official actions. Official actions stemming from ANMAT inspections included the commencement of 22 administrative proceedings and 22 criminal fraud allegations.

5.4 Drug prescription by international nonproprietary name

The Argentine regulation of drugs requires that doctors prescribe medicine by generic name or international nonproprietary name (INN). The Argentine Government imposed this requirement in 2002 through the passage of Law No. 25 649.

According to Article 2 of Law No. 25 649, all prescriptions for medical drugs must indicate the generic name of the drug or the INN, followed by the pharmaceutical form and dosage/unit information, with detailed information on concentration levels. The prescription may also indicate the drug's commercial brand. The pharmacist is obliged to substitute the medication for a lower-priced substitute that contains the same active ingredients, concentrations, form and similar number of units at the request of the consumer.

5.5 Patents

The Argentine Congress passed the nation's first patent law, Law No. 111, in 1864. Law No. 111 prohibited the patenting of pharmaceutical products and was considered one of the key elements in the emergence of the national pharmaceutical industry. The introduction of new minimum standards of protection under the TRIPS Agreement, combined with international pressure from the United States and several European countries, led to the passage of a new Patent Law No. 24 481 that went into effect in September 1995 (Genovesi, 1995). Unlike Law No. 111, the 1995 law did not contain a prohibition on the patenting of medicinal drugs.

Argentine Patent Law No. 24 481 attempts to take advantage of many of the flexibilities built into the TRIPS Agreement. The Argentine law emphasizes the following elements: the non-patentability of therapeutic, surgical and diagnostic methods for human beings; the international exhaustion of patent rights; an exception for research and educational activities; and compulsory licensing as a remedy for anticompetitive practices, including international price discrimination, or refusing to license a patent on reasonable commercial terms. Compulsory licences are also authorized for health emergencies. Later, in 1996, Law No. 24 766 introduced the Bolar exception (permitting the use of patented substances for the purpose of requesting marketing approval of generic copies of a patented medicine) and INPI dictated the non-patentability for second uses of pharmaceutical products. INPI has accepted patent applications for pharmaceutical products as of 1 January 1995 (including applications with a priority date after 1 January 1994). However, patents were only granted on these applications after 23 October 2000.

46 Source: ANMAT.

As explained above, the United States initiated two consultation processes against Argentina under the WTO Dispute Settlement Understanding.[47] In addition to the issues previously discussed, these consultations also included allegations of inconsistencies within the new Argentine Patent Law. The mutually agreed upon solution of 2002 included the Argentine Government's agreement to send a bill amending Patent Law No. 24 481 to Congress (WTO, 2002). The proposed amendments established, inter alia, the protection of products obtained directly through a patented process and also clarified how the burden of proof shifts to the alleged patent infringer in civil cases, and preliminary injunctions (WTO, 2002). In January 2004, Law No. 25 589 went into effect, amending Patent Law No. 24 481.

As of the time of writing of this report, Argentina has yet to ratify the Patent Cooperation Treaty (PCT); nor has Argentina signed any free trade agreement that contains provisions related to patents and the protection of test data.

INPI has a considerable backlog in the number of patent applications under its review. Due to this backlog, the time from solicitation of a patent to its concession has typically been 6–8 years. INPI employs approximately 60 patent examiners, of which 17 work in the pharmaceutical field and 7 work in the area of biotechnology. In 2008, ANP received 5582 patent requests; of these requests, foreigners submitted 4781, and Argentine residents submitted the remainder (MINCyT, 2008a). In 2008, the dependency rate was 5.97, the auto-sufficiency rate was 0.14, and the invention coefficient rate was 0.20 (MINCyT, 2008a).[48]

5.6 Transfer of technology and foreign direct investment

Law No. 22 426 regulates the transfer of technology by people located outside Argentina to people or companies in the country. INPI is the authority responsible for the application of Law No. 22 426.

Contracts between a foreign-owned local business and a company that directly or indirectly controls it are subject to approval by INPI. INPI will approve these contracts if its review finds that the business dealings adhere to standard business practices between independent parties and that the agreed upon consideration relates to the transferred technology.[49] Once the review process has begun, the contract in question is automatically approved after 90 days unless INPI rejects the contract. Contracts between independent parties are not subject to INPI approval; nor do these contracts require registration.

47 WT/DS171/1. Geneva, World Trade Organization, 5 May 1999. WT/DS196/1. Geneva, World Trade Organization, 6 June 2000.

48 The dependency rate means the ratio number of nonresident patent applications per number of resident patent applications; the auto-sufficiency rate refers to the ratio number of resident patent applications per number of total patent applications; and the invention coefficient rate indicates the ratio number of resident patent applications per 100 000 of the population.

49 Law No. 22 426, Article 5.

The absence of approval of a contract between related parties or failure to register a contract between independent parties does not affect the validity of the contract or the validity of the agreed upon benefits. Nevertheless, failure to gain approval will result in the denial of tax benefits to the parties. First, the payments realized by the transferee may not be considered as capital gains for tax purposes.[50] Second, the sum of the payments received by the transferor is considered net earnings of the provider. When a contract is properly authorized by INPI, the applicable tax will be reduced from 35% to 21% of the total received.[51]

The Argentine Constitution guarantees equal treatment and rights for local and foreign investors.[52] Law No. 21 832 regulates foreign direct investment (FDI) and permits foreign investors to send profits abroad and repatriate their investments. Argentina has signed 58 bilateral investment treaties, 55 of which are in effect (Nofal et al., 2010).

UNCTAD estimates that 1800 foreign affiliates operate in Argentina (UNCTAD, 2009). In 2007, approximately 330 of the 500 largest national and international non-financial companies operating in Argentina were affiliates of foreign companies and accounted for roughly 405 365 jobs and US$ 121 billion in sales. In the same year, affiliates of foreign companies accounted for 83.8% of gross value added and 90.2% of the total profits of those 500 largest non-financial companies (INDEC, 2009b).

In 2008, inward FDI stock in Argentina was US$ 79.902 billion. In 2008, Argentina ranked fourteenth among emerging markets in terms of FDI stock. Manufacturing, natural resources and services each accounted for approximately one-third of the total inward FDI stock. The top five investors by value of their FDI stock in 2008 were Spain, the United States, the Netherlands, Brazil and Chile. In the same year, earnings as a percentage of FDI stock were 9.1% on average.

In December 2001, Argentina experienced a devastating economic and financial crisis that caused 6 presidents to assume and leave office within 10 days. Argentina defaulted on its debt and Congress passed the Emergency Law, which, inter alia, devalued the Argentine peso by eliminating the dollar–peso peg, established varying exchange rates for different transactions, and terminated public utilities' right to adjust tariffs. Alleging that Argentina took measures in violation of its commitments to foreign investors, foreign investors filed 44 arbitration claims against Argentina in the International Centre for Settlement of Investment Disputes (ICSID). To date, 2 of these claims have been concluded under Annulment Process; 4 awards have been rendered pending annulment proceedings; 13 claims have been discontinued; 11 claims have been suspended; and 14 claims are still pending (INDEC, 2009b). Since this period of economic crisis, no foreign pharmaceutical investor has requested arbitration against Argentina at ICSID.

50 Law No. 22 465, Article 9.

51 Earnings Tax Law (1997), Article 93 §a.

52 Constitución Nacional (National Constitution), Article 20.

5.7 Industrial policies

The Argentine pharmaceutical industry is not subject to a special industry policy and does not receive specific incentives. Furthermore, as discussed above, there is no difference in treatment for foreign-owned companies or those companies that do not have manufacturing plants in Argentina. Argentina does not require, either wholly or partially, that medical drugs or their inputs be manufactured locally.

Regarding tariffs, the pharmaceutical sector is very open and often finds itself subject to intense external competition. Imports from Mercosur countries, Chile and Bolivia are exempt from import duties. Mercosur's Harmonized Tariff System (HTS) applies to imports from all other countries. The HTS applies to the cost, insurance and freight (CIF) value of the imported product. The tariff rate on pharmachemical products varies from 0% to 14%, depending on the tariff position. The rate allocation criterion requires a higher tariff for those products with higher value added. In line with these criteria, pharmachemical products are, for the most part, charged a 2% tariff and finished pharmaceutical products are subject to a 14% tariff.

Pharmaceutical and pharmachemical exports are subject to a 5% tax, calculated against the free on board (FOB) value of the merchandise.

In 2007, Congress passed Law No. 26 270, which is designed to promote research in biotechnology and the production of biotechnology products. There are multiple benefits under the law; for example, there is accelerated depreciation of capital goods, equipment, parts and components, and early reimbursement of value-added tax (VAT) paid on the purchase of capital goods, equipment, parts and components. Additionally, listed property is not taxable under the minimum presumed income tax, and contributions to social security and expenses for the contracting of R&D services from public institutions are treated as tax credits. The law also includes a special fund to promote new biotechnological projects. However, the Executive Branch has not published regulations for the law; therefore, the law is not yet in force.

The pharmaceutical and pharmachemical industries are the beneficiaries of common horizontal policies promotion to all industrial sectors. The main aspects of these policies are detailed below.

First, Law No. 26 360 promotes investment in new capital goods for manufacturing. The Executive Branch implemented Law No. 26 360 in 2007, and the law remained in force until December 2010. The benefits granted by Law No. 26 360 include (i) accelerated reimbursement of VAT paid on purchases of capital goods and other materials related to investment projects; and (ii) accelerated depreciation for machinery and equipment related to investment projects. Investors may apply for both benefits for export-oriented projects and environmentally friendly projects. For all other types of projects, companies must choose one of the options. The granting of the law's benefits is subject to the fulfilment of several requirements, one of which is the generation of

a certain number of jobs. The Argentine Government has budgeted US$ 314 million per year to distribute between all of the projects; US$ 52 million of these funds are earmarked for small and medium-sized enterprises.

Second, Decree No. 509/2007 provides a zero import duty on a broad range of capital goods. Most of these goods fall under HTS Chapters 84–87, 89, 90 and 94.[53] The exemption applies only to imports of new equipment.

Third, numerous decrees, in particular Decrees No. 493/2001, 496/2001, 615/2001, 733/2001 and 959/2001, have reduced the VAT paid upon the acquisition of capital goods. Included in these VAT reductions is the application of a preferential rate of 10.5%, rather than the standard 21% for other, non-capital goods, and on the sale or import of finished capital goods and computer and telecommunications hardware, including parts.

Fourth, Decree No. 256/2000 established a special import regime for large industrial investments projects. Under this regime, companies pay no tariffs on imports of capital goods that are part of an autonomous and complete production line. The regime allows for the import of spare parts up to 5% of the line's FOB value.

5.8 Science and technology policies

Investment in R&D in Argentina represented 0.52% of the GDP in 2008, an amount equivalent to US$ 1.973 billion (RICYT, 2010). Investment in R&D occurred in both the public and private sectors – 70.6% and 28.8%, respectively. Medical research accounted for 13.3% of R&D investment, while the exact and natural sciences accounted for 16.6% (MINCyT, 2008a).

In 2008, 79 400 people worked in the R&D field in Argentina, 50 816 of whom were researchers and 15 536 of whom were doctors. In the same year, the number of citations in the Science Citation Index (SCI) totalled 7928, 18.9% of which related to medical sciences, 25.3% life sciences, and 24.2% physics, chemistry and earth sciences (MINCyT, 2008a).

Ministerio de Ciencia y Tecnología (Science and Technology Ministry; MINCyT) is the highest authority in the Argentine scientific arena. In addition to the budgetary resources of the Argentine state, MINCyT has US$ 925.7 million of financing from the Inter-American Development Bank and the World Bank at its disposal for its projects (MINCyT, 2009).

The Argentine R&D sector has a significant amount of qualified human resources. In particular, Argentina has a long history of success in biomedical research, and its achievements include two Nobel Prize winners.[54] A third

53 Decree No. 509/2007.

54 Bernardo Houssay was awarded the 1947 Nobel Prize in Physiology or Medicine for his discovery of the course of catalytic conversion of glycogen (see http://nobelprize.org/nobel_prizes/medicine/laureates/1947/). In 1970, Luis Federico Leloir won the Nobel Prize in Chemistry for his discovery of sugar nucleotides and their role in the biosynthesis of carbohydrates (see http://nobelprize.org/nobel_prizes/chemistry/laureates/1970/leloir-bio.html).

Nobel Prize was granted to an Argentine-educated researcher who carried out his work in the United Kingdom.[55]

Weaknesses in the scientific technology sector include low levels of investment in R&D, particularly by the private sector; lack of coordination between projects; a weak culture of intellectual property protection; scant communication between the public and private sectors; and the difficulty of preventing the most highly qualified scientists and technicians from accepting other employment opportunities internationally.[56] Over the past 20 years, the Argentine Government has implemented diverse policies in an attempt to overcome these weaknesses.

ANPCyT is the executing arm of MINCyT. ANPCyT manages several programmes aimed at the promotion of R&D. Specifically, it has instituted the Fondo Tecnológico Argentino (Argentine Technology Fund; FONTAR) and the Fondo para la Investigación Científica y Tecnológica (Scientific and Technological Research Fund; FONCYT).

FONTAR supports projects designed to improve productivity in the private sector through technological innovation. FONTAR broadcasts public calls for applicants and rewards those qualified with funding. The organization also has some funds that are permanently open to applications. In 2009, FONTAR approved 501 projects, totalling approximately US$ 72 million (MINCyT, 2009).

FONCYT engages in the promotion of research projects that aim to create new scientific and technological know-how. There are various promotion instruments and funds awarded through government bids for applicants. In 2009, FONCYT approved 1010 projects and provided funding in the amount of approximately US$ 109 million (MINCyT, 2009).

In addition to these instruments, which are applied generally to all industrial sectors, MINCyT focuses on three strategic knowledge areas and four strategic sectors. The strategic knowledge areas are the three cross-technology platforms: biotechnology, nanotechnology and ICT. The four MINCyT strategic sectors include the health, agroindustrial, energy and social development sectors.[57] As a result, the manufacture and development of vaccines and medicinal drugs are at the intersection of the principle axes of the Argentine scientific-technological policy.

The Fondo Sectorial Argentino (Argentine Sectoral Fund; FONARSEC) is a fund created in 2009 and dedicated to investing in MINCyT's strategic knowledge

55 César Milstein won the 1984 Nobel Prize in Physiology or Medicine for his theories concerning the specificity in development and control of the immune system, and the discovery of the principle for production of monoclonal antibodies (see http://nobelprize.org/nobel_prizes/medicine/laureates/1984/press.html).

56 In relation to the problem of retaining qualified scientists and technicians in Argentina, the Argentine Government established the highly successful Roots programme to repatriate scientists. As of March 2010, 714 researchers had returned to Argentina through this programme. The programme was declared a Policy of the State by Law No. 26 421.

57 See Subsecretaría de Políticas en Ciencias, Tecnología e Innovación Productiva, Regulations No. 002/2010 (11 February 2010), 003/2010 (15 February 2010) and 004/2010 (15 February 2010).

areas and sectors. FONARSEC aims to improve competition in these sectors, contribute to finding solutions to diagnosed problems, and answer the demands of society, business and the state. FONARSEC has financed projects to refurbish works, update infrastructure and equip universities with technology, and projects aimed at creating specialized university programmes to train managers and technology linkers. In its first year, FONARSEC approved 51 projects and provided funding of US$ 30 million.[58]

6. Analysis of ELEA

Since 2002, the Argentine pharmaceutical market has experienced very high rates of growth. As the market, in general, has grown, ELEA has also grown. It has increased its market share and doubled its sales over the past 5 years. Now, the company's principal objective is to maintain its leadership position in the local market and to increase its position in the Latin American market as a whole. ELEA's current position is the result of the strategies described below.

First, ELEA adopted the traditional model implemented by other Argentine laboratories of competing in the market without obtaining patent protection for its own branded products. Following the paradigm that serves as the foundation of this model, ELEA has introduced over 50 new products and presentations into the market since 2007, the launch of which allowed the company to consolidate its market share. By implementing this strategy, ELEA has achieved significant success, as evidenced by its positioning as the absolute leader in various market segments.[59] The majority of the products for which ELEA is a leader are those that it manufactures under its own brand, although in a few instances the position was gained through the production of licensed products.

Second, ELEA's successful merger with GYM, which granted to ELEA the exclusive licence for Parke Davis products, also propelled the company to the levels at which it currently operates. Through its merger with GYM, ELEA became the fifth largest laboratory in Argentina in terms of sales, as well as a much more efficient enterprise. However, considering that the licence is more than 20 years old and that Pfizer could end the relationship at any time, assuming compliance with the contractual requirements as regards indemnification and minimum notice periods, the question arises as to how ELEA would be affected if the licence agreement came to an end and how it would offset the lost income stemming from termination of the licence.

Third, ELEA's growth strategy is based on the development of new medications and diagnostic kits based on biotechnology, which has also led to the company's commercial success. ELEA's own R&D unit, working alone or in conjunction with the Argentine and Cuban universities and public research centres with which the company has formed strategic alliances, realized these

58 Ibid.

59 Source: ELEA and IMS Health Argentina.

discoveries and inventions. Some of these innovations are already available on the market.

The strategic alliances that ELEA formed with research centres and universities have generated a process of transfer of knowledge and technology from the public to the private sector; however, these partnerships have certainly generated positive impacts for the institutional partners as well. The researchers' work has been the subject of numerous publications in international magazines and digests, scientific works and textbooks. Furthermore, the researchers, universities and research centres have realized increased income since entering into partnerships with ELEA. One source of this increased income is the royalty charged on the knowledge that the partner generated and for the provision of the partner's services. Also, from a human resources perspective, the strategic alliances with ELEA have had a large impact, particularly regarding the hiring and retention of doctors, fellows and support staff, the modernization of laboratories and the acquisition of new equipment. All of these externalities are positive in and of themselves, but their impact has been amplified through the cross-fertilization of ideas and synergies between ELEA and its strategic alliance partners. It is also important to note that the success of ELEA and its partners demonstrates that it is feasible to reap the fruits of an R&D model based on South–South international cooperation, cooperation between universities, research institutions and private enterprise, and public and private financing.

The main challenge that lies ahead for ELEA and its partners is the completion of the phase III studies for racotumomab and completion of the development of the other cancer vaccines and drugs based on molecular biotechnology that the company has in development.

The participation of ELEA in the Sinergium consortium also deserves special mention. ELEA's participation in the consortium affords the company the opportunity to grow in the vaccine market, which represented only 0.2% of the company's sales in 2009 (see Figure 1). Although the contract awarded by the Argentine Government is for the production of influenza vaccines, the investment could be more attractive if the consortium is able to erect a multipurpose plant that would permit the manufacture of vaccines for other diseases as well.

ANMAT's interaction in the construction of the plant and the transfer of technology will be key to the project's success. It may be advisable for the consortium to establish a consultative mechanism with ANMAT to ensure that plant construction and the transfer of technology comply with ANMAT's requirements from the commencement of construction of the plant, so as to avoid wasting time and resources.

On the other hand, if the project is limited to the production of the influenza vaccine, Sinergium should not lose sight of the possibility of building extra capacity in order to have the opportunity to export surplus vaccines and fulfil the demands of other international organizations, such as United

Nations Children's Fund (UNICEF), other United Nations (UN) organizations or PAHO's Revolving Fund. However, for Sinergium to provide vaccines to these organizations, it must meet all of the criteria for prequalification that are provided by the World Health Organization (WHO, 2011). In conclusion, Sinergium and its individual members must work very closely with ANMAT to optimize the benefits of the future vaccine manufacturing facility.

ELEA's shareholders and their ties to organizations at all points on the supply chain, and their links to the pharmachemical sector, provide an enormous competitive advantage. Although the company is not vertically integrated, in that it does not produce APIs, formulate the drugs and directly distribute them, the company has obtained similar efficiencies through relationships with domestic and international companies that have been brokered by its shareholders.

The relationship with Chemo Group has provided ELEA with early access to therapeutics that are new to the Argentine or regional market or have few competitors. This access has allowed ELEA to gain control over portions of the market before competitors enter or are able to consolidate their positions. Although the relationship with Disprofarma has contributed to the company's improved efficiency, it is also viewed as a motivation to maintain current licences and to obtain new licences.

Finally, it seems that the company still enjoys a high level of international growth potential, particularly in the Latin American market. The company exports to diverse destinations but has thus far been unable to acquire a significant volume of business in relation to its overall size.

7. Implications of local production and related technology transfer on access to medicines

ELEA has contributed to the improvement of access to medicines in Argentina by making available new treatments. In the area of biotechnology, the company produces, inter alia, a diagnostic kit for the early diagnosis of diabetes mellitus and other autoimmune diseases and develops a tumour indicator for melanoma. In addition, ELEA is currently developing new vaccines against cancer, as illustrated by ongoing phase III clinical trials on racotumomab as a vaccine for non-small-cell lung cancer. Finally, ELEA's has developed a new antitussive drug, which is marketed throughout Latin America.

The focus by ELEA on biotechnology-based new medications and diagnostic kits represents a first step in longer-term efforts to establish itself in the important area of vaccines production. Capacity in this area, including for exports, could assist ELEA in finding a niche market vis-à-vis large foreign producers of high-volume, affordable generic chemical products.

The research team was not able to obtain comparative pricing data between ELEA and other firms in the Argentine market. In the absence of such data, it is not possible to conclude the effect of ELEA products on overall prices in Argentina. Argentina has a market, however, where branded generics are available at slightly below the prices charged by foreign originator companies for similar products.

Of particular note are Argentina's efforts at becoming a producer of APIs. Although these are mainly niche APIs, these raw materials represent a significant effort at expanding the source for APIs globally and could perhaps serve as a model for other countries seeking to develop API production capacity (see next section, finding no. 3).

8. Policy-relevant findings

The information gathered on the Argentine pharmaceutical market in general and on ELEA in particular gives rise to the following principal policy-relevant findings:

1. Although ELEA seems to be one of the most advanced pharmaceutical producers in Argentina, especially as far as its efficient R&D networks are concerned, the core of its success, i.e. a well-skilled workforce, is typical for the entire pharmaceutical sector in Argentina. This case study shows that some firms in Argentina have attained a level of sophistication and technical capacity that contributes to greater access to medicines through discovery and development of new medicaments and vaccines. Argentine pharmaceutical laboratories, particularly the large and medium-sized enterprises, have evolved into entities that are developing original products that go beyond traditional innovations on new formulations, associations or processes. In some cases, the Argentine laboratories' R&D departments have devised original innovations, especially in the fields of biotechnology and nanotechnology.

2. Argentine pharmaceutical companies took form over several decades. During this time there were several significant policy and economic factors that supported this gradual development: the availability of skilled personnel as a result of a solid educational system; the prohibition of pharmaceutical product patents (that expired in 1995); the protection of the domestic sector through tariffs on foreign products (modified in the 1990s); consistent access to APIs on the international market; a governmental system for granting marketing authorization by similarity (i.e. no exclusive rights in originator test data); and a gradual and yet continuous increase in the levels of GMP that permitted a gradual phasing-in of the necessary investments that would allow compliance with increasingly strict regulatory requirements.

The practice of approving drugs by similarity and the requirement that bioequivalence tests be conducted only on high-risk drugs and ARVs has contributed to the preservation of a competitive pharmaceutical market in

Argentina, and favours new entrants and high levels of competition in the generic drug market.

3. The existence of a strong domestic pharmaceutical industry is not necessarily sufficient to establish a pharmachemical sector with the power to have significant impact in the substitution of imported APIs. The primary obstacle is not technological in nature. In the interviews conducted for this case study, it became evident that the country employs qualified technical personnel – although it would be helpful to improve basic training in chemistry – and possesses the capacity to generate requisite information for health authority registries (e.g. drug master files).

The main impediment to the creation of self-sufficiency in APIs production is that the volume of the Argentine market does not facilitate the ability of local firms to compete with Indian and Chinese pharmachemical laboratories. For this reason, the sector must work to widen its market in order to increase its ability to compete with international firms. Following the example set by ELEA, the sector could consider identifying market niches and specialize in low-volume, high-value APIs such as hormonal products, and focus on the development of biotechnology-based molecules.

4. An important element playing in favour of the Argentinean industry is its close geographical, linguistic and cultural relationships with other Latin American countries. It is for this reason that Argentine exports of pharmaceutical products and APIs have become increasingly significant, in particular for the fellow Mercosur countries, followed by the rest of Latin America. This trend has also contributed to the creation and consolidation of Argentine multinational pharmaceutical companies such as Roemmers, Bagó, and Raffo/Tecnofarma. These companies have established subsidiaries, branches and plants in other countries, permitting production on greater scales and, consequently, improving competitiveness in the global market.

Therefore, the challenges that lie ahead are to consolidate and grow the industry's exporter profile, raise the technological value of exported products, and increase the volume of exports to developed countries where the volume of Argentine exports still lags. To this end, domestic pharmaceutical companies will need to invest significantly to achieve the levels of GMP required by the regulatory agencies of those countries, and to develop commercial networks abroad.

5. Parts of the Argentine pharmaceutical industry have demonstrated their market competitiveness on the national and regional level, in particular through their ties with Latin American export markets, their ability to reverse-engineer, and their cooperation with universities and R&D centres. The industry has also shown that it has the wherewithal to achieve further development in the pharmachemical sector. Furthermore, the industry possesses the necessary infrastructure, human capital and knowledge to receive transferred technology for the production of drugs and vaccines for type I, II and III diseases.

6. The traditional north–south models for the transfer of technology between private companies with the support of effective technology no longer appear to be a valid option. Agreements therefore focus on trademark licences rather than transfer of technology. On the one hand, the formulation of licensed drugs does not cause insurmountable problems for technologically developed licensees such as ELEA or even for smaller firms, which do not have limitations on the supply of APIs in the international market. On the other hand, when licences are granted to market drugs that are truly therapeutic innovations, whether patented or not, the licensees merely act as distributors or, at most, packagers of finished products imported in bulk. In this context it seems that the main incentive for a multinational laboratory to grant a licence to a domestic laboratory is the understanding that the licensee has of the local market and the licensee's position in the distribution chain, rather than the transfer of technology.

The transfer of technology to Sinergium that will facilitate the construction of the plant to manufacture influenza vaccines is an exception to the previously described scenario. Various factors give rise to this exception, such as the participation of Novartis in the joint venture, the presence of an unmet global demand for the vaccines, and the exclusive 10-year supply arrangement with the Argentine Government.

7. A significant portion of Argentine innovation is generated through associations with universities and public research centres. In Argentina, there exists a favourable environment for private entities to enter into these associations, which, although in their infancy and not very widespread, have led to increased R&D activity. The development of the racotumomab cancer vaccine is one example of a drug developed through one of these associations. As explained above, this model is supported by a network of public and private entities, self-funding, cooperation among companies from different countries, and an effective use of state-offered aid for R&D.

Nevertheless, this model must be consolidated over time. Although public and private investment in R&D has increased in recent years, the levels remain below those in developed countries. Also, many laboratories are unaware of available R&D incentives or underutilize them. To overcome this ignorance and to increase exploitation of the available incentives, there must be strengthened communication efforts and a strengthening of the relationship between R&D centres and universities, and the private sector.

Some companies have opted to implement similar strategic alliances as ELEA with the assistance of research centres or companies based in developed countries. For example, Gador partners with the British firm PeptiCel to develop a vaccine against Chagas disease and the Dutch Leiden University in the area of bisphosphonates.

8. ELEA and its partners have developed a creative model to finance the phase III studies of racotumomab. In addition to assistance from the Argentine Government, ELEA and its partners are financing these studies with funds

received as a prepayment of a portion of the royalties for licences granted to companies in other parts of the world for the future use of the new molecule in their respective markets upon authorization of the health regulator.

9. Argentine laboratories' investment is directed towards drugs and vaccines for the treatment of type I diseases. According to the interviews conducted for this study, the market for type II and type III diseases does not justify investment from the perspective of private Argentine investors. This is due to the fact that most people with type II and type III diseases tend to be poor and without sufficient resources to buy medicines. In this context, traditional mechanisms to incentivize investment, such as patents and test data protection, are insufficient.

This issue therefore requires the implementation of new mechanisms for incentives and funding. The federal state could play a fundamental role as coordinator of the various lines of research that are moving forward with regard to type II and type III diseases in Argentina. It would be helpful if the Argentine Government could see its role in ensuring the prioritization of these diseases, and oversee the administration and direction of funding. The productive relationship between the public and private sectors over the past few years is one example of a potential, but as yet unused, source for research on these diseases.

10. The state's purchasing power should be explored as an alternative tool to promote the development of vaccines and drugs for the treatment of type II and type III diseases. The mechanism adopted by the Argentine Government to grant an exclusive 10-year contract for the purchase of influenza vaccines in exchange for the installation of a plant to produce the vaccines in the country could be applied not only to the transfer of technology for type I diseases but also for the generation of new medicines and vaccines for type II and type III diseases.

References

ANMAT. La ANMAT y la bioequivalencia. *Consultor de Salud*, 2006a, 375:4.

ANMAT. La ANMAT y la bioequivalencia. *Consultor de Salud*, 2006b, 376:4.

ANMAT. *Medicamentos de alto riesgo autorizados para su comercialización*. Buenos Aires, Administración Nacional de Medicamentos, Alimentos y Tecnología Médica, 2011a (http://www.anmat.gov.ar/listados/Listado_Alto_Riesgo_03-2011.pdf).

ANMAT. *Listado de antiretrovirales*. Buenos Aires, Administración Nacional de Medicamentos, Alimentos y Tecnología Médica, 2011b (http://www.anmat.gov.ar/listados/Listado_antirretrovirales.pdf).

CILFA. *Plan estratégico para el desarrollo del sector farmacéutico y farmoquímico nacional 2007–2011*. Buenos Aires, Cámara Industrial de Laboratorios Farmacéuticos Argentinos, 2006 (http://www.cilfa.org.ar/archivos/File/biblioteca/planestrategico/Plan-estrategico%20CILFA.pdf).

CILFA. *Programa de fortalecimiento del comercio exterior de la industria farmacéutica y farmoquímica Argentina 2008–2012*. Buenos Aires, Cámara Industrial de Laboratorios Farmacéuticos Argentinos, 2007.

De la Puente C et al. *Propiedad intelectual y medicamentos: el caso de la República Argentina*. Serie de Estudios ISALUD No. 9, Buenos Aires, Universidad ISALUD, 2009.

Genovesi LM. *Patentes y medicamentos: Un tema para debater*. Buenos Aires, Fundación Argentina y el Mundo, 1995.

INDEC. *Encuesta permanente de hogares continua*. Buenos Aires, Instituto Nacional de Estadística y Censos, 2006.

INDEC. *La industria farmacéutica en la Argentina: Informes cuatrimestrales 2009*. Buenos Aires, Instituto Nacional de Estadística y Censos, 2009a.

INDEC. *Grandes Empresas en Argentina, February 2009*. Buenos Aires, Instituto Nacional de Estadística y Censos, 2009b.

INDEC. *Censo 2010: Resultados provisionales*. Buenos Aires, Instituto Nacional de Estadística y Censos, 2010.

Katz J. *La industria farmacéutica Argentina: Estructura y comportamiento*. Buenos Aires, Centro de Investigaciones Económicas, Instituto Torcuato Di Tella, 1973.

Katz J. *Oligopolio, firmas nacionales y empresas multinacionales: La industria farmacéutica argentina, Editorial Siglo XXI*. Buenos Aires, 1974.

Katz J. *La industria farmacéutica y farmoquímica: desarrollo histórico y posibilidades futuras (Argentina, Brasil y México)*. Estudios e Informes de CEPAL no. 65. Santiago de Chile, Economic Commission for Latin America, 1987.

Katz J, Burachik G. *La industria farmacéutica y farmoquímica argentina en la década del noventa*. Buenos Aires, 1992.

MINCyT. *Indicadores de ciencia y tecnología Argentina 2008*. Buenos Aires, Ministerio de Ciencia, Tecnología e Innovación Productiva, 2008a (http://www.mincyt.gov.ar/multimedia/archivo/archivos/Indicadores_WEB4mb.pdf).

MINCyT. *Anuario FONTAR 2008*. Buenos Aires, Ministerio de Ciencia, Tecnología e Innovación Productiva, 2008b (http://www.mincyt.gov.ar/multimedia/archivo/archivos/Anuario_Fontar_2008.pdf).

MINCyT. *Resultados de gestión 2009*. Buenos Aires, Ministerio de Ciencia, Tecnología e Innovación Productiva, 2009 (http://www.mincyt.gov.ar/documentos/Presentacion_2009.pdf).

Ministerio de Salud, PAHO. *Indicadores básicos: Argentina*. Buenos Aires, Ministerio de Salud and Pan American Health Organization, 2009.

Nofal B et al. *Inward FDI in Argentina and its policy context: Columbia FDI profiles*. New York, Vale Columbia Center on Sustainable International Investment, 2010.

Panadeiros M. *Nuevas estrategias competitivas en la industria farmacéutica Argentina y reconocimiento de la propiedad intelectual*. Córdoba, Fundación de Investigaciones Económicas Latinoamericanas, 2002.

RICYT. *Red de Indicadores de Ciencia y Tecnología Iberoamericana e Interamericana*. Buenos Aires, Red de Indicadores de Ciencia y Tecnología, 2010 (http://bd.ricyt.org/explorer.php/query/submit?excel=on&indicators[]=GAS&syear=1990&eyear=2008&).

Santoro FM. *Innovación y sendero evolutivo en la industria farmacéutica: los casos de Argentina y España*. Cadernos de Gestão Tecnológica no. 48. São Paulo, Universidad de São Paulo, Programa Ibero-americano de Ciencia y Tecnología para el Desarrollo, 2000.

UNCTAD. *The least developed countries report 2007*. New York and Geneva, United Nations Conference on Trade and Development, 2007.

UNCTAD. *World investment report 2009: Transnational corporations, agricultural production and development*. New York and Geneva, United Nations Conference on Trade and Development, 2009.

UNDP. *Human development report 2009*. New York, United Nations Development Programme, 2009.

WHO. *Procedure for assessing the acceptability, in principle, of vaccines for purchase by United Nations agencies*. WHO/IVB/05.19. Geneva, World Health Organization, 2011 (http://www.who.int/immunization/documents/WHO_IVB_05.19/en/index.html).

WTO. WT/DS171/3, WT/DS196/4, IP/D/18/Add.1, IP/D/22/Add.1, Argentina – patent protection for pharmaceuticals and test data protection for agricultural chemicals (WT/DS171) and Argentina – certain measures on the protection of patents and test data (WT/DS196), Notification of Mutually Agreed Solution According to the Conditions Set Forth in the Agreement, 22 June 2002. Geneva, World Trade Organization.

Annex: Interviewed individuals and institutions

The following 18 individuals/institutions were interviewed:

Pharmaceutical experts

Alberto Álvarez Saavedra, CEO, Gador S.A., Argentina

Néstor Annibali, Biotechnology Manager, Laboratorio Beta S.A., Argentina

Julio Andrés Bellomo, Medical Director, Laboratorio Roemmers S.A.I.C.F., Argentina

Jorge Belluzzo, CEO, Laboratorios Raffo S.A., Argentina

Cesáreo Lachiondo, Chief Financial Officer, Laboratorio Beta S.A., Argentina

Mirta Levis, Intellectual Property Director, Cámara Industrial de Laboratorios Farmacéuticos Argentinos (CILFA), Argentina

Luis Alberto Rodríguez, Chief Financial Officer, Gador S.A., Argentina

Patricio Rodríguez-Espósito, Director, Tecnofarma S.A., Argentina

Federico Santoro, Business Development Director, Elea, Argentina

Hugo Sigman, Elea and Chemo Group shareholder

Representatives of the Argentine Government

Carlos Chiale, Director, ANMAT

Adrián Galli Basualdo, Chief, Judicial Matters Department, ANMAT

Vanessa Lowenstein, Advisor, MINCYT

Eduardo Arias, Patent Commissioner, INPI

María Georgina Gerde, Patent Legal Advisor, INPI

Representatives of universities

Alberto Boveris, Dean, Pharmacy and Biochemist School, University of Buenos Aires

Darío Codner, Under Secretary of Research and Transfer of Technology, Quilmes National University

Representative of nongovernmental organizations

Graciela Ciccia, Innovation and Technological Development Director, Fundación Mundo Sano, Argentina

Case study 2

Bangladesh

This study on Bangladesh was carried out by Padmashree Gehl Sampath, Economic Affairs Officer, UNCTAD and formerly Technical Officer at the Secretariat for Public Health, Innovation and Intellectual Property, WHO, and Ermias Biadgleng and Christoph Spennemann, legal experts of the Intellectual Property Unit, Investment Capacity-Building Branch, Division on Investment and Enterprise of UNCTAD. Inputs for the study were collected during a field mission to Dhaka, Bangladesh from 19 to 26 February 2010. The case study report was finalized under the supervision of Kiyoshi Adachi, Legal Officer and Chief, Intellectual Property Unit, and the overall responsibility of Mr James Zhan, Director of the Division on Investment and Enterprise, and Mrs Nazha Benabbes Taarji, Officer-in-Charge, Investment Capacity-Building Branch.

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Abbreviations

ADF	Asthma Drug Facility
BAPI	Bangladesh Association of Pharmaceutical Industries
BPL	Beximco Pharmaceuticals Ltd
CFC	chlorofluorocarbon
DGDA	Directorate General of Drug Administration of Bangladesh
GSK	GlaxoSmithKline
GIZ	Gesellschaft für Internationale Zusammenarbeit
IV	intravenous
KfW	Kreditanstalt für Wiederaufbau
MDI	metered dose inhaler
OSD	oral solid dosage
Square	Square Pharmaceuticals Ltd.
TGA	Therapeutic Goods Administration (Australia)

1. Background and methodology

This case study is designed to investigate pharmaceutical production in a least-developed country (LDC) where there is a thriving pharmaceutical industry, the sources of the industry's technology, and the reasons for its sustainability. Specifically, this case study examines how Bangladesh, an LDC, managed to build a technological base for pharmaceutical production and considers the issues that its firms currently face, including the challenges of producing low-cost, high-quality active pharmaceutical ingredients (APIs).

UNCTAD thanks Beximco Pharmaceuticals Ltd (BPL) and Square Pharmaceuticals Ltd. (Square) for agreeing to be the subject firms for this case study. UNCTAD also thanks the German Gesellschaft für Internationale Zusammenarbeit (GIZ) and the Kreditanstalt für Wiederaufbau (KfW) offices in Bangladesh for assisting UNCTAD in facilitating the arrangement of interviews during the field mission to Dhaka.

The study uses a case study research methodology consisting of collection of data through open-ended, face-to-face interviews in Bangladesh, as well as reviews of relevant regulations, public policy documents and academic literature. Interviewees were identified through purposive sampling. During the fact-finding mission to Bangladesh from 19 February to 3 March 2010, the following 27 individuals/institutions were interviewed: 8 representatives from the pharmaceutical industry (from BPL, Square, Bangladesh Association of Pharmaceutical Industry (BAPI), Acme Pharmaceuticals and Aristopharma), 6 members of the pharmaceutical distribution network (with visits to 4 independent pharmacies), 6 Bangladeshi Government representatives (Directorate General of Drug Administration, Ministry of Health and Family Welfare and Ministry of Industries), 3 representatives of academia (University of Dhaka), 3 international organizations (including the World Bank), and 1 research institute representative (International Centre for Diarrhoeal Disease Research).[1]

In addition, a semi-structured questionnaire designed to capture the dynamics of firm-level activities related to production and technology transfer was administered to the firms, the results of which are included in the case study where relevant.[2]

This case study defines "innovation" as any new products, processes and organizational changes that are new to the enterprise, context and country in question, although not necessarily to the world at large (UNCTAD, 2007). In keeping with the scope of the project, "technology transfer" was defined as all components of technology, both codified (in terms of blueprints, hardware, machine parts and plant technologies) and tacit (know-how and skills), that are essential to enhance the capacity of the organizations in the recipient country to produce pharmaceutical products.[3]

1 See Annex: List of interviewed individuals and institutions.

2 See Annex: Field questionnaire.

3 A uniform definition of technology transfer was used for all components of the project, including the trends survey, the regional dialogues and the stakeholder analysis.

2. Description of the firms, structure and range of products

BPL and Square are among the largest pharmaceutical companies in Bangladesh in terms of capital and market share. Square and BPL started as private limited companies in 1958 and 1976, respectively. Both companies produce and market branded generics and, although on a smaller scale and from advanced intermediaries, APIs. The manufacturing and marketing of pharmaceuticals form the core business of the BPL and Square conglomerates. The conglomerates have, however, branched out to other sectors following their initial successes in pharmaceuticals.

The Beximco Group, of which BPL is a part, includes 21 companies in pharmaceuticals, information and communication technologies (ICT), media, textiles, travel services, ceramics, jute production, finance and investment, energy and aviation. BPL has been trading in the domestic capital market since 1985, and soon after this it expanded its plants for oral solid dosage (OSD), metered dose inhalers (MDIs) and intravenous (IV) fluids. BPL started producing and exporting a limited quantity of APIs in 1992 and entered export markets such as the Russian Federation and Singapore in addition to several other countries in Africa, Asia and Latin America. Today BPL is among the biggest pharmaceutical companies in Bangladesh, employing 2310 people, with authorized capital of 2000 million taka (approximately US$ 29.4 million at the time of writing) and paid-up capital of 1259.57 million taka (approximately US$ 18.5 million) held by around 66 000 shareholders. In addition to debt financing, BPL is listed on the Chittagong Stock Exchange and the Dhaka Stock Exchange in Bangladesh, and in 2005 it was listed on the Alternative Investment Market (AIM) of the London Stock Exchange (BPL, 2009).[4] BPL registered a net profit of 545 341 million taka (approximately US$ 8 million) in 2008 (BPL, 2008). According to interviews with BPL officials, the Beximco Group as a whole accounts for approximately 0.8% of the gross domestic product (GDP) of Bangladesh.

BPL controls around 7.22% of the local market.[5] It has 410 generic brands and is strong in IV fluid products (28 products, which make up approximately 45% of the local market, according to interviews with BPL officials) and niche products such as MDIs. BPL manufactures the APIs for paracetamol and penicillin from an advanced intermediate stage.

BPL demonstrated significant growth in 2009, with a very strong sales performance in the domestic market, achieving around 43% growth in the

4 AIM is the London Stock Exchange's international market for smaller growing companies, including those at an early stage, those backed by venture capital, and more established companies that seek access to growth capital. BPL is listed on AIM by issuing a London Global Depository Receipt (GDR).

5 Statistical information on market share is not conclusive. According to the 2008 survey conducted by Intercontinental Marketing Services (IMS), a global pharmaceutical intelligence company, of the 250 companies, the top 10 – Square, BPL, Eskayef, Incepta, Acme, ACI, Opsonin, Renata, Aristopharma and Drug International – take up nearly 70% of the total domestic market. See the review of the IMS report from the Bangladesh Economic News (http://bangladesheconomy.wordpress.com).

first quarter, compared with the same period in 2008 (BPL, 2009).[6] BPL is a listed supplier for the United Nations Children's Fund (UNICEF) and the Asthma Drug Facility (ADF) for its chlorofluorocarbon (CFC)-free MDI, which is part of a new scheme launched under the 1987 Montreal Protocol on Substances that Deplete the Ozone Layer. BPL is qualified by multinational companies, including GlaxoSmithKline (GSK) for the manufacture of MDI and Global F Hoffmann La Roche for the production of OSD. It is also accredited for compliance with good manufacturing practices (GMP) by the Therapeutic Goods Administration (TGA) of Australia for its new OSD, MDI and spray manufacturing facilities. BPL also received GMP certification from the Gulf Central Committee for Drug Registration, the Executive Board of the Health Ministers' Council for the Gulf Cooperation Council, and the National Health Surveillance Agency (Anvisa) of Brazil (BPL, 2008, 2009).

The Square conglomerate includes 15 companies in the textile, consumer products, pharmaceuticals, ICT, media, finance, media and health sectors. Square went public in 1994, started its own production of APIs the next year, built a new plant in Dhaka in 2001, and launched its state-of-the-art cephalosporin[7] manufacturing facility in 2005 (Square, 2009). Today, Square is the largest Bangladeshi pharmaceutical firm, employing 3811 people, and with authorized capital of 5000 million taka (approximately US$ 73.5 million), of which 1207.22 million taka (approximately US$ 17.7 million) is paid up by 31 688 shareholders, registering a net profit of 1.89 billion taka (approximately US$ 28 million) in 2009. In addition to debt financing, Square is listed on the Chittagong Stock Exchange and the Dhaka Stock Exchange. It exports to around 34 countries (Square, 2009).[8] It has been the leading pharmaceutical company in the local market since 1985.

Square controls around 19.48 % of the local market.[9] Square markets branded generics in 611 preparations and is strong with its 44 products within the therapeutic range of injectables. The top-selling brands in Bangladesh have been Neoceptin (indicated for the treatment of ulcers) and NAPA (indicated for pain relief), manufactured and marketed by BPL; and Seclo (indicated for gastro-oesophageal reflux disease) and Neotack (indicated for the treatment of ulcers), manufactured and marketed by Square (Haq & Minul, 2008).

Like Beximco, Square expanded its production and growth by over 20% between 2008 and 2009. Its facilities include the Pabna Unit, its oldest plant, which started operation when the company was launched in 1958. The Dhaka unit is dedicated for OSD formulation and production and started operation in 2002. The Dhaka unit also includes a separate ophthalmic plant. Square

6 BPL's manufacturing facilities are spread across a 20-acre site near Dhaka. The facilities consist of an OSD plant, an MDI plant, an IV-fluid manufacturing plant, facilities for liquids, ointments, creams, suppositories, ophthalmic drops, injectables and nebulizer solutions, and an API unit for the production of paracetamol. It has API facilities outside the site for penicillin production and formulation. BPL maintains its own facilities for power generation to supply its manufacturing plants.

7 Cephalosporin is a class of antibiotics.

8 See also http://www.squarepharma.com.bd.

9 Statistical information on market share is not conclusive.

Cephalosporins Ltd. is a subsidiary of Square that was established in 2006, with a facility dedicated to the manufacturing of cephalosporin. The facility was built under the supervision of TELSTAR S.A. of Spain. Having started operations in 1995, Square also has an API unit, where it carries out activities from an advanced intermediate stage. Additionally, it has two other units, for animal health and pesticides. Finally, in 2009 Square opened an insulin bottling plant that started operation by importing crystals from China and acquiring their formulation from Biogen (Switzerland). The plant can produce up to 13 million insulin vials per year.

One of Square's pharmaceutical production facilities is approved by the United Kingdom Medicines and Healthcare Products Regulatory Agency (MHRA) and enlisted by UNICEF. Its oldest facility at Pabna complies with World Health Organization (WHO) current/good manufacturing practices (cGMP) requirements and earned an ISO 9001 Certificate in 1998; but none of its products is currently cGMP-qualified.[10]

3. Technological capacity of BPL and Square

The establishment of Square and BPL dates back to the pre-1982 investment framework of Bangladesh, when eight multinational corporations controlled up to 70% of the local market. Both of these private-sector initiatives of Bangladeshi entrepreneurs built their capacity at the early stage through technical collaboration with multinational corporations operating in Bangladesh, and followed it up under licensing arrangements, as well as marketing and contract manufacturing to branch off on their own.

Although the first school of pharmacy was established at the University of Dhaka in 1964, the public sector institutions were not strong enough to support the pharmaceutical sector in the 1980s.[11] As a result, field interviews with Square reveal that the expertise was gained from India in the initial stages of its operation. Square expanded its production from its modest start with minor formulations of different types of pharmaceuticals. The founder and current chairman of Square attributes the success of the company to its initial licensing arrangements with various multinational corporations.[12] Major expansion took place when Square entered a third-party licensing agreement with Jansen Pharmaceuticals of Belgium (a subsidiary of Johnson and Johnson International, United States of America) in 1974. The agreement allowed Square to manufacture and sell Jansen's products in Bangladesh. Similarly, BPL was producing in the 1980s under licences for two major foreign multinational corporations – Bayer AG (Germany) and Pharmacia & Upjohn Inc. (United States). These collaborations provided Square and BPL with their initial training and exposure to international standards of quality manufacturing.

10 See http://www.squarepharma.com.bd/DhakaUnit.html.

11 It is important to note that Bangladesh attained independence only in 1971, and the real task of setting up institutions for industrialization began in the 1980s.

12 Source: field interviews.

Following the implementation of the National Drug Policy of 1982, which placed several restrictions on local production of drugs by multinational corporations and launched government-established pharmaceutical companies for the manufacture of drugs for local needs, private entrepreneurial ventures in the sector received encouragement. Both Square and Beximco (along with several other local companies at the time) began to launch their own generic brands after 1982 (see detailed discussion below).

In their current operations, both Square and BPL continue to use the expertise of companies from developed countries for building and upgrading facilities and the introduction of new products, both of which involve the transfer of technology to Bangladesh. Some examples include:

- Square has hired the support of foreign experts to undertake bioequivalence studies for submission of its products for registration in countries such as Malaysia. Square officials, however, think that the capacity for bioequivalence is increasing in Bangladesh. Square also has plans to establish a bioequivalence centre, leveraging the Square Group's capacity in health care.
- BPL is now producing pharmaceutical products under contract for multinational companies following the changes in the National Drug Policy of Bangladesh in 2005 (see below). These include contract manufacturing of MDI for GSK. BPL considers the partnership with GSK as providing it with "much valuable expertise and know-how to manufacture world-class products".[13]
- Square is commissioning the construction of facilities for newer products such as MDI and IV fluids, and topical sprays for skin allergies. Field interviews reveal that Square intends to build these facilities in compliance with applicable European and United States standards. Square is currently relying on United States expertise in product development, quality assurance, manufacturing, regulatory and other relevant areas. Square officials revealed that a good number of generic products that go under the name of "new drug delivery systems" (NDDS)[14] are currently under development in-house for introduction in the United States market, upon approval by the United States Food and Drug Administration (FDA). Although the implementation of this project is not complete, at the time of the interviews, Square expected technology transfer gains to occur from the process of building United States-standard facilities and the formulation of products and establishment of manufacturing practices consistent with FDA standards.

Aside from BPL and Square, Bangladeshi pharmaceutical companies are increasingly involving foreign firms (in their private capacity as consultants) for improving their capacity. Asia Pacific Consultants Pty Ltd (an Australian company) provides specialized consultancy and support, especially in

13 See http://www.beximco-pharma.com.

14 New drug-delivery systems are also called "speciality generics". The name refers to generic products that rely on various drug-release mechanisms such as sustained release and heat resistance.

process development, facility design and construction management, GMP auditing, and introduction of laboratory information management systems for pharmaceutical companies in Bangladesh. It lists Aristopharma Ltd., Aventis, BPL, Opsonin Pharma Ltd., Popular Pharmaceutical Ltd., Renata Pharmaceuticals, Eskayef Bangladesh Ltd, Fisons Bangladesh Limited and Novartis (Bangladesh) Limited as some of its clients.[15]

Field interviews reveal that accreditation and expected proceeds from sale in the United States, the United Kingdom of Great Britain and Northern Ireland, Australian and other regulated markets (including some semi-regulated markets of Latin America) seem to be the key drivers for technological upgrading in the case of both firms. As noted above, BPL is qualified for certain products by multinational companies, including GSK and Global F Hoffmann La Roche. It is also accredited for GMP compliance by a number of foreign regulatory bodies for certain products. Square's facility in Dhaka is approved by the MHRA. Square was also expecting an inspection of its facility by TGA in the third quarter of 2010.

Both BPL and Square have the capacity to produce antiviral and antiretroviral (ARV) products. BPL currently produces six first-line ARV combinations and introduced its generic version of Tamiflu under the name of Oseflu in 2006. Roche has recently announced a technology transfer agreement with BPL for the production of a second-line human immunodeficiency virus (HIV)/ acquired immunodeficiency syndrome (AIDS) medicine, saquinavir (Fortovase or Invirase). At the time of the field interviews with Beximco, the activity had not commenced and the market value of the drugs produced was unclear, since the WHO (2006) ARV guidelines advise against the use of the drug as an independent medicine as such and recommend its use only as a booster in antiretroviral therapies (see also WHO, 2003).[16]

Square has produced first-line ARV combinations since 2007 (Gehl Sampath, 2007) but, despite plans for WHO prequalification for Square's products since 2007, field interviews show that little or no progress has been made on this front. Local firms in Bangladesh have tended to focus exclusively on the local market in designing firm-level production strategies historically, with a new trend of focusing on developed markets for select exports given the expectation of huge profit margins. BPL currently exports to 38 countries, including emerging economies such as Singapore, China, Hong Kong Special Administrative Region (Hong Kong SAR) and the Russian Federation. BPL has also received marketing authorization from Chilean authorities (Instituto de Salud Publica de Chile) for a number of products, thus becoming the first Bangladeshi company to enter into the Latin American market. Square is also exporting to many developing countries, emerging economies and the United

15 See list of clients at http://www.a-p-c.com.au.

16 Beximco officials participating in the field interview were unsure as to what extent the WHO ARV Guidelines were a factor in Roche's decision to transfer technology for the drug, but they welcomed it nevertheless, on grounds that the technology and expertise gained could be used to improve production capacity more generally beyond the production of saquinavir.

Kingdom.[17] The export activities of both companies are a small portion of their businesses (below 5% of total production, according to field interviews), although with highly diversified destinations, including LDCs, especially those in the Asia-Pacific region.

Bangladesh has very low HIV infection rates, according to both national and international estimates, and field interviews with company officials of Square and BPL reveal that the low local demand for ARV drugs is a major deterrent to scaling up production. Although field interviews with Square revealed that the company still intends to apply for GMP prequalification, its incentives to embark on expansion and GMP prequalification over the mid-term are unclear. Square and BPL also produce various antimalarial products for export, which would benefit from WHO prequalification.

The technological capacity of neither firm extends to being able to produce APIs from inception. The production of APIs constitutes a significant portion of the inputs needed to manufacture any drug (Gehl Sampath, 2010a). No company in Bangladesh produces APIs from scratch. Most firms import APIs from an advanced intermediate stage and perform the last few stages of API production in-house. However, the ability of firms to reverse-engineer drugs completely and manufacture APIs within the country will be critical to make their exports more competitive vis-à-vis the branded generic firms from China and India, from where most APIs for Bangladeshi pharmaceuticals are currently sourced. This case study found that pharmaceutical companies in Bangladesh have yet to fully master the capacity to produce APIs. They import 80% of the APIs needed to produce the finished products. For example, field interviews show that BPL is able to produce APIs for paracetamol and penicillin from advanced intermediate stages, and it imports the APIs it requires for all its other formulations. BPL's API production is for its own use, unlike Square, which also supplies APIs to many competitors, including BPL, Aventis, Novartis Bangladesh, Advanced Chemicals Industry, Eskayef Bangladesh, Opsonin Chemicals, Renata and Essential Drugs Co. (Business Monitor International, 2010).

To support the development of API production in Bangladesh, the Bangladeshi Government approved the establishment of an API industrial park during 2008–2010 (Business Monitor International, 2010). The only recent development in this regard was the acquisition of land for the industrial park in September 2009, and ongoing land filling for the park during 2010–2011, but actual groundwork has yet to start.[18]

4. The pharmaceutical market in Bangladesh

The population of Bangladesh has reached 153 million, according to a 2008 estimate, making it the seventh most populous nation in the world and one

17 See http://www.squarepharma.com.bd/CurrentExportMarket.html.

18 See http://bangladesheconomy.wordpress.com/2010/12/28/pharma-sector-to-get-api-park/.

of the world's most densely populated countries (Economic Intelligence Unit, 2009). Bangladesh's GDP in 2008 measured at purchasing power parity (PPP) stands at US$ 213.5 billion, according to World Bank data.[19] The GDP is projected to reach US$ 355.6 billion by 2014 at PPP. However, per-capita income is so low that the United Nations classifies the country among the 49 LDCs (UN-OHRLLS, 2010).[20] Despite being an LDC, Bangladesh is among the few developing countries that could be considered relatively self-sufficient in pharmaceutical products. Currently there are 5300 registered brands covering 450 generic drugs, most of which are produced locally (Gehl Sampath, 2007).[21]

According to the most recent (at the time of writing) data posted on the web site of the Directorate General of Drug Administration (DGDA) of the Ministry of Health of Bangladesh, there are 245 registered pharmaceutical companies in Bangladesh,[22] of which 135 are considered to be actively operational (Gehl Sampath, 2007). The companies include medium to large Bangladeshi companies with international links, specialized subsidiaries of multinational corporations, and a number of small companies (Gehl Sampath, 2007).[23] Despite the presence of such a large number of firms, the market is highly concentrated, with the top 10 companies (including Square and BPL) controlling 70% of the market (Gehl Sampath, 2007; World Bank, 2008a). As mentioned earlier, Square and BPL jointly control approximately 26% of the market.

Estimates of the local pharmaceutical market vary. A 2010 report notes in this regard that the total value of the local market for pharmaceuticals was about US$ 1.13 billion in 2009 (Business Monitor International, 2010). However, the BAPI executive director, Abdul Muktadir, founder and manager of Incepta Pharmaceuticals Ltd., which also ranks in the top five firms in the market in 2010, estimates the market size to be around US$ 700–800 million. Despite the very low per-capita income in Bangladesh, Bangladesh's economy has experienced dynamic growth over the past decade, with a very clear rise in exports in the key sectors of textiles and ready-made garments, agro-processing and pharmaceuticals (UNCTAD, 2007). In addition to the growing GDP, income from remittances accounts for the increase in per-capita expenditure on pharmaceuticals in the country.[24] The local market is also expanding due to a marked increase in newer forms of illnesses, mainly in the cardiovascular

19 The service sector contributes 52.4% of GDP, followed by industry at 27.4%; the rest is contributed by agriculture. See Economic Intelligence Unit (2009).

20 The second largest Asian LDC (of 15 in the region) in terms of population is Myanmar, which has 47 million people (2008 estimate) and covers a surface area much bigger than Bangladesh

21 There have been no new surveys of the sector since 2007 to update these figures.

22 See http://ddabd.org/allopathic.htm.

23 Of these, 34 companies are marked as "suspended" in the list of manufactures on the DGDA web site, although the reason for suspension is not provided.

24 The economy has grown by 5–6% over the past few years, despite inefficient state-owned enterprises, delays in exploiting natural gas resources, insufficient power supplies, and slow implementation of economic reforms (UN-OHRLLS, 2010). Bangladesh is the fifth country outside the Organisation for Economic Co-operation and Development (OECD) in terms of the total amount of remittances received from abroad. Remittances from Bangladeshis working outside their country stood at US$ 9.6 billion in 2008–2009 (Bangladesh Bank, 2010).

and respiratory ailment categories. These factors are considered to be some of the drivers for growth of the pharmaceutical industry in Bangladesh (Gehl Sampath, 2007). During interviews, pharmaceutical companies identified as drivers the growing income due to such remittances, expanding disease patterns, and a larger demand for pharmaceutical products in rural parts of the country.

Small independent pharmacies and drug stores are the principal means of distribution of pharmaceuticals in Bangladesh. The distributors are supplied by the pharmaceutical companies. Square, for example, operates 11 depots throughout the country (LankaBangla Securities Ltd, 2008). Of the 200 000 pharmacies and drug stores spread across the country, the government recognizes only 76 000 as licensed, indicating the presence of a large "grey" market (i.e. medicaments from non-authorized sources) for medicaments (World Bank, 2008a). Poor people cannot always afford to visit hospitals and clinics and have to rely on self-medication and advice from pharmacy staff.

The 1982 National Drug Policy (revised in 2005 and again in 2010) mandates price control to ensure access to medicines. The DGDA is vested with the mandate of controlling prices, but the implementation of the price control system is conditional on the issuance of a regulatory order by the Ministry of Health. A 1993 Price Control Order reduced the number of drugs that were under price control from 150 (as of 1982) to 117 drugs. A new update created in 2009 found that of these 117 drugs, an estimated 100 were obsolete and proposed 209 new drugs to be placed under price control in the interests of public health and greater access to medicines in Bangladesh. However, at the time of the field interviews, the DGDA was still awaiting a governmental order to implement the new 2009 update. In the absence of this, the DGDA will be able to control only 50 drugs from the previous 1993 list of drugs that were placed under price control, most of which have been found to be obsolete.

The pricing of all other pharmaceutical products is based on the indicative value for money price. The maximum retail price is broken down into trade price (75.5%), wholesale commission (2.3%), retail commission (12.0%) and value-added tax (VAT; 12.5%). Imported finished products are priced by adding a fixed percentage of mark-ups to the cost and freight price to arrive at the maximum retail price. The breakdown for the imported products includes trade price (88.89%) and retail commission (11.11%).[25]

Interviews with ministry officials and donor organizations active in the health sector conducted for the case study revealed a broad consensus that price control is nonfunctional or not effective at a general level. For all the other drugs being sold that are not under price control, in the absence of pressure on public expenditures or other incentives by the Ministry of Health, the indicative price may not be an optimal price.

25 These figures seem to suggest that retail commission is higher for locally produced pharmaceuticals than for those that are imported. See Bangladesh Ministry of Health and Family Welfare (1982, 2004) and Uddin Ahmad (2008).

Even in the absence of an effective price control mechanism, the presence of a competitive market with a large number of medium and large companies should theoretically be sufficient to provide ample space for price-based competition that is essential for greater access to medicines. This does not seem to be the case in the Bangladesh market, however. The increased concentration of the pharmaceutical market and the importance of company-based distribution networks for distribution of medicinal products both contribute to a market where branded competition does not necessarily contribute to lowering prices as close to the margin as could be expected.

5. The framework for local production and technology transfer in Bangladesh

5.1 National Drug Policy and regulations

As in all countries, medicines must be registered in order to distribute them in Bangladesh. Bangladesh's National Drug Policy in 1982 changed the broad framework for pharmaceutical production in the country by deregistering medicines considered unnecessary or useless by the health authorities.[26] It also prohibited all prescription chemicals not included in the latest edition of the British Pharmacopoeia or British Pharmaceutical Codex as medicine.[27] Subsequently, and for the first time, a list of 150 essential medicines and 100 specialized drugs was established.[28] The policy was motivated largely due to the lack of essential medicines in the market resulting from high prices of medicines being sold locally. These factors have been attributed primarily to certain restrictive business practices of multinational corporations at that time, the need to purchase raw materials at inflated prices from tied sources by multinational corporations, and the inability to access appropriate technology for local production at reasonable costs.

The multinational corporations, which lost a significant part of their product portfolio due to deregistration of products, were further de facto restricted to producing injectable vitamins for local supply by the 1982 National Drug Policy. Bangladeshi companies were also restricted from producing pharmaceuticals for multinationals under contract manufacturing or licence. As a result of these new restrictions, several multinational corporations sold out their companies to local entrepreneurs. For example, Pfizer (Bangladesh) is now Renata Limited, Imperial Chemical Industry is now Advanced Chemical Industries Limited (ACI), and Organon is now Nuvista Ltd, all of which are fully owned by Bangladeshis (Chowdhury & Rahman Kabir, 2009). The restrictions on alliances between local and multinational companies forced companies such as Square and BPL to adjust their businesses accordingly and to launch their own brands. Finally, the policy also set out a strategy for importation of

26 The Drug (Control) Ordinance, 1982 (order number VIII of 1982) deregistered and removed from the market medicines considered unnecessary and useless, including vitamin mixtures, tonics, alkalizers, cough mixtures, digestive enzymes and palliatives.

27 Bangladesh, National Drug Policy (1982), Annex III, no. x.

28 Bangladesh, National Drug Policy (1982), Annexes I and II.

APIs at an acceptable quality and at a competitive price. In any event, the 1982 policy appears to have had a major impact on the composition of the market: before 1982 multinationals controlled 70% of the local market, but now the position has been reversed, with local firms controlling the market.

The 1982 National Drug Policy was revised in 2005 and relaxed some of the earlier restrictions. For example, the 2005 Policy permits multinational corporations producing in Bangladesh to manufacture any pharmaceuticals for export to international markets. The 2005 Policy also lifted the ban on Bangladeshi companies to manufacture under contract and license for multinational corporations.[29] This served as a boost to local companies such as Beximco, which has now started contract manufacturing for the research and development (R&D)-based pharmaceutical transnational corporations.

A key restriction of the 1982 Policy has been retained in the 2005 version, however, and this relates to the restriction on importation of a pharmaceutical product or a close substitute of any pharmaceutical product thereof, so long as the pharmaceutical product is being produced in the country. This provision, originally intended to support local production, has now rendered the local firms controlling the market with no threat of any price-based competition from outside. The absence of any external price-based competition and the increasingly concentrated internal market leave the top local firms with ample scope to establish prices and engage in other potentially anticompetitive practices, to the detriment of the interest in greater access to medicines (Gehl Sampath, 2007; World Bank, 2008a; Bangladesh Health Watch, 2010).

The development and revision of the drug policy was led by a National Drug Policy Review Committee, with members from all relevant sectors. From the interviews, the local pharmaceutical industry took a lead role in determining the scope of the revised National Drug Policy of 2005. The industry is consulted through directly participating in various decision-making processes or through its representation by BAPI, although many dispute the effectiveness of the latter due to rivalries among its members.

The 2005 National Drug Policy also seeks to enforce cGMP. WHO promotes cGMP for good-quality production of medicines in developing countries. The responsibilities of assessing GMP compliance lie with the DGDA. The DGDA is the main body in Bangladesh empowered to supervise and implement all prevailing regulations related to importation, production and export of pharmaceuticals, in addition to promoting cGMP. It was upgraded from "department" status under the Ministry of Health and Family Welfare to "directorate general" status after the adoption of the 2005 revised National Drug Policy. The new status is supposed to provide the DGDA with full regulatory authority and responsibility in matters of drug registration and control. However, the DGDA suffers from extreme funding, staffing and technical competence constraints. During interviews, DGDA officials indicated that more than half of the currently government-approved posts for human resources necessary for the running of the DGDA are vacant and unlikely

29 Bangladesh, National Drug Policy (1982), Annex III, no. xii, xiii, xiv, xv and xvi.

to be filled soon. The civil service recruitment policies are said to be the bottlenecks in implementing DGDA capacity-building efforts. There are two government drug-testing laboratories, one in Dhaka at the Institute of Public Health and another in the Chittagong region. However, these laboratories have extremely limited capacity, with three technical staff in the Chittagong laboratory and eight technical staff in Dhaka. The entire country has only 28 post-surveillance personnel, of which 12 are active in Dhaka alone.[30] None of the DGDA laboratories has the capacity to test drugs for safety, efficacy or bioequivalence. There is neither a central reference laboratory nor any independent contract research organizations in the country. Companies that are exporting to international markets have their products tested and certified in established laboratories in other countries (for example, Square sends its products regularly to Malaysia) (Alam, 2009). The problem of pricing and quality of drugs is therefore very acute in the absence of any mechanism to check the efficacy of all the drugs being sold in the local market.

The DGDA's effectiveness is further constrained by the administrative quagmire of various organizations and committees involved in the relevant regulatory processes. The recommendation for registration of drugs by the DGDA comes from the Drug Control Committee. The National Drug Advisory Council advises on implementation of the National Drug Policy and the promotion of local pharmaceutical industries. There are also a Pricing Committee (which approves pricing decisions on medicaments) and a Standing Committee for Procurement and Import of Raw Materials and Finished Drugs (GIZ, 2007). Adding to this structure, the National Research Ethics Committee is responsible for reviewing all clinical trials of medicinal substances and advises the DGDA to ensure that the drugs available in the country fulfil the necessary requirements for safety, quality and efficacy. There is a clear public health need, therefore, for this governance structure to be reconciled with the changes introduced since 2005, especially in making the DGDA a full regulatory body, in ensuring the necessary facilities are available to the DGDA, the office is fully staffed and its authorities are not diluted. This is also important when considering the wide practice of self-medication by poor people who cannot afford physicians, and overuse of drugs, including in children.[31]

At the time of the field interviews, a new drug policy (2010) was being formulated for introduction in the country later in 2011. Some of the aforementioned issues could be tackled through this new drug policy.

30 Source: field interviews.

31 During interviews, the Child Health Unit, International Centre for Diarrhoeal Disease Research (ICDDR) stated that children take a lot of antibiotics, higher than the amount recommended by WHO, and are rapidly developing resistance. Marketing of drugs would need active regulation, as businesses are pushing drugs to each home and there are more unlicensed vendors than licensed drug stores in Bangladesh. Here, the work of the Child Health Unit, ICDDR on the social marketing system and treatment guidelines for pubic sector hospitals would need to be supported by the drug regulatory system.

5.2 Intellectual property

Bangladesh is among the few LDCs utilizing to some extent the various flexibilities provided for LDCs by the World Trade Organization (WTO) that support pharmaceutical production and marketing. The transition period lasting until 2016 (WTO/IP/C/25) exempted Bangladesh and other LDCs from implementing the provisions of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) on patent and protection of undisclosed information with respect to pharmaceutical products. The transition period also includes a waiver from obligations to provide exclusive marketing rights, granted by the WTO General Council in a separate decision in 2002.[32] According to the Bangladesh Patent and Design Law (1911), patents are available for new processes for the manufacture of chemical compounds, pharmaceutical compositions and microorganisms and for the article prepared or produced by the process. This provides a process patent regime in accordance with the flexibility provided for LDCs.[33] The Bangladeshi Government has issued an order for suspension of granting patents for pharmaceutical products, despite the fact that the Patent and Design Law does not provide for such patents.[34] In addition, the order introduces a "mailbox" for receiving patent applications during the time that pharmaceutical product patents continue to be unavailable (WTO, 2010). According to the Registrar of Patents, Designs and Copyrights, the mailbox system contains several pharmaceutical patent applications (Gehl Sampath, 2010b). If these applications are granted after 1 January 2016, any pharmaceutical substances addressed in granted applications could become unavailable to local generic producers (see also Box 1).

Bangladesh does not provide protection for undisclosed information submitted for pharmaceutical product approval/registration purposes concerning new chemical entities (WTO, 2006). Bangladesh currently does not provide exclusive marketing rights for pharmaceutical products, which is fully consistent with the flexibility provided for LDCs under the WTO General Council waiver decision from 2002 on exclusive marketing rights (see above). Another transition period allows LDCs to delay compliance with the rest of the provisions of the TRIPS Agreement until 2013.

32 WTO General Council decision: "Least-developed country members – obligations under Article 70.9 of the TRIPS Agreement with respect to pharmaceutical products", 8 July 2002, WTO document WT/L/478, 12 July 2002.

33 See Article 2(8), which defines "invention" as any manner of new manufacture and includes an improvement and an alleged invention, and Article 2(10), which defines "manufacture" as inclusive of any art, process or manner of producing, preparing or making an article, and also any article prepared or produced by manufacture (Patent and Design Act, Bangladesh, 1911). A similar conclusion is made on the interpretation of Bangladeshi legislations by the GIZ (2007) study.

34 It is not clear to the drafters of this study whether the Bangladeshi Government is of the view that pharmaceutical product patents have been granted before issuing the suspension order. Nor is it clear whether there are any actually granted patents on pharmaceutical products in Bangladesh. For these reasons, our analysis will be based on the provisions of the Bangladesh Patent and Design Law (1911), which excludes pharmaceutical product patents.

Box 1 Mailbox applications

When the TRIPS Agreement was adopted in 1995, there were several countries that were not making patent protection available for pharmaceutical product inventions. These countries were granted a transition period until 1 January 2005 to change their laws and make patent protection available for pharmaceutical product inventions (Article 65.4 of the TRIPS Agreement). The use of the transition period was based on two conditions.

Countries not providing pharmaceutical product patents had to allow the filing of such patents between 1995 and 2005 in order for the pharmaceutical companies to establish priority of claims over each pharmaceutical product invention (Article 70.8 of the TRIPS Agreement). Such filing is known as "mailbox" procedure, since patents were not examined or granted during the transition period. At the end of the transition period in January 2005, the countries had to open the mailbox and provide patent protection for the remainder of the patent term, counted from the filing date, for applications that meet the patentability criteria as defined in Article 27.1 of the TRIPS Agreement.

Also during the transition period, exclusive marketing rights had to be granted for a period of 5 years after obtaining marketing approval or until a product patent was granted or rejected, whichever is shorter. This was conditional on a patent being granted and marketing approval obtained in another WTO Member (Article 70.9 of the TRIPS Agreement).35

The mailbox procedure can be applicable to LDCs during the (extended) transition period before 2016,36 provided that they were among the countries that were not making pharmaceutical product patents available on 1 January 1995 (i.e. the date of entry into force of the TRIPS Agreement). This appears to be the case in Bangladesh.

Source: UNCTAD, 2011

35 An exception applies to LDCs, which have been exempted from the obligation to provide for exclusive marketing rights for pharmaceutical products until 1 January 2016 (see above).

36 The mailbox obligation already applied to LDCs during the original transition period (i.e. up to 1 January 2006). This follows from TRIPS Article 70.8(a), which obligates all WTO Members to apply the mailbox, "notwithstanding the provisions of Part VI" of TRIPS. The provisions of Part VI contain precisely the LDC transition period under Article 66.1. Under the 2013 and 2016 extension decisions, this same transition period under Article 66.1 was extended into 2013 (i.e. on the implementation of TRIPS obligations in general) and 2016 (i.e. on the implementation of TRIPS provisions on patents and the protection of undisclosed information in the area of pharmaceutical products). The extension decisions expressly refer to the LDC transition period "under Article 66.1" of the Agreement, i.e. the transition period under which LDCs had to respect the mailbox obligation under Article 70.8(a). This reference has to be understood as carrying over into 2013/2016 the original mailbox obligation under the original transition period. Although the 2013 decision refers only to TRIPS Articles 3–5 as remaining obligations for LDCs, it makes clear in its heading that what is extended is the transition period as subject to the mailbox obligation.

An update of the patent regime that took into account the flexibilities of the TRIPS Agreement was proposed under the draft Patent Act of 2007, prepared by the Bangladesh Law Commission. The draft Patent Act of 2007 was delayed due to a few observations of the Ministry of Law and Parliamentary Affairs on a couple of clauses that were conflicting in the law, which were then reconciled through detailed stakeholder consultations (Gehl Sampath, 2010b). The draft Act, which dealt with both patents and designs, has now been separated into a Patent Act and a Designs Act in accordance with World Intellectual Property Organization advice. According to all Ministry officials interviewed in March 2010, the new draft Patent Act 2010, which contains several changes to the earlier draft Patent Act of 2007, was supposed to be enacted during 2010. However, as of March 2011, this does not appear to be the case.[37]

The legislature is to enact the draft as a law no later than the date set by the TRIPS Agreement (WTO, 2006). This date could be 1 July 2013, although there could be a specific exclusion from patentability of pharmaceutical products until 1 January 2016. The draft incorporates the mailbox application procedure that will be operational until 2016 with respect to pharmaceutical products (Law Commission, 2006). In this regard, in the case of a further extension of the LDC transition period, the mailbox system would have to be extended for the same period. During interviews, many of the companies and BAPI consider the WTO flexibilities as an important factor for their successes. Companies interested in investing in the country profile Bangladesh as an LDC benefiting from TRIPS flexibilities with significant pharmaceutical production capacity (Hassan, 2009).

In 2010, Bangladesh submitted to the WTO Council for TRIPS a communication on its priority needs for technical and financial cooperation in order to implement the TRIPS Agreement by 2013 (WTO, 2010). The submission provides an overview of the current state of play of intellectual property rights legislation in Bangladesh and highlights some of the work outstanding (WTO, 2010, Annex I). Importantly, it refers to the need to incorporate in domestic patent law a provision regarding the exportation of pharmaceutical products made under compulsory license, in line with the 2005 Decision by the WTO General Council to amend the TRIPS Agreement (WTO, 2005). Such exportation could potentially provide important opportunities to the domestic pharmaceutical industry after the introduction of full patent protection in Bangladesh. This is because the 2005 Decision waives the requirement, under Article 31(f) of the TRIPS Agreement, to reserve the predominant share of the production under a compulsory license to the domestic market of the exporting country.

In addition, the submission also illustrates that TRIPS implementation is not only about legal transposition of rights and obligations resulting from an international treaty into domestic legislation; it also includes thorough consideration of the manner in which such implementation can best benefit

37 The World Intellectual Property Organization's WIPO Lex website, which contains domestic intellectual property laws enacted in WIPO Member states, still refers to the Bangladesh Patents and Designs Act of 1911 (see http://www.wipo.int/wipolex/en/results.jsp?countries=BD&cat_id=3).

domestic development objectives, including, in particular, public health and the role of the pharmaceutical sector, which has been identified as a priority in Bangladesh. The submission puts particular emphasis on the vital role of technology transfer for the area of pharmaceuticals and the need to further enhance such transfer.[38]

5.3 Industrial and investment policies

The industrial and investment policies of Bangladesh aim at increasing the contribution by the industrial sector to GDP and employment. The policy aspiration includes that the manufacturing sector, which includes pharmaceutical production, will account for 30% of GDP and about 20% of employment in the economy by 2021. The 2009 Industrial Policy lists pharmaceutical goods as one of the "thrust sectors" for the first time (Ministry of Industries, 2008). The thrust sectors are considered as export-oriented and receive various fiscal incentives and investment facilities and as preferences for allocation of land.

In terms of investment in pharmaceutical production, the key policies are found in the National Drug Policy of Bangladesh adopted in 1982 and revised in 2005, as explained above. Additionally, the 2009 Industry Policy of Bangladesh targets foreign investment to bring about technology transfer, management and marketing skills and to facilitate access to export markets (Ministry of Industries, 2008).[39] However, the participation of multinational corporations is limited to production for export markets under the 2005 National Drug Policy of Bangladesh. An Indian pharmaceutical company, Sun Pharmaceuticals, began its operations in Bangladesh in a "green field" investment in 2007. Interviews revealed that there is not full agreement on opening the market for essential medicines to foreign companies. Some question the wisdom of this policy while the domestic industry is still at a nascent stage, while others think that the Bangladeshi companies have built their capacity and can face competition from foreign companies.

Financing of the investment and operation of pharmaceutical manufacturing in Bangladesh is primarily through bank loans at commercial rates, and trading on the domestic capital market. During the field mission, the pharmaceutical companies stated that there are no facilities for bank loans at low interest rates and long-term repayment terms. Both Square and BPL are trading on the Chittagong Stock Exchange and Dhaka Stock Exchange. Use of supplier credit to finance acquisition of technology or importation of raw materials is highly regulated by the Bangladeshi Bank (the central bank).[40] The industrial and

38 See Paragraph 8 of the submission of 23 March 2010.

39 The Bangladesh Government envisages admitting research and development expenses for tax rebate, facilitates need-based industrial technology studies at universities, and facilitates patenting of innovations and taking adequate measures to comply with the TRIPS agreement of the WTO.

40 The Bangladesh Bank (1996) states that industrial enterprises in the private sector may, with prior approval from the Board of Investment, enter into supplier's credit and other foreign currency loan contracts with lenders abroad if the effective rate of interest does not exceed the London interbank offered rate (LIBOR) +4%, the repayment period is not less than 7 years, and the down payment is not more than 10%.

investment policies of Bangladesh related to pharmaceutical production are further supplemented by tariff concessions and import policy, fiscal incentives for investment, and export policy.

5.3.1 Income tax holiday for reinvestment

Tax holidays are available for 5 or 7 years, depending on the location of the industrial enterprise.[41] BPL and Square benefited from tax holidays for each new investment facility and subsidiary. Square, for example, enjoyed a tax holiday for 5 years for its Dhaka Unit, with effect from April 2002 (Square, 2006). The tax holidays are conditional on creating a reserve for profit acquired from the tax holiday. BPL had a 442 354 953 taka (approximately US$ 6.5 million) tax holiday reserve in 2007 that expired the following year (BPL, 2008). Square maintained a 1 101 935 237 taka (approximately US$ 15.9 million) tax holiday reserve as of March 2009 (Square, 2009). Companies are required to invest their benefits from the tax holidays within 2 years from the end of the tax holiday in the same undertaking or in any new industrial undertaking, or in stocks and shares of listed companies, or in government bonds or securities, or for other purposes as required by the Income Tax Ordinance of 1984. Hence, BPL and Square acquired capacity to expand and improve productive capacity by using tax holidays.

5.3.2 Tariff regime and import policy

The Bangladeshi import regime consists of banned items, restricted items and free importable items. Pharmaceuticals are classified as either restricted items or freely importable items under the Import Policy Ordinance of Bangladesh for 2009–2012. Importation of final products of medicines and vaccines is based on a list of importable items published in the government gazette by the DGDA. The importation of raw materials and packaging materials for the pharmaceutical industry takes place at tariff rates that are much lower than the most-favoured-nations rate of 100% for export. The procedures for importation are further facilitated by creating a "block list" of imports for each recognized pharmaceutical company approved by the Director of the DGDA. The block list provides the description of the raw material and packaging material, value and quantity according to the annual production plans of the pharmaceutical companies. The list is usually prepared as part of product registration. Companies importing raw materials have to present an import invoice and analysis report of the quality, value and quantity for each import. The analysis report of the raw materials must be certified by the DGDA or be prepared by a government-approved pre-shipment inspection agent (Bangladesh Ministry of Commerce, 2007).

5.3.3 Export policy

The export policy of Bangladesh has included the pharmaceutical sector in the highest priority sector category since 2006. With exports emerging as a new direction for growth and competitiveness of the industry, BLP, Square and many other pharmaceutical companies are extensively upgrading their

41 See http://www.nbr-bd.org/incometax.html.

facilities and products, leading to export-led quality improvement. The main incentives available for pharmaceutical export include up to 50% income tax exemption for export earnings, duty-free import of capital machinery for export-oriented facilities and 10% of spare parts of capital machinery every 2 years, a tax holiday and duty-drawback scheme, and up to 15% retention of foreign currency for reuse (Export Promotion Bureau, 2009). However, during interviews, Square, BPL, Aristopharma and Advanced Chemicals Industries complained about the inadequacy of foreign currency allocation for export operations of pharmaceutical companies. Unlike other exports, pharmaceutical exports entail huge operational expenses in relation to representatives or agents in export markets, and registration of products.

Companies' activities in Bangladesh are rendered more difficult by the country's unsatisfactory infrastructure, which is prone to frequent flooding. The electricity supply per head is very low, power generation being primarily from abundant natural gas reserves (Economic Intelligence Unit, 2008). All industries in Bangladesh, including pharmaceuticals, rely on their own generators, because of the irregular supply of electricity. Pharmaceutical companies complain about the insufficiency and unreliability of gas-generated electricity, and the related costs (field interviews). Where the pharmaceutical companies are not enjoying a tax holiday, they enjoy accelerated depreciation allowances for their investment capital. Given that the pharmaceutical sector is now a priority sector according to the Industrial Policy of 2009, this might mean that new incentives to address infrastructure deficits might be introduced.

5.4 Science, technology and innovation policy

Bangladesh adopted its National Science and Technology Policy in 1986. The Policy builds on the prevailing thought at the time of focusing on self-reliance and import substitution, while stressing the need to coordinate science and technology with the socioeconomic, cultural, educational, agricultural and industrial policies of the country. Bangladesh is currently reviewing the policy. The revision as of February 2010 proposes a bottom-up approach in which specific science and technology policies are developed for each sector under the overall objectives of the policy. The policy proposes increased collaboration among research institutions and with the private sector, including international cooperation. The pharmaceutical sector is proposed to be covered under the larger group of "large-scale industries including engineering and metal industries". This, in addition to the new Industrial Policy of 2009, creates a policy framework for the provision of all key elements required by the sector to build API capacity – human resources (that are technically competent in chemistry, biochemistry and advanced areas of clinical chemistry and biotechnology), improved physical infrastructure and common scientific infrastructure, such as the API park and advanced testing laboratories within the country.

The revision proposes various institutional mechanisms for coordination and linkage. The Science and Technology Policy is also complemented by the National Information and Communication Technology Policy (2002), which

outlines action plans for human resources development, ICT infrastructure, research and development, and the ICT industry.

5.5 Education

In 2007, only 7% of the population of tertiary age was in tertiary education, which is lower than the regional average estimated at 12%. In all primary, secondary and tertiary levels of education, Bangladesh performs below the regional average (UIS, 2007). In 2007, the government spent 15.8% of its total expenditure on education (UIS, 2007).

Public and private higher education facilities train pharmacists and chemists. About 15 institutions provide a diploma in pharmacy, and another 6 public universities and 21 private universities provide graduate and postgraduate programmes, according to the Pharmacy Council of Bangladesh. The pharmacy graduates are mainly trained to work in the pharmaceutical industry as formulation scientists and manufacturing experts. The clinical aspects of the training and courses on biomedical sciences have been insufficient (Habib & Ahmed, 2007).

According to Article 13(a) of the National Drug Act of 1982, pharmaceutical companies are required to maintain at least two qualified people: one of them must be a graduate pharmacist from a recognized university in Bangladesh, but the other may be a graduate in pharmacy, chemistry, biochemistry or microbiology. The companies can satisfy this legal requirement from the local labour market. Going beyond the legal requirements, field interviews revealed that there are various problems in maintaining an adequate supply of skilled labour in Bangladesh. The pharmacy schools are training students for marketing and do not have incentives to upgrade their scientific curriculum. Furthermore, there is an inadequate supply of engineering staff.

Companies such as BPL and Square demonstrated a preference for graduates from the School of Pharmacy at the University of Dhaka. The School, however, produces only 70 graduates per year. During interviews with the School, it was noted that its 15 or 16 faculty members undertake research under collaborations established by the School with universities and research centres in the United States, United Kingdom and Japan. The School is undertaking continuous curriculum reviews to meet international standards, including meeting the United States requirements for pharmacy education, publishing periodicals and inviting visiting professors from collaborating institutions, including its graduates working in different parts of the world.

5.6 Good governance

Bangladesh enjoys significantly better peace and security compared with many other countries in the South Asian region, according to the Global Peace Index ranking for 2009. However, this has not translated into improving domestic institutions in terms of ensuring regulatory quality and dealing with corruption. Bangladesh scored poorly in 2008 in regulatory quality and

controlling corruption according to the World Bank governance indicator.[42] Government effectiveness, the rule of law and accountability also stand at significantly lower rates than in other countries in the region (Table 1).

***Table 1** Governance indicators in selected developing countries*

Country	2010 Global Peace Index	Governance indicators (percentile rank, 0–100)				
		Regulatory quality	Government effectiveness	Rule of law	Control of corruption	Voice and accountability
India	128	46.9	53.6	56.5	44.4	58.7
Sri Lanka	133	44.4	46.9	54.5	54.1	33.7
Pakistan	145	34.8	25.6	19.1	24.6	19.2
Nepal	82	26.6	24.2	24.9	29	25
Bangladesh	87	20.8	22.7	27.3	10.6	30.8
Myanmar	132	1	1.9	4.8	1	0

50–75 percentile
25–50 percentile
10–25 percentile
0–10 percentile

Sources: Institute for Economics and Peace (2010) and World Bank (2008b).

6. Analysis of BPL and Square

The early collaboration by Square and BPL with multinational corporations provided the opportunity for technology transfer and exposure to standards of good-quality manufacturing in developed country markets. Square and BPL took advantage of their earlier experiences and moved to active learning and mastery of formulation technology. They did so by building in-house capacity and securing the services of companies from advanced countries for further learning. The in-house capacity of Square and BPL is strong in the formulation and marketing of pharmaceuticals for local and underregulated markets. Both are building their capacity to formulate and develop products in-house, with the help of foreign companies for export to regulated markets. They have important success in accreditation of their facilities by regulatory authorities of advanced countries such as the United Kingdom and Australia. As a sign of strong product formulation capacity, both developed the capacity for manufacturing of medicines in many therapeutic categories, including ARVs and various antimalarial products. If Square and BPL secure WHO prequalification for their ARVs, they will be able to export and tap into the large market in Africa, provided that they have a strong and viable marketing strategy. They have already established their presence in foreign markets, including some emerging markets.

The market share of the two companies, supported by the National Drug Policy, has provided them with the opportunity to generate revenue and use

42 BPL considers 2007–2008 a difficult period, when charges of corruption were brought against two senior mangers of the larger Beximco Group. Profit in 2007 was lower than in the previous year, which later bounced back in 2008 (Business Monitor International, 2010).

resources to secure technologies and know-how at arm's length trade from companies in advanced countries. However, in terms of export, common perceptions of the country and questions regarding the local quality-control system may pose challenges for exporters. Regulatory control continues to be a problem and requires further reform. The extent to which Square and BPL can deal with their image challenges by securing foreign accreditation is uncertain.

The main shortcomings in terms of technological capability of Square and BPL pertain to the capacity for the production of insulin, anticancer drugs and vaccines where there is growing interest, undertaking research and development, and manufacturing APIs. Square is tackling the problem by launching an insulin bottling facility. In their export ventures, Square and BPL undertake bioequivalence studies, hiring the support of foreign companies. In Bangladesh, bioequivalence studies are required only for importation of drugs and thus there is no incentive to build research capacity for this purpose. When exporting products, regulated markets demand the filing of bioequivalence studies. No independent domestic contract research organization or any research facility is accredited by foreign regulatory bodies to undertake bioequivalence and other studies in securing qualification or WHO prequalification.

The success in mastering formulation and production capacity in pharmaceuticals by Square and BPL has not yet translated into capacity for producing APIs, which is a technologically more challenging activity for pharmaceutical firms. Square and BPL produce various APIs only from an advanced intermediary stage. Furthermore, Square's attention and investment capacity may be distracted by its venture into pesticides and animal health, where the company has predicted more short-term gains. The bigger challenge is the lack of clear strategy by both the private sector and the Bangladeshi Government to enter into API production, as plans for an API park in Bangladesh have all but stalled (field interviews). The original plan was for the API industrial park to be established during 2008–2010. The incentive for API production in Bangladesh could be undermined by the short-term challenge of competition with other countries in the region that have been producing APIs for four decades or more, such as China and India. The existing API production from an intermediary basis seems to be motivated by the desire to export and the need to comply with regulations of export markets rather than the local market.

The companies that move to produce a specific API take the risk of increased initial costs of production for their final formulation compared with companies that import APIs from highly competitive producers in China and India at tariff rates lower than the most favoured nation or at zero if final products are for export. This could explain the stagnation of API production observed in Bangladesh, despite a long history of pharmaceutical production. Strategic intervention and investment would be required by local producers to develop the capabilities to domestically produce APIs. On a positive note, the Bangladeshi Government is intending to establish a common effluent

treatment plant for all producers of APIs in a bid to revitalize the API park project. Undertaking water treatment for pharmaceutical production and waste management is an expensive operation for each company to do separately. The common effluent treatment plant, if implemented, could at least place Bangladesh's infrastructure on a par with other countries in the region for API production. With respect to API production, ensuring the quality of education and human resource training, and a supply of skilled labour in chemistry and engineering fields, would need particular attention.

7. Implications of local production and related technology transfer on access to medicines

Square and Beximco, as the two oldest companies in the local sector, have contributed throughout their growth phase to promoting greater access to medicines in Bangladesh. Both companies have focused on producing cheaper, local versions of drugs for use by the local population and maintain a wide area of therapeutic coverage. These changes, although promoted by the National Drug Policy of 1982, have been sustained at the firm level by a series of technology transfer and tacit know-how-building alliances between the firms and their international counterparts.

Technology transfer from foreign companies, as highlighted in this study, has been extremely important for (i) establishing production capacity, (ii) expanding product portfolios to include several new product categories, and (iii) technological upgrading of the kind required to produce good-quality medicines at reasonable cost. The case study method, although well suited to exploring a particular case in detail, is not suitable for gathering time-series data (over a period of time) to see the impact of the companies' activities on promoting access to medicines in the country. The impact of all the companies in the local sector on reducing the burden of disease in the country similarly calls for the generation of much more rigorous data. A last question on firm-level activity and access to medicines pertains to whether the products manufactured by the local companies are priced cheaply enough to promote access to medicines, when compared with generic substitutes that could be obtained from other countries or sources.

On this issue, although the study was unable to ascertain the extent to which the medicines produced by both companies are cheaper than those in other generic markets, such as China and India, it is clear that the drugs manufactured by both companies are significantly cheaper than the generic versions of drugs that can be obtained from multinational companies (Ahmed, 2009). A study on pricing differentiation of 35 essential medicines between local producers and multinational pharmaceutical companies in Bangladesh found that the majority of locally produced anti-infectives were less expensive than the counterparts of their multinational corporations, notwithstanding the business reasons for still maintaining high per-pill profits locally (Chowdhury & Rahman Kabir, 2009).

8. Policy-relevant findings

The two companies that form the subject of this case study are fairly typical of the larger companies in the local pharmaceutical sector in Bangladesh. The other local companies in the market share the historical factors that led to the emergence of the firms, along with the technological strengths and limitations described in the study, even though the other local companies vary in size and market share when compared with Square and BPL. Several important lessons may be drawn from this case study that also could apply to the other firms in the sector:

1. Both of the researched firms initially acquired the technological capacity to manufacture good-quality pharmaceutical products through collaborations with foreign pharmaceutical companies, which at the time were controlling the market in Bangladesh.

2. Through targeted infant industry protection, the Bangladeshi Government provided the legal and economic framework for domestic companies to develop their market share. Important elements of these policies were the 1982 National Drug Policy (revised in 2005) limiting imports of pharmaceuticals where local production was sufficient; the potential of a large domestic market; intellectual property legislation favouring domestic generic producers; cheap labour costs; and access to APIs. Against this favourable policy framework, firms such as BPL and Square have managed to thrive even without WHO prequalification of any product, which they are currently seeking in their bid to reach export markets served by international organizations, aid agencies, philanthropic initiatives and nongovernmental organizations (NGOs). Bangladesh's pharmaceutical companies have the capacity to produce drugs in most therapeutic categories and dosage forms, available at low (but oligopolistic) prices in the domestic market.

3. In the context of access to medicines, the study shows that both long-term and short-/medium-term considerations have to be taken into account when designing policies for local production. The long-term public health objective is to enable the population's access to affordable, good-quality medicines. While the replacement, to some extent, of foreign imports by domestic production, as pioneered by the 1982 Drug Policy, was an important medium-term step towards the creation of local pharmaceutical capacities, this industrial policy objective has not been well coordinated with access to medicines and pricing policies. In particular, lack of monitoring of company pricing practices and lack of systematic emphasis on ensuring that the local production is in the interests of public health are evident. Controlling pricing practices of local firms, ensuring an up-to-date essential medicines list and drug regulation are some of the safeguards required to make sure that access to medicines and public health is well-integrated into industrial policy promoting the sector. These need to be further strengthened through new measures that promote dynamic competition in the local market, and through establishing checks and balances on the pricing and behaviour of local firms through a strong DGDA

and other policy measures, such as, for instance, the gradual introduction of price-based competition from abroad.

4. The case study shows that important long-term issues remain to be addressed. The field interviews and other data collected for the study point towards the need to determine (i) whether and how local production contributes towards providing access to drugs identified under the essential medicines list within Bangladesh, (ii) the access gaps, and (iii) how these gaps are being alleviated through the new incentives of the Industrial Policy of 2009. A clearer link between the new industrial incentives and the public health needs that the firms can cater to (both locally and through exports) is required. The biggest challenge with respect to export markets will be building capacity for local API production from the initial stage, which is seen as the principal means to lower the price of medicaments to a level where domestic firms could compete with Chinese and Indian manufacturers. In the medium to long term, increased API production capacity in Bangladesh could potentially provide good opportunities for outsourcing production for firms from China and India.

5. Seeking to address this issue, the Bangladesh Science, Innovation and Technology Policy (currently in preparation) identifies the pharmaceutical subsector with a view to building capacity in the production of basic chemicals and pharmaceuticals. Developing a pharmaceutical subsector science, innovation and technology policy could help to systematically address strategies for the industry, and for the problems regarding the quality of human resources and education, especially for building the capacity for the production of APIs from the initial stage. A science, innovation and technology policy may help to address issues relating to inadequate infrastructure, especially reliable energy and water and land allocation, and the problems of linkage between research organizations and the private sector.

6. In the context of the affordability of medicines, the study illustrates the importance of effective price monitoring systems that ensure ethical pricing practices and the gradual introduction of foreign competitors to the market, now that the domestic producers have reached a sufficient degree of technological capacity to face competition. A phased, locally suited technology regime is not new: countries have used highly interventionist technology policies in the past to build local sectors (e.g. Chang, 2002, 2003). In this respect, ensuring the quality of locally produced drugs is essential. The regulatory authority plays a key role in this respect. It needs to be performing and fully operational in order to support local producers in their efforts to improve quality.

7. The lessons listed above make clear that access to affordable, good-quality medicines through local production depends on the availability of scientific and technological capacities. The design and effective functioning of a country's educational system is therefore an important long-term consideration for public health and other policy-makers.

References

Ahmed S. Drug regulations: the need for an appropriate regulatory system. *Bangladeshi-American Pharmacists' Association Journal*, 2009, 18:31–35.

Alam SZ. *Report on legal and ethical issues in drug industry: Directorate of drug administration point of view* [thesis]. Bangladesh, School of Business, Independent University, 2009 (http://www.scribd.com/doc/17187626/Legal-and-Ethical-Issues-in-Drug-Industry-Directorate-of-Drug-Administration-Point-of-View).

Bangladesh Bank. *Guidelines for foreign exchange transactions*. Dhaka, Bangladesh Bank, 1996.

Bangladesh Health Watch. *Bangladesh Health Watch report 2009: How healthy is health sector governance?* Dhaka, The University Press, 2010 (http://www.bracuniversity.net/I&S/sph/publications/reports/bhw/2009/BHW%20REPORT%202009.pdf).

Bangladesh Bank. Major economic indicators. *Monthly Update*, 2010, 03.

Bangladesh Ministry of Commerce. Government of the People's Republic of Bangladesh, Import Policy Order 2006–2009. *Bangladesh Gazette Extraordinary*, 16 May, 2007.

Bangladesh Ministry of Health and Family Welfare. *Drug (control) ordinance of 1982*. Dhaka, Bangladesh Ministry of Health and Family Welfare, 1982.

Bangladesh Ministry of Health and Family Welfare. *Report of the Expert Committee for Drugs on the National Drug Policy 1982*. Dhaka, Bangladesh Ministry of Health and Family Welfare, 1986.

Bangladesh Ministry of Health and Family Welfare (2004). *Drug (control) ordinance of 2004*. Dhaka, Bangladesh Ministry of Health and Family Welfare, 2004.

BPL. *Annual report, 2008*. Dhaka, Beximco Pharmaceuticals Ltd, 2008.

BPL. *Half year report, 2009*. Dhaka, Beximco Pharmaceuticals Ltd, 2009.

Business Monitor International. *Bangladesh pharmaceuticals and healthcare report, Q2*. London, Business Monitor International, 2010.

Chang HJ. *Kicking away the ladder: Development strategy in historical perspective*. London, Anthem Press, 2002.

Chang HJ. *Globalization, economic development and the role of the state*. London, Zed Press, 2003.

Chowdhury N, Rahman Kabir R. Per pill price differences across therapeutic categories: a study of the essential drug brands marketed by multinational and local pharmaceutical companies in Bangladesh. *African Journal of Marketing Management*, 2009, 1.

Economic Intelligence Unit. *Country profile 2008: Bangladesh*. London, Economic Intelligence Unit, 2009.

Export Promotion Bureau. *Export policy*. Dhaka, Export Promotion Bureau, Bangladesh Ministry of Commerce, 2009 (http://www.epb.gov.bd/export_Policy_2009-12.php).

Gehl Sampath P. *Innovation and competitive capacity in Bangladesh*'s pharmaceutical sector. Working paper series. Maastricht, UNU-MERIT, 2007.

Gehl Sampath P. *Reconfiguring global health innovation*. London, Routledge, 2010a.

Gehl Sampath P. *TRIPS flexibilities and local pharmaceutical production capacity in Bangladesh: An update*. Gesellschaft für Technische Zusammenarbeit, 2010b.

GIZ. *Study on the viability of high quality drugs manufacturing in Bangladesh*. Eschborn, Federal Ministry of Economic Cooperation and Development, 2007.

Habib MJ, Sharif A. Update pharmacy curricula: A wake up call for Bangladeshi pharmacy schools. *BAPA Journal*, 2007, August:15–17.

Haq AI, Minul I. *Equity research Bangladesh: Valuation of Square Pharmaceutical Ltd*. Dhaka, Institute of Business Administration, Dhaka University, 2008.

Hassan N. *Future prospects of pharmaceutical industry of Bangladesh, 2009*. Presented at the 3rd Chittagong Stock Exchange Capital Market Fair 2009, Chittagong (http://www.csebd.com/cse/start.html).

Institute for Economics and Peace. *Global peace index*. Sydney, Institute for Economics and Peace, 2010 (http://www.visionofhumanity.org).

LankaBangla Securities Ltd. *Bangladesh equities: Square Pharmaceuticals Ltd*. Dhaka, LankaBangla Securities Ltd, 2008.

Law Commission – Bangladesh. *Final report on the Patents and Designs Act, 200*-----. Dhaka, Law Commission, 2006.

Ministry of Industries. *Industrial policy 2009*. Dhaka, Ministry of Industries, 2008 (http://www.ibfb.org/pdfs/Industrial%20Policy.pdf).

Square. *Annual report, 2005–2006*, Dhaka, Square Pharmaceuticals Limited, 2006.

Square. Annual report, 2008–2009. Dhaka, Square Pharmaceuticals Limited, 2009.

Uddin Ahmad AK Monaw-war. *Competition, regulation and the role of the state: The case of Bangladesh, 2008*. Lecture delivered at the Asiatic Society of Bangladesh, Dhaka, 30 August 2008.

UIS. *Statistics in brief: Bangladesh*. Montreal, UNESCO Institute for Statistics (http://stats.uis.unesco.org/).

UNCTAD. *The least developed countries report: Knowledge, technological learning and innovation for development*. New York and Geneva, United Nations Conference on Trade and Development, 2007.

UN-OHRLLS. Landlocked developing countries and small island developing states, facts and figures. United Nations Office of the High Representative for the Least Developed Countries (http://www.unohrlls.org/en/ldc/related/63/, accessed 7 April 2010).

WHO. *Scaling up antiretroviral therapy in resource-limited settings: Treatment guidelines for a public health approach*. 2003 revision. Geneva, World Health Organization, 2003.

WHO. *Guidelines for antiretroviral therapy for HIV infection in adults and adolescents*. Geneva, World Health Organization, 2006.

WHO. *Report of the WHO Expert Committee: The selection and use of essential medicines*. WHO Technical Report Series 914. Geneva, World Health Organization, 2009.

World Bank. *Public and private sector approaches to improving pharmaceutical quality in Bangladesh*. Bangladesh Development Series Paper No. 23. Washington, DC, World Bank, 2008a.

World Bank. *The governance indicators*. Washington, DC, World Bank, 2008b (http://info.worldbank.org/governance/wgi/index.asp).

WTO. *Amendment of the TRIPS Agreement*. General Council Decision, 6 December 2005. WT/L/641. Geneva, World Trade Organization, 2005.

WTO. *Trade policy review, Bangladesh*. Report by the Secretariat. WT/TPR/S/168/Rev.1 (2006). Geneva, World Trade Organization, 2006.

WTO. Priority needs for technical and financial cooperation. Communication from Bangladesh. IP/C/W/546 (2010). Geneva, World Trade Organization, 2010.

Annex: List of interviewed individuals and institutions

The following individuals/institutions were interviewed:

Representatives of pharmaceutical companies

Muhammadul Haque, Chief Marketing Officer, Square Pharmaceuticals Ltd.

SM Noor Hossain, General Manager, Marketing and Sales, Aristopharma

Mahammad Masud Parves, Board Executive, Beximco Pharmaceuticals Ltd

Shamin Momtaz, Executive Director, Manufacturing, Beximco Pharmaceuticals Ltd

Abdul Muktadir, Managing Director, Incepta Pharmaceuticals Ltd.; and Secretary General, Bangladesh Association of Pharmaceutical Industry

Mohammad Rafiqui Islam, Director, Marketing and Sales, Acme Pharmaceuticals

Mohd Tahir Siddique, Executive Director, Quality, Beximco Pharmaceuticals Ltd.

M Mohibuz Zaman, Chief Operating Officer, Advanced Chemical Industries Limited

Representatives of the Bangladeshi Government

Mr Jnanendra N Biswas, Joint Secretary, Office of the (Permanent) Secretary, Ministry of Industries

Salim Burani, Deputy Director, Directorate for Drug Administration

Mr Amir Hossain, Additional Secretary, Ministry of Health and Family Welfare, Bangladesh Secretariat

Mr Zahidul Islam, Assistant Secretary, International Cooperation, Ministry of Industries

Major General MD Abul Kalam Azad, Directorate for Drug Administration

Ms Habibun Nahar, Senior Assistant Secretary, Public Health-I

Representatives of academia and research centres

Shams El Arifeen, Senior Scientist and Head, Child Health Unit, International Centre for Diarrhoeal Disease Research

Dr Abul Hasnat, University of Dhaka

Dr MD Abdur Rashid, Dean Faculty of Pharmacy, University of Dhaka

Dr ATM Zafrul Azam, Associate Professor, Department of Pharmaceutical Chemistry, University of Dhaka

Representatives of international organizations

Tania Dmytraczenko, Senior Economist, World Bank

Daniel Seidl, Director, German-Bangladesh Chamber of Commerce

Dr Sergei, Immunization Officer, World Health Organization, Dhaka

Case study 3

Colombia

This case study on Colombia was carried out by Luis Mariano Genovesi, UNCTAD Consultant and Law Professor at Universidad de Buenos Aires, Argentina. Mr Genovesi and Maximiliano Chab, ICTSD Regionalism Programme Officer, collected input for the study during a field mission to Bogotá and Cali, Colombia from 25 to 29 January 2010. The case study report was finalized by Kiyoshi Adachi and Christoph Spennemann of the Intellectual Property Unit, under the overall responsibility of Mr James Zhan, Director of the Division on Investment and Enterprise, and Mrs Nazha Benabbes Taarji, Officer-in-Charge, Investment Capacity-Building Branch.

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Abbreviations

ANDI	Cámara Farmacéutica de la Asociación Nacional de Empresarios de Colombia
ASINFAR	Asociación de Industrias Farmacéuticas Colombianas
BK+	Bacillus Koch positive
CECIF	Centro de la Ciencia y la Investigación Farmacéutica (Centre for Science and Pharmaceutical Research)
CIDEIM	Centro Internacional de Entrenamiento e Investigaciones Médicas (International Medical Research and Training Centre)
CIDEPRO	Centro de Investigación para el Desarrollo de Productos contra Enfermedades Tropicales (Research Centre for the Development of Products to Fight Tropical Diseases)
CNPM	Comisión Nacional de Precios de los Medicamentos (National Commission of Drug Price Surveillance)
Colciencias	Departamento Administrativo de Ciencia, Tecnología e Innovación (Administrative Department of Science, Technology and Innovation)
CONPES	Consejo Nacional de Política Económica y Social (National Board of Economic and Social Policy)
CSC	Colombia Sales Company
DANE	Departamento Administrativo Nacional de Estadística
DNP	Departamento Nacional de Planeación
EPSS	Entidades Promotoras de Salud Subsidiada
FOSYGA	Fondo de Solidaridad y Garantía del Sistema General de Seguridad Social en Salud
ICESI	Universidad ICESI
IFARMA	Fundación Instituto para la Investigación del Medicamento en los Sistemas de Salud
INVIMA	Instituto Nacional de Vigilancia de Medicamentos y Alimentos
MSD	Merck, Sharp and Dohme Corporation
POS	Plan Obligatorio de Salud (Mandatory Health Care Plan)
rEGF	recombinant epidermal growth factor
RICYT	Red Iberoamericana de Indicadores de Ciencia y Tecnología
SGSSS	Sistema General de Seguridad Social en Salud (General System of Social Security in Health)
SNCTeI	Sistema Nacional de Ciencia, Tecnología e Innovación (National System of Science, Technology and Innovation)

1. Background and methodology

This case study was designed to investigate the trends in transfer of technology in the pharmaceutical field in Colombia, the source of their technology, the factors behind their sustainability, and the issues that local and multinational companies currently face. Specifically, this case study examines the technological innovation strategy of the largest Colombian pharmaceutical company through its research and development (R&D) efforts; the evolution of transfer of technology from multinational R&D-based firms in the past 20 years; the role that active pharmaceutical ingredients (APIs) and equipment suppliers play in transfer of technology, as well as other means for this purpose such as hiring of professionals or skilled technicians; and the place that universities and R&D institutions have in the transfer of technology in a developing country.

UNCTAD thanks Tecnoquímicas S.A. (Tecnoquímicas) for agreeing to be the subject firm for this case study.

A case study research methodology was used in this study. Data were collected from academic literature and policy documents and through open-ended, face-to-face interviews with individuals in Colombia. Interviewees were identified through purposive sampling. During the fact-finding mission to Bogotá and Cali, Colombia from 25 to 29 January 2010, 18 people from various sectors of the pharmaceutical industry were interviewed, including 9 pharmaceutical experts (affiliated with Laboratorio Franco Colombiano S.A. (Lafrancol), Tecnoquímicas, Asociación de Industrias Farmacéuticas Colombianas (Association of Colombian Pharmaceutical Industries; ASINFAR), Cámara Farmacéutica de la Asociación Nacional de Empresarios de Colombia (Pharmaceutical Chamber, National Business Association of Colombia; ANDI), and TopPharma Consulting); 7 government representatives (from Departamento Administrativo de Ciencia, Tecnología e Innovación (Colciencias) (Administrative Department of Sciences, Technology and Innovation), Fideicomiso de Promoción de Exportaciones Proexport Colombia (Proexport) (Export Promotion Trust Proexport Colombia), and Instituto Nacional de Vigilancia de Medicamentos y Alimentos (National Institute for Medicines and Food Surveillance; (INVIMA)); and 2 representatives of Fundación Instituto para la Investigación del Medicamento en los Sistemas de Salud (Institute for Research in Medicines and Health Systems Foundation; IFARMA), a nongovernmental organization (NGO).[1] Furthermore, four representatives from three different innovative multinational pharmaceutical companies were interviewed during the field mission, which included a visit to a plant operated by one of these companies; however, these multinational laboratories did not authorize their Colombian branches to participate in the case study, so these four representatives agreed to be interviewed off the record.[2]

1 See Annex I.

2 Their views are accordingly unattributed in this study.

In addition, a semi-structured questionnaire designed to capture the dynamics of firm-level activities related to production and technology transfer was administered to the above-listed firms, the results of which are included in the case study where relevant.[3]

This case study defines innovation as any new product, process or organizational change that is new to the enterprise, context and country in question. This need not be novel to the world at large. In keeping with the scope of the project, technology transfer was defined as all components of technology, both codified (such as blueprints, hardware, machine parts and plant technologies) and tacit (such as know-how and skills), that are essential to enhance the capacity of the organizations in the recipient country to produce pharmaceutical products.[4]

2. Description of the firm, structure and range of products

Tecnoquímicas is a Colombian laboratory, located in Cali. It was founded in 1934. Two brothers (Francisco José Barberi and Juan Manuel Barberi) control, in an equal share, 90% of this laboratory through holding companies. The remaining 10% belongs to the International Finance Corporation (IFC), which is part of the World Bank Group. IFC purchased its participation in TECNOQUÍMICAS with a US$ 25 million investment in 2008.

Tecnoquímicas manufactures pharmaceutical drugs, baby care products, personal care products, and animal and veterinary health products. This is done either directly or through companies controlled by Tecnoquímicas. The most noteworthy of these companies are Adhesivos Internacionales S.A. (which manufactures adhesive bandages under the CureBand trademark), Tecnosur (which manufactures disposable nappies/diapers) and Indugráficas (which manufactures packaging materials).

2.1 Colombian market

Tecnoquímicas is the largest pharmaceutical laboratory in the Colombian market in terms of value of sales, among both domestic and foreign laboratories, with sales of US$ 361 million in 2009 (La Nota Económica, 2010). The company is also among the bigger firms in the Colombian economy, ranking sixtieth on the list of the largest manufacturing companies in 2008 (Superintendencia de Sociedades, 2002–2008).

Tecnoquímicas's main strength is in the over-the-counter (OTC) market, but it also ranks fifth in the prescription drugs market. Tecnoquímicas sells generic products under the McKesson (MK) trademark. It also sells branded generics, of both its own trademarks and of trademarks licensed from third parties.

3 See Annex: Field questionnaire.

4 A uniform definition of technology transfer was used for all components of the project, including the trends survey, the regional dialogues and the stakeholder analysis.

Figure 1 shows a package of an MK generic product. Annex II to this case study shows a list of MK generic products and the corresponding therapeutic groups and APIs.

Figure 1 *MK generic product package*

Figure 2 shows a package of a branded generic product distributed by Tecnoquímicas. Annex III to this case study shows the branded generics line and the corresponding therapeutic groups.

Figure 2 *Branded generic package distributed by Tecnoquímicas*

Tecnoquímicas and its subsidiaries have eight manufacturing plants in Colombia. The company manufactures 87% of the products it sells. It handles about 5000 raw materials and manufactures about 2800 different finished

products. The San Nicolás plant specializes in the production of human sterile products, cosmetics, talcum and alcohols. The Jamundí plant specializes in solid and liquid pharmaceutical products and veterinary sterile products. The Yumbo plant focuses its production on effervescent products, ointments and lotions. The Villa Rica plant, which opened in 2005 and is the most modern of the plants, produces liquids, lotions and effervescent products.

The origins of Tecnoquímicas date back to 1934, when the Colombia Sales Company (CSC) was established in the city of Bogota. CSC imported and distributed raw materials, medicines and personal care products. CSC started its own manufacturing activity in 1951. However, it never abandoned the importation and distribution business, of both its own products and those of others. As one of the main logistics companies in Colombia, this company is vertically integrated. Its current name Tecnoquímicas was adopted after a merger with Laboratorios Filaxia in 1957.

Also in the 1950s, Tecnoquímicas became a licensee of several companies, including SmithKline & French (renamed SmithKline Beecham), Richardson Merrel (renamed Procter & Gamble; for the manufacture and sale of Vick Vaporub), and Bayer de Colombia. These licences, together with its distribution network, were Tecnoquímicas's main assets for more than three decades. In the early 1970s the company manufactured 60% of the products it distributed. Another milestone in the history of Tecnoquímicas was the acquisition of the Merck, Sharp and Dohme Corporation (MSD) plant in 1986; at that time, this plant was considered the best in Colombia. The impact of this purchase was two-pronged: Tecnoquímicas had access to the highest technology available in the country, and Tecnoquímicas became an MSD licensee for the Colombian market.

The 1990s witnessed a process of transformation in the Tecnoquímicas business model. The loss of their two most important licences (SmithKline Beecham and MSD) and of other, less important licences as a consequence of several ongoing processes (mergers of large multinational laboratories and the rise of the Colombian generic pharmaceutical industry) raised doubts about the future of the company. Confronted with this new challenge, the company developed a strategy that included (i) diversifying its range of products by penetrating or furthering its presence in other markets, such as bleaches, nappies/diapers, adhesive bandages and agrochemical products; and with the addition of new products to the OTC range;[5] (ii) the acquisition of third-party trademarks and the development of its own trademarks; (iii) enhancing its generic products line; (iv) manufacturing products for other companies; and (v) increasing its exports.

Most relevant for this case study is the development of the generic products line. The basis for this development was the acquisition of Organización

5 In 1993, Tecnoquímicas purchased Organización Farmacéutica Americana and Distribuidora Farmacéutica Calox Colombiana and, with these purchases, many OTC products. In 1996, it founded Tecnosur to manufacture nappies/diapers in the Páez area of the Cauca Department – a joint venture of Tecnoquímicas and the local branch of Kimberly-Clark; the Adhesivos Internacionales company was founded in the Free Trade Zone of the Pacific to manufacture adhesive bandages. In 1998, it consolidated the position of the Agroveterinarian Division with a stake in an agrochemicals national plant.

Farmacéutica Americana S.A. in 1993, which added the MK generic products range of the McKesson Corporation. This trademark had long been present in the Colombian, Ecuadorian, Peruvian and Brazilian markets. This strategic decision of Tecnoquímicas also coincided with the implementation of national health reform (see Section 5) and the development of the institutional market for generic products. Tecnoquímicas thus managed to grow hand in hand with the development of the generic market to become a market leader in this field in 2006. At the time of writing, the generic products business unit accounts for half the amount of sales, both in value and in volume. Tecnoquímicas's distribution network is of considerable size.[6]

2.2 Presence in overseas markets

Tecnoquímicas is a company with a presence outside the Colombian market. This has been achieved through (i) exports, (ii) a subsidiary in Ecuador and (iii) a controlled laboratory in El Salvador. Tecnoquímicas exports medications, but its main exports are adhesive bandages under the CureBand trademark. These adhesive bandages are sold in 19 countries (Aruba, Netherlands Antilles (until 2010, now Curacao and Sint Maarten, as well as the Dutch public bodies Bonaire, Saint Eustatius and Saba), Bolivia, Canada, Chile, Costa Rica, Dominican Republic, Ecuador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, the United States of America, Venezuela and El Salvador). These exports account for US$ 5 million in sales per year.

Tecnoquímicas has a fully controlled subsidiary in Ecuador. In 1993, this company started up under the name of Grufarquímicas S.A., which was later renamed Tecnoquímicas del Ecuador S.A. This subsidiary does not have an industrial plant, since it is supplied by its headquarters, but it possesses a main office in Guayaquil and branches in Quito and Cuenca. Tecnoquímicas del Ecuador markets OTC products and MK generic products. It also sells veterinary and agrochemical products. It has positioned itself as the market leader in volume of sales in Ecuador. Sales of the Ecuadorian subsidiary are at US$ 20 million per year.

Tecnoquímicas acquired Laboratorios Terapéuticos Medicinales S.A. de C. V. (Teramed), a Salvadorian laboratory, in October 2009. Teramed produces generic products and is the most important laboratory in El Salvador in terms of sales value. Unlike Tecnoquímicas de Ecuador, Teramed has a modern production plant with the capacity to produce solid products, semi-solid products, liquid products and injectable products in the city of San Salvador. Teramed exports medications to Honduras, Nicaragua, Guatemala, Belize and the Dominican Republic. Teramed controls two distributors in El Salvador

6 The firm possesses six regional logistic centres in the main Colombian cities: Bogotá, Cali, Medellín, Barranquilla, Bucaramanga and Pereira. It delivers to 27 000 clients in 600 locations all over the country. It distributes directly to 100% of the 1500 points of sale of private self-service stores and compensation funds; to 70% of the 4000 self-service stores; to 100% of all the drug warehouses; to 100% of the different points of sale of several drugstore chains; and to 5000 independent pharmacies. It also distributes to 275 clinics, entidades promotoras de salud (health-promoting entities), hospitals and official entities in Colombia.

(Nacional and Galemi) and another in Guatemala (Farmont), which is why Tecnoquímicas acquired other strategic assets.

3. Tecnoquímicas's technological capacity

The four pharmaceutical plants that tecnoquimicas operates in Colombia, either directly or through controlled companies, allow it to produce pharmaceutical products in many different pharmaceutical forms: human sterile products, solid products, semi-solid products, liquid products, effervescent products, ointments and lotions. The four plants posses a valid good manufacturing practice (GMP) certification granted by INVIMA.[7] The Jamundi plant also possesses ISO 9001 certification, version 2000, from the Instituto Colombiano de Normas Técnicas y Certificación (Colombian Institute of Technical Norms and Certification).

These plants show an uneven level of technological development, however. There are machines and processes from the 1960s and 1970s operating next to fully automated processes and modern equipment acquired in the past 5 years. The company has centralized the quality control system of all its plants in the Quality Control Centre at the Jamundi plant. The Quality Control Centre approves raw materials and carries out controls at different stages of the productive processes. It also controls the finished products to verify their quality. Most of the members of the quality control team are university graduates with degrees in chemistry or pharmacy.

The current and potential technological capacity of Tecnoquímicas is based on diverse issues (know-how conveyed by its licensors in its 76 years of existence; in-house R&D; technology introduced by its API and equipment suppliers; technicians and highly trained professionals; technological developments with partners in the biotechnology area and with universities and research centres). These issues are discussed below.

3.1 Know-how conveyed by Tecnoquímicas's licensors

Tecnoquímicas's main business until the mid-1990s was to manufacture and market products licensed by large international pharmaceutical companies, such as SmithKlineBeecham and MSD. According to estimates of the Tecnoquímicas officials interviewed during the field mission, around 70% of the products sold by the company in 1995 were licensed, whereas now only 10% of the Tecnoquímicas products are licensed.

Incident to these licences, Tecnoquímicas received transfer of technology in terms of galenical formulation and analytical methods to manufacture the different products, but above all it signified receiving the know-how and GMP training that each of its licensors demanded. Tecnoquímicas was, to a certain

7 The Yumbo plant has a GMP certificate valid until 30 June 2011 granted by INVIMA; the San Nicolás plant until 23 May 2011; the Jamundí plant until 5 April 2011; and the Villa Rica plant until 20 September 2011 (INVIMA, 2010).

extent, the sum of all the know-how of all the companies that had been its licensors, which gave Tecnoquímicas a huge competitive advantage.

An important milestone in the history of Tecnoquímicas's technological capacity was the purchase of the MSD plant in 1986, which allowed Tecnoquímicas to make a great technological leap forward, since this plant was the most modern in Colombia at the time.

The time of the big licences to produce pharmaceutical products came to an end in the 1990s, with globalization and the departure of the large multinational laboratories. Related transfer of technology also came to an end.

3.2 In-house research and development

Tecnoquímicas has an R&D laboratory that dates back to 1995. This laboratory is in the San Nicolás plant. The plant has 20 professionals and it is run by a graduate of the University of Buenos Aires with a degree in pharmacy and 20 years' experience in the R&D area, both in generic products laboratories and in multinational companies in Argentina. The main function of the R&D laboratory is to develop the galenical formulations and the analytical methods of control of the new pharmaceutical products that Tecnoquímicas will manufacture and market. This laboratory develops 50–60 new products per year. This area has a small plant that allows Tecnoquímicas to produce pilot batches and to carry out production trials and analytical methods. This area is also in charge of industrial scaling.

Typical innovations are in new pharmaceutical forms, new combinations of known active principles, new methods of manufacturing, and improvements or changes to existing products. In this sense, the R&D activity does not differ substantially from what other Colombian and Latin American generic products laboratories do – that is, to improve and adapt known products. The R&D laboratory has experience in the development of the following pharmaceutical forms: tablets; gel and powder capsules; oral and topical solutions, suspensions and syrups; lotions and semi-solids; liquid and dry powder injectable products; solid and suspension ophthalmological products; softgel capsules; and effervescent tablets and powder.

The sources of information used to support the galenical development and the analytical methods are (i) information supplied by the API manufacturer, (ii) bibliographic reviews from paid databases, such as the Chemical Abstracts Service, and (iii) patent documents.

A distinctive trait of Tecnoquímicas is the importance of marketing for its development of new products. Product development is achieved through a combined effort. The Tecnoquímicas medical representatives impart information about the needs and preferences of doctors and patients, while the marketing staff analyse trends and preferences of the Colombian consumers. All the information gathered is summarized in a document detailing the traits that a product must possess. This document is sent to the R&D laboratory,

where it brings about improvements or changes in the products to make them more appealing to Colombians (Mejía et al., 2009).

Lastly, Tecnoquímicas has to date requested two national patents and a Patent Cooperation Treaty (PCT) patent for a new formulation of softgel capsules, a new association of naproxen and ibuprofen, and a system of controlled release. These patents show the kind of in-house innovations achieved by this company. Whether it is advisable, from the perspective of both public health and innovation policy, to make available patent protection for this kind of incremental pharmaceutical innovation, is an entirely different question, which would go beyond the scope of this study.[8]

3.3 Transfer of technology by suppliers and contractors

The main source of acquisition of technology available to Tecnoquímicas now is through its API and equipment suppliers. Tecnoquímicas considers essential that API suppliers guarantee the constant quality of the product, which is why the company has rejected less expensive suppliers in India and China in favour of other companies – even in those countries – that provide more expensive alternatives but that guarantee the quality of their APIs. In addition, suppliers usually transfer, together with the API, know-how and confidential information regarding formulation. This type of transference is highly valued by Tecnoquímicas, since it allows the company to shorten development times and to place its products on the market before its competitors.

The equipment suppliers also play an important role in the enhancement of the company's technological assets, both because of the technology added to the equipment and because of the training in the use of the equipment provided by the suppliers.

A good example of this is the recent incorporation of the softgel capsules production plant. Tecnoquímicas was involved in a project to launch softgel capsule products. To do this, Tecnoquímicas had reached an agreement with Procaps S.A.,[9] a pharmaceutical laboratory, to outsource to Procaps the production and development of the softgel capsule products; but at the last minute the agreement fell through. For this reason, Tecnoquímicas decided not to depend on third parties and to manufacture these products directly, but Tecnoquímicas had to acquire the new technology to achieve this.

The company explored several alternatives in the international market. It shortlisted companies in India, South Korea and the United States. A first obstacle was the language barrier, which made negotiations difficult and made Tecnoquímicas reject the Indian and Korean options. Finally, it decided in favour of the company GIC Engineering, Inc. (GIC) of Tampa, in the United States. Although GIC is an American company, the managing executives are

8 On the appropriate incentives for small scale innovation in the area of pharmaceuticals, see UNCTAD (2011, Part 2, Section 2.3.2).

9 Procaps S.A. is a Colombian laboratory that has achieved a remarkable development in the manufacturing of softgel caps. It is one of the key players in this market. It exports to the five continents and has plants in Colombia, Venezuela and Brazil.

Ecuadorian and speak Spanish, which made negotiations and the process of technology transference easier.

The selected production line was the SUPRA II. GIC carried out the plant design, manufactured the equipment, gave technical support, delivered two formulations, supplied technology regarding processes and trained the Tecnoquímicas staff. Tecnoquímicas hired a technician from another company, who had experience and expertise in the handling of softgel capsules.

Production of the plant was not free from difficulties. First, Tecnoquímicas had problems with the engineering works related to dry air and water supply. The companies that had been hired did not possess the degree of expertise necessary to comply with the standards that the technology required. This caused problems in the manufacturing of the capsules. The company then had to make adjustments in the equipment to deliver a product that would meet the required quality standards.

Second, there were intellectual property problems. Procaps S.A. held several patents regarding processes and formulations of softgel capsules. The Tecnoquímicas R&D department had to find alternative processes and formulations that would not infringe these patents. This development brought about a patent application under the company name.

3.4 Skilled workers and professionals

Like other laboratories controlled by Colombians, Tecnoquímicas resorted to one of the most effective techniques for acquiring technology: hiring staff who had previously worked for multinational laboratories. These technicians and professionals are highly trained and bring fresh knowledge, which is why they are much sought after by the national laboratories.[10] This informal way of making technology flow was very important until the mid-1990s. In the past few years, however, this type of flow has become less common, since most of the multinational plants in Colombia have closed down.[11]

In general, the chemical-pharmacological training in Colombia is very good, although some of the interviewees pointed out that it is outdated. There are five universities where future graduates in chemistry and pharmacy study.[12] During the interviews, it was stressed that, in general, the training in maths and English is poor, which makes it difficult to take advantage of the available resources and to receive transfer of technology from foreign companies.[13]

10 A high-ranking official of a multinational innovative laboratory that still has a plant in operation in Colombia was interviewed during the mission. He claimed that the constant job offers that his staff members receive constitute "harassment".

11 The closure of the multinational plants left many workers, technicians and professionals unemployed. The national laboratories jumped at the opportunity. They added these unemployed people to their payrolls, thus enhancing their technological assets without making a considerable investment.

12 Universidad Nacional de Colombia (Bogotá), Universidad de Antioquía, Universidad del Norte (Barranquilla), Universidad de Cartagena and Universidad ICESI (ICESI).

13 The same official quoted in footnote 10 mentioned that, of all the plant staff on the payroll, only two professionals were able to receive training and communicate fluently in English.

During interviews with the Tecnoquímicas managers, they emphasized that, regardless of the technical knowledge acquired by professionals at university or by technical staff and manual workers at high school, the most important part of the training process takes place in the plant through "learning by doing".[14]

Regardless of this, Tecnoquímicas runs an external technical training programme for its staff. This training is carried out both in and outside Colombia. The company invested US$ 1.2 million in this programme in 2007.[15]

3.5 Developments in the biotechnological area

Tecnoquímicas has taken some timid steps into the biotechnological area in recent years. It took part in a joint venture with Limor de Colombia S.A. (Limor) to manufacture and market an anti-tick vaccine for cattle. It has also benefited from transfer of technology, including through training in Cuba, from the company Heber Biotec S.A. (Heber Biotec) and from the Centro de Investigaciones Genéticas y Biológicas (Center for Genetic and Biologic Research) of the Polo Científico de La Habana (Habana Scientific Pole), to formulate a healing cream whose API is recombinant epidermal growth factor (rEGF).

Tecnoquímicas is considering the possibility of widening its range of biotechnological products. An Argentine company has offered to transfer biotechnological product technology to Tecnoquímicas, and Tecnoquímicas is considering hiring a consultancy firm to carry out a feasibility study into this. This third step into the biotechnology area would entail manufacturing technologically mature products, such as erythropoietin, interferon alfa and beta, filgrastim and human growth hormone.

3.6 Partnerships with universities and research centres

Tecnoquímicas has always followed an intelligent policy of giving financial support to universities and research centres.[16] Although these donations have more to do with the firm's corporate social responsibility policies, Tecnoquímicas obtains important benefits from its relationships with these institutions. While the universities and research centres benefit from Tecnoquímicas's financial support, Tecnoquímicas benefits from the chance to recruit and train staff from

14 Universidad del Valle researchers have carried out an interesting investigation on the traits and organization of the Tecnoquímicas workforce (Mejía et al., 2009).

15 Tecnoquímicas also encourages its staff to enrol on graduate and postgraduate courses. The company grants scholarships to chosen members of staff. These staff are selected according to the courses chosen by them and the needs of the company. For example, of the 221 Tecnoquímicas employees with postgraduate degrees, 108 had been the recipients of scholarships that covered 70% of tuition costs. In 2007, US$ 1 million was spent on scholarships.

16 Among the research centres and universities that Tecnoquímicas has supported, the most important are ICESI, Centro Internacional de Entrenamiento e Investigaciones Médicas (International Medical Research and Training Centre; CIDEIM), Universidad de Antioquía (University of Antioquía), Centro de la Ciencia y la Investigación Farmacéutica (Center for Science and Pharmaceutical Research; CECIF), Fundación Valle del Lili (Valle del Lili Foundation) and Centro de Investigación para el Desarrollo de Productos contra Enfermedades Tropicales (Research Centre for the Development of Products to Fight Tropical Diseases; CIDEPRO).

these institutions and use them to undertake the studies and clinical trials[17] (bioavailability and bioequivalence[18]) for which Tecnoquímicas does not have the necessary equipment or staff and, in some cases, to obtain transfer of technology. In a public–private partnership, Tecnoquímicas is involved in R&D on pharmaceutical products, vaccines and diagnostic tests for tropical diseases such as leishmaniasis.[19]

4. The pharmaceutical market in Colombia

Colombia's estimated population in 2010 was 45 508 205 (DANE, 2010). Approximately 45% of the Colombian population lives below the poverty line (Ministerio de la Protección Social & PAHO, 2008). In 2008, the infant mortality rate was 15.5 deaths per 1000 live births (Ministerio de la Protección Social & PAHO, 2008). Colombia has 160 doctors and 80 nurses for every 100 000 inhabitants (Ministerio de la Protección Social & PAHO, 2008).

The principal infectious diseases found in Colombia are malaria, dengue, human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) and tuberculosis. Colombia reported 84 525 cases of malaria and 71 079 cases of dengue in 2009 (Instituto Nacional de Salud, 2009). The tuberculosis incidence and the tuberculosis Bacillus Koch positive (BK+) rates are 24.9 and 16.4 cases per 100 000 inhabitants, respectively (Ministerio de la Protección Social & PAHO, 2008). The incidence rate for HIV/AIDS is 1.9 per 1 000 000 inhabitants (Ministerio de la Protección Social & PAHO, 2008). Leishmaniasis has become an endemic pathology: 12 727 cases were reported in 2009, a significant increase over the average number of cases reported in the 1990s (6500). However, the situation may be even worse, since it is believed that government statistics may not be accurate because a large number of cases of leishmaniasis are not reported.

The Colombian pharmaceutical industry consists of approximately 143 industrial plants that are GMP-certified by INVIMA, 133 of which belong to Colombian businesses and 10 of which belong to foreign-owned laboratories.[20] The Colombian pharmaceutical sector offers about 1447 products with

17 For example, on valsartan (for arterial hypertension), oxcarbazepine (for epilepsy), gabapentin (for epilepsy), carbamazepine (for epilepsy and bipolar disorder), gliclazide (for diabetes mellitus), clonazepam (an anxiolytic) and metformin (for diabetes mellitus).

18 "Bioavailability is the rate and extent at which the active pharmaceutical ingredient or active moiety is absorbed from a pharmaceutical dosage form and becomes available at the site(s) of action" (WHO, 2006, p. 213). See also Ministry of Health, Resolution No. 1400, 24 August 2001. "Two pharmaceutical products are bioequivalent if they are pharmaceutically equivalent or pharmaceutical alternatives and their bioavailabilities, in terms of peak (Cmax and Tmax) and total exposure (area under the curve (AUC)), after administration in the same molar dose under the same conditions, are similar to such a degree that their effects can be expected to be essentially the same" (WHO, 2006).

19 CIDEPRO is a public–private partnership founded at the initiative of the Universidad de Antioquia, IPS Universitaria, Universidad Pontificia Bolivariana, CECIF, Tecnoquímicas and Humax Pharmaceutical S.A. in January 2009. Currently, CIDEPRO is carrying out six research projects related to leishmaniasis.

20 Source: INVIMA.

different APIs or combinations thereof, which make up more than 14 000 different presentations (Econometría Consultores, 2005).

In 2009, sales in the Colombian pharmaceutical market totalled US$ 2.232 billion (ANDI, 2010b). Prescription drugs account for 68.2% of the market and OTC sales comprise the remaining 31.8%, as of 2008 (ANDI, 2010b). The pharmaceutical industry represents 2.31% of industrial gross domestic product (GDP) (ANDI, 2010b). The pharmaceutical industry directly employs 22 264 people (ANDI, 2009).

Colombian laboratories control approximately 66% of the domestic market by sales, foreign-owned generic laboratories 10%, and foreign innovative laboratories the remaining 23% (Proexport, 2008). In 2009, 3 of the 15 largest laboratories located in Colombia were domestic companies: Tecnoquímicas (first), Procaps S.A. (ninth) and Lafrancol (twelfth) (Table 1) (La Nota Económica, 2010).

***Table 1** Main Colombian laboratories by sales, 2009*

Position	Company	Sales (US$ million)
1	Tecnoquímicas	361
2	Pfizer	310
3	Merck/Schering-Plough	270
4	Roche	257
5	Baxter	244
6	Abbott	201
7	Bayer	191
8	Novartis	149
9	Procaps S.A.	148
10	sanofi-aventis	147
11	GlaxoSmithKline	131
12	Lafrancol	118
13	Boehringer Ingelheim	95
14	Genfar	90
15	AstraZeneca	58

Source: La Nota Económica (2010).

Products on the Colombian market are classified as either generic or branded. Among the branded products there are two different types: patented products and branded generics (products in the public domain but sold by domestic laboratories under trademarks). Most generic products are destined for the institutional market that belongs to the national health-care system. The generic market is dominated by domestic laboratories, although some multinational companies such as Novartis and sanofi-aventis participate in this sector through their respective generic divisions, Sandoz and Winthrop.

Table 2 shows the market share of branded and generic products in Colombia in volume and in value terms. In 2009, the market share of generic products was 34% of the total units sold, but the sales of these products account for

only 11.5% of the total value of sales. The table illustrates that although the generic market share in volume terms increased slightly in the period 2006–2009, the market share in value remained stable over the same period, despite a more prominent increase in 2009.

***Table 2** Market share in value and volume*

	Market share (value)				Market share (volume)			
	2006	**2007**	**2008**	**2009**	**2006**	**2007**	**2008**	**2009**
Generic products	10.5%	10.7%	10.8%	11.5%	31.1%	31.6%	33.0%	34.3%
Branded products	89.5%	89.3%	89.2%	88.5%	68.9%	68.4%	67.0%	65.7%

Source: La Nota Económica (2010).

The Colombian pharmaceutical sector came into existence in the early twentieth century with the establishment of a pharmaceutical industry funded with capital of foreign origin (Gallo Castro, 2010). In the 1940s and 1950s the industry gained momentum thanks to the establishment of a government policy that restricted the import of pharmaceuticals and fostered the domestic production of such products. This policy motivated companies such as Abbott (1944), Bristol Myers Squibb (1944), Whitehall Laboratorios (1946), Química Schering (1950), Hoechst Colombiana (1955), Baxter Colombia (1956), Glaxo Wellcome de Colombia (1957), Merck Colombia (1957), Productos Roche (1957) and Bayer de Colombia (1957) to build their plants in Colombia (DNP, 2004). The establishment of these laboratories allowed Colombia to become an important Latin American production centre. It also contributed to advances in the processes of transfer and assimilation of technology (Vallejo Díaz et al., 2007).

Although the Colombian pharmaceutical industry started operating relatively early in the twentieth century (DNP, 2004), it was not until the 1970s and 1980s that a large number of domestic laboratories appeared. This was prompted by a combination of three factors: the lack of patent protection for pharmaceutical products, the existing health care legislation, and a policy that encouraged the prescription of generic products (DNP, 2004).[21]

In the 1990s, changes in public policies in the sector had an impact on the development of the pharmaceutical industry in the following years. First, significant changes were introduced in the patent regime: patenting pharmaceutical products was no longer forbidden, and using patented manufacturing methods in the country ("local working") was no longer mandatory (see Section 5.7).

Second, there were significant changes in the pharmaceutical industry regulations (Ministerio de la Protección Social & PAHO, 2003), such as the creation in 1994 of INVIMA,[22] a public health regulation authority that introduced stricter GMP requirements (see below). The other important change

21 See also Gallo Castro (2010).

22 Decree No. 1290 of 1994.

was the establishment of new GMP standards in April 1995 through Decree No. 677, which contained the recommendations included in the thirty-second report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations (WHO, 1992) (see Section 5.3).

Third, a new general social security system in health was implemented when Law No. 100 was enacted in 1993. This law applies the principles of universal health coverage, solidarity and obligatory participation. As a consequence of the passing of this law, the number of people who benefited from the social security system rose from 25% in 1993 (Glassman et al., 2010) to 86% in 2008 (DANE, 2008). This increase had a great impact on the demand for medications due to the consolidation of the institutional market, which favoured the purchase of generic products. This trend allowed the entrance of new domestic players, whose aim was to supply this increasing demand.

These changes in public policy brought about significant structural changes in the industry (Econometría Consultores, 2005; Gallo Castro, 2010). In the mid-1990s a process of divestment on the part of international pharmaceutical companies began. Illustrative of this is the decrease in the number of operating plants owned by multinational laboratories (down from 100 in 1995 to 10 in 2010, according to INVIMA), and the consequent increase in the number of operating plants owned by domestic laboratories (up from 32 in 1995 to 133 in 2010).[23] These domestic laboratories built up their strength through the purchase of some of the plants that belonged to the multinational companies undergoing the process of divestment and that had been closed down (Gallo Castro, 2010). This process may have been caused by several factors, including the level of political violence experienced in Colombia in the 1990s. However, the academic literature and data collected during the field interviews suggest that endogenous factors within the pharmaceutical industry may have caused such a phenomenon.

With the introduction of the new GMP guidelines, many plants that did not comply with these parameters became obsolete. A considerable investment was required to make the plants meet new GMP requirements established by INVIMA. This situation, together with a globalization process in the pharmaceutical industry that involved closing some plants and concentrating production processes in more modern plants in a search for efficiencies, made many companies close their Colombian plants and supply this market through imports.

The fact that these plants were closed had an impact on how the domestic market was supplied. In the 1980s, the number of existing plants was such that it was possible to meet almost all the demand of the Colombian market: 95% of the products sold had been domestically produced (Econometría Consultores, 2005; Vallejo Díaz et al., 2007). In 1994 the market share of domestically produced products fell to 90.4%, and in 2007 it dropped to 73.0% (Econometría Consultores, 2005); this brought about an increase in the volume of imports of finished products. In 2009, the imports of these products

23 Source: INVIMA and Gallo Castro (2010).

accounted for 59% of total imports,[24] an indication that the market is open to international competitors.

In 2009 the export of pharmaceutical products represented 1.19% of Colombia's total exports, while the import of pharmaceutical products made up 3.36% of the country's total imports.[25] For 2009, Colombian imports and exports of APIs, excipients and finished and semi-finished products totalled US$ 1.105 billion and US$ 391.21 million, respectively. Consequently, the foreign trade balance showed a deficit of US$ 714 million in 2009.[26]

Of these totals, APIs and excipients comprised roughly US$ 234 million of imports and US$ 19.3 million of exports. The import of finished and semi-finished pharmaceutical products totalled US$ 656 million and US$ 214, respectively; and the export of finished and semi-finished products totalled US$ 370 million and US$ 1.5 million, respectively (see Table 3) (ANDI, 2010a).

Table 3 Finished and semi-finished pharmaceutical products, APIs and excipients: imports and exports, 2009

	Imports 2009		Exports 2009	
	Value CIF (US$)	Variation 2009/2003	Value FOB (US$)	Variation 2009/2003
Finished pharmaceutical products	656 790 712	98.39%	370 662 598	84.68%
Semi-finished pharmaceutical products	213 959 138	112.08%	1 415 310	29.23%
APIs	227 005 713	45.05%	18 321 498	149.34%
Excipients	7 850 764	61.71%	814 551	–18.33%
Total	1 105 606 328	105.67%	391 213 957	105.37%

CIF, cost, insurance and freight; FOB, free on board.
Source: ANDI (2010a).

Table 4 shows the origins of imports to Colombia. According to the data, 87.16% of imports to Colombia come from 12 countries. Since 2003, Colombia has experienced a spectacular growth in imports from China (363.06%) and Germany (207.70%). It is not clear from the information gathered during the interviews the extent to which investments withdrawn from Colombia were relocated by multinational corporations to production sites in these countries, or to other countries that have witnessed considerable growth in exports of pharmaceutical products to Colombia, such as Argentina, Brazil and India. Although the available information does not distinguish between imports of APIs and semi-finished and finished pharmaceutical products by country, the growth in imports of Chinese origin may be explained by the fact that

24 Conclusion of the author based on information from ANDI (2010a).

25 Conclusion of the author based on information from ANDI (2010a) and DANE (2010b).

26 Conclusion of the author based on information from ANDI (2010a).

China has become an important supplier of APIs for the generic industry in recent years. The growth in imports from Germany, however, may be the result of two factors. First, Bayer, Merck and Boehringer Ingelheim have kept their production plants in Colombia, and therefore they import APIs and semi-finished products from their headquarters to add them to industrial processes, thus turning Colombia into a production and distribution hub to supply other countries in the region (see Table 6). Second, many finished products that are not locally produced come from Germany.

***Table 4** Pharmaceutical product imports by country, 2008*

Country	Value CIF (US$)	Percentage of imports	Growth 2003/2008
Germany	133 283 508	12.84%	207.70%
United States	118 558 480	11.42%	37.48%
France	82 688 638	7.97%	112.80%
China	81 831 133	7.88%	363.06%
Mexico	79 090 897	7.62%	55.22%
Italy	67 531 356	6.51%	190.17%
Brazil	58 870 774	5.67%	112.74%
India	53 746 764	5.18%	146.62%
Switzerland	52 319 106	5.04%	24.40%
Argentina	49 934 885	4.81%	170.18%
Netherlands	29 920 957	2.88%	n/a
Puerto Rico	29 741 254	2.87%	n/a
Others	133 283 508	12.84%	55.56%
Total	1 037 871 328	100%	93.07%

CIF, cost, insurance and freight; n/a, not applicable.
Source: ANDI (2010a).

Table 5 shows information about the ten main importers of pharmaceutical products in Colombia. The table shows that all of these importers are multinational laboratories, which is a result of the previously mentioned process of divestment and the decision to supply the market with imports of finished products.

***Table 5** Main importers of pharmaceutical products in Colombia, 2008*

Company	Value FOB (US$)	Percentage of imports
Abbott Laboratories de Colombia S.A.	74 898 346	7.22%
Pfizer S.A.	46 829 231	4.51%
Bayer S.A.	45 095 265	4.34%
Productos Roche S.A.	44 800 789	4.32%
Laboratorios Wyeth Inc.	41 860 523	4.03%
GlaxoSmithKline Colombia S A	41 832 712	4.03%

Company	Value FOB (US$)	Percentage of imports
Novartis de Colombia S.A.	38 789 950	3.74%
Sanofi Aventis de Colombia S A	37 339 873	3.60%
Bayer Cropscience S.A.	28 546 304	2.75%
Merck S.A.	27 239 468	2.62%
Total	427 232 461	41.16%

FOB, free on board.
Source: ANDI (2010a).

Exports of pharmaceutical products increased dramatically in the 1990s due to the widening of the overseas market as a result of the conclusion of the international trade agreements (Free Trade Agreement Colombia–Venezuela–Mexico (G3) and Comunidad Andina de Naciones (Andean Community)) (DNP, 2004). In 2007, 17.1% of local production was exported (ANDI, 2010b). The main destinations for these exports were the Andean countries, among which Venezuela (28.73%), Ecuador (24.74%) and Peru (8.72%) stand out, since they account for 62% of total exports. Table 6 shows the export destinations and the percentages of pharmaceutical products exported to those destinations.

***Table 6** Pharmaceutical product exports by country, 2008*

Country	Value FOB (US$)	Percentage of exports	Growth 2003/2008
Venezuela	98 712 070	28.73%	147.77%
Ecuador	84 989 595	24.74%	68.50%
Peru	29 972 742	8.72%	39.17%
Panama	25 963 785	7.56%	19.27%
Chile	17 323 506	5.04%	71.69%
Cucuta Free Trade Zone	16 733 497	4.87%	96.32%
Mexico	11 981 021	3.49%	–58.90%
Guatemala	9 665 314	2.81%	n/a
Others	48 194 422	14.03%	154.11%
Total	343 535 951	100.00%	

FOB, free on board.
Source: ANDI (2010b).

Table 7 gives information about the ten main exporters. Four of these exporters are domestic laboratories. Colombian-produced pharmaceutical exports are either finished products produced by multinational laboratories that have kept their Colombian plants or generic products for the Andean region produced by domestic laboratories. Table 7 shows that the multinational laboratories that have remained in Colombia have considerable production capacities, as illustrated by the rather high percentage of exports. This important potential may have been a reason for their being unaffected by the divestment process that took place during the 1990s.

Table 7 Main exporters of Colombia, 2008

Company	Value FOB (US$)	Percentage of exports
Laboratorios Baxter S.A.	30 077 408	8.76%
Boehringer Ingelheim S.A. UAP 164	29 245 531	8.51%
Procaps S.A.	26 774 765	7.79%
Merck S.A.	26 774 662	7.79%
W-L LLC	21 335 395	6.21%
Genfar S.A.	19 895 298	5.79%
Laboratorios La Sante S.A.	19 231 864	5.60%
C.I. Procaps S.A.	17 368 109	5.06%
Schering Plough S.A. Uap Cod. 442	13 930 131	4.05%
Sanofi Aventis de Colombia S.A.	13 536 803	3.94%
Total	218 169 966	63.51%

FOB, free on board.
Source: ANDI (2010b).

Colombia produces locally very few APIs, such as paracetamol,[27] and must therefore import APIs and semi-finished products (DNP, 2004). As a result, international costs of raw materials have a direct impact on the cost of local production (Gallo Castro, 2010). ANDI statistics shown in Table 3 demonstrate the existence of API exports. The main products included in this table are stearic acid (7.28%), paracetamol (18.5%) and vitamins (23.60%).[28]

The percentage of imports of semi-finished products has increased steadily, causing a reduction in the contribution to the national production process in terms of added value (Abbott, 2007; Econometría Consultores, 2005). Consequently, in 2003–2009, the import of semi-finished products increased by 112%, while that of APIs increased by only 45.05% (field interviews).

Colombian pharmaceutical laboratories, both domestic and foreign, mainly formulate medicines. Many of these medicines have been on the market for many years, and they are not among the latest therapeutic novelties. There is no research or development of new molecules.

27 Industria Química Andina manufactures paracetamol (Abbot, 2007).

28 Conclusion of the author based on information from ANDI 2010a.

5. The framework for local production and technology transfer in Colombia

5.1 The health security system

The Sistema General de Seguridad Social en Salud (General System of Social Security in Health; SGSSS) has exerted an enormous influence on the evolution and current profile of the pharmaceutical industry in Colombia. First, medications covered by the Plan Obligatorio de Salud (Mandatory Health Care Plan; POS) are supplied for free, which has increased the demand for generic medications. Second, the demand for inclusion in the POS of medications so far not covered caused a serious financing problem to the system, which has put the viability of the SGSSS at risk in the short term (see below).

SGSSS has had enormous success in terms of achieving near-universal coverage, an increase in health-care expenses and a change in its composition of health-care spending. In 1993, when Law No. 100 was passed, only 25% of the population had access to health care (Glassman et al., 2010). In 2008, the SGSSS provided coverage to 86% of the Colombian population (DANE, 2008). Spending in health care rose from 6.2% of GDP in 1993 to 7.8% in 2003. As a consequence of the implementation of the SGSSS, private spending on health care went down from 3.3% of GDP in 1993 to 1.2% in 2003.

Progress in coverage notwithstanding, SGSSS faces several problems. According to Glassman et al. (2010), "a decade after the reform, 15 percent of the population remains uninsured; benefit plans under the contributory regime and the subsidized regime still differ. There are deficiencies in the quality of care and not all public hospitals are modernized. The stewardship function needs to be strengthened; the financial sustainability of the system is continually at risk". It has also been pointed out that the percentage of the rural population that has joined the SGSSS is smaller than that of the urban population, and that poor people have a nominal rather than real access to health care (Contraloría General de la República, 2009).

Requests for coverage and judicial orders for non-POS medications (medicines not covered by POS) or therapies have increased dramatically. The Ministry of Social Protection estimates that between 1997 and 2000, requests for recovers on medications not included in POS were 387 and there were 701 judicial

orders that mandated the recovery of non-POS medications. By November 2009, the health system received 1 412 462 requests for non-POS medication recovers and 945 406 judicial orders.[29]

In an attempt to accommodate the increased request for non-POS medicines, the Colombian Government in a new law sought to increase the coverage of the POS. The Constitutional Court, however, considered this law unconstitutional, as it favoured certain parts of the population. The Court claimed that the public health system should cover all non-POS medications. According to the Colombian Government, this ruling had the effect of producing a dramatic change in the demand for non-POS services and medications, which caused an increase in the number of applications and in their costs, causing an untenable deficit in fiscal and financial terms.[30] In addition, several NGOs (e.g. IFARMA, 2010; Federación Médica Colombiana, 2008) denounced the existence of mechanisms to influence prescriptions that did not comply with sanitary and business ethics codes. They also denounced the fact that some laboratories that marketed non-POS products encouraged doctors to prescribe those.[31]

On 23 December 2009, the Colombian Government declared a social emergency in health (social emergency) through Decree No. 4975 to enable the issuing of measures to address the SGSSS crisis. Between 23 December 2009 and 21 January 2010, the Colombian Government issued 17 decrees on the grounds of the social emergency. These decrees included anticorruption measures for the public health system,[32] and they reassigned resources in the SGSSS, set marketing margins for medications, and created new resources for the public health system through tax increases on, for example, beer, liquor and gambling.[33] However, the Constitutional Court later declared the unconstitutionality of almost all the decrees issued on the grounds of the social emergency.[34]

But not all the measures established in the social emergency decrees fell through. In July 2010, the Congress, through Law No. 1393, ratified the tax reform established by Decree No. 127. In addition, decrees and resolutions were issued where maximum marketing margins for medications and medical devices were set; a regime of parallel imports was established; and prices were agreed with suppliers.

29 Established by the Corte Constitucional (Constitutional Court) in judgment T-288/10 (http://www.corteconstitucional.gov.co/relatoria/providencia.php).

30 See Decree 126 of 2010.

31 See also "El Tiempo", "Dádivas y regalos a médicos para que formulen drogas, cuestionados en E.U.; en Colombia son la norma Federación Médica Colombiana", 16 July 2008.

32 See Decree No. 126 of 2010.

33 Decrees Nos 4373 and 4376 of 2009; and Nos 119, 120, 073, 074, 075, 126, 127, 128 129, 130, 131, 132, 133, 134 and 135 of 2010.

34 Ibid. Judgments C-288/2010 (Decree No. 128 of 2010), C-289/2010 (Decree No. 131 of 2010), C-290/2010 (Decree No. 075 of 2010), C-291/2010 (Decree No. 129 of 2010), C-292/2010 (Decree No. 135 of 2010), C-297/2010 (Decree No. 134 of 2010), C-298/2010 (Decree No. 074 of 2010), C-302/2010 (Decree No. 126 of 2010), C-332/2010 (Decree No. 130 of 2010), C-374/2010 (Decree No. 132 of 2010) and C-399/2010 (Decree No. 073 of 2010). See http://www.corteconstitucional.gov.co/relatoria/providencia.php.

At the time of writing, the problems, financial and otherwise, that prompted the declaration of the social emergency remained unsolved, and civil society, health-related companies and the Colombian Government were still debating how to solve the crisis.

5.2 Drug regulation

INVIMA is the national regulatory authority on drugs and food in Colombia. INVIMA was created through Law No. 100 of 1993, Article 245, and its functions and area of influence were regulated by Decree No. 1290 of 1994. INVIMA is a public, scientific and technological institution with legal capacity and independent assets. It is established under the Ministry of Social Protection.[35]

In the opinion of the individuals interviewed during the visit to Colombia, generally INVIMA fulfils its task satisfactorily and has made remarkable progress compared with the performance of the entity (the Ministry of Health) previously responsible for this task. In June 2010, the Pan American Health Organization (PAHO) named INVIMA a level IV national regulatory authority for reference drugs, the highest level granted by PAHO, thus placing INVIMA at the same level as the Brazilian and Argentine national regulatory authorities.

5.3 Marketing authorization

The Colombian drug manufacturing, importing, exporting and marketing regime is regulated by Law No. 100 of 1993, Decree No. 677 of 1995 (with several modifications introduced over a period of time) and other regulations issued by the Ministry of Social Protection and INVIMA. Decree No. 677 establishes that pharmaceutical plants that produce medicines either in Colombia or for the Colombian market must have GMPs certified by INVIMA.[36] With this aim in mind, this decree adopted the GMP standards included in the thirty-second report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations (WHO, 1992).

In 1995, when Decree No. 677 officially took effect, many plants did not meet the new GMP standards. Therefore, the decree drew up a schedule that established the deadlines for investments and changes that had to be made by those companies that did not meet the new standards. Both domestic and foreign laboratories with plants in Colombia were given enough time to be able to adjust to the new regulatory framework, and competition was minimally affected. At the time of writing, 174 plants operating in Colombia were GMP-certificated by INVIMA and another 202 plants operating abroad possessed this certification.

Decree No. 677 also establishes that the production, import, export, manufacture, packing, packaging, marketing and sale of medications in Colombia are subject to obtaining marketing authorization issued by INVIMA.[37]

35 Law No. 100 of 1993, Article 245; and Decree No. 1290/1994, Article 1.

36 Decree No. 677/1995, Article 6.

37 Decree No. 677 of 1955, Article 19.

INVIMA issues six types of marketing authorization: (i) manufacture and sale, (ii) importation and sale, (iii) importation, packing and sale, (iv) importation, semi-manufacture and sale, (v) semi-manufacture and sale and (vi) manufacture and exportation.[38] If a new medicine has already been authorized in at least two countries of reference,[39] and its registration has not been denied in any of those countries, then to comply with the pharmacological evaluation it will suffice to present a summary of the clinical information together with the corresponding bibliography.[40] In this way, the process of registration takes less time and is less cumbersome.

The practice of approving drugs by reference and a requirement that bioequivalence tests be conducted only on high-risk drugs has contributed to the preservation of a competitive pharmaceutical market in Colombia, and favours new entrants and high levels of competition in the generic drug market.

It is worth noting that Decree No. 2086 of June 2010 established a speedy process to obtain marketing authorization in cases of general or public health interest that had been so declared by the Colombian Government.[41] However, medications whose APIs are subject to data protection in accordance with Decree No. 2085 of 2002 are excluded from this process (see Section 5.4).

5.4 Data exclusivity

The Colombian Government introduced data protection for an exclusivity period through Decree No. 2085 of 2002. This decision was controversial because of its impact on the generic products market: it does not allow the obtaining of marketing authorization by reference before the expiration of the exclusivity period (i.e. 5 years from the granting of marketing authorization). This decree has established a highly effective barrier to the entrance into the market of competitors of the protected medication, regardless of the existence of patent protection. Subsequent free trade agreements concluded with the United States and the European Union (EU) adopting the same standard, laying down an obligation to provide for a 5-year term of exclusivity of regulatory test data.[42]

A study of the information published by INVIMA regarding approvals of new chemical entities (NCEs) allows conclusions to be drawn about the strategy that multinational innovative laboratories have implemented in Colombia. For example, almost all the applications for marketing authorization of NCEs

38 Decree No. 677 of 1995, Article 14 (in accordance with a modification introduced through Decree No. 2091 of 1997).

39 Decree No. 677 of 1955, Article 27 § 1.

40 Ibid.

41 Decree No. 2086 of June 2010.

42 See Article 224.2 of the FTA EU–Colombia/Peru. Under the United States FTA with Colombia, parties have the possibility of reducing the term of protection to less than 5 years where the test data originator has not involved considerable efforts and expenditures. For details, see Roffe and Vivas-Eugui (2007) and UNCTAD (2011, Box 12). Note that at the time of writing (December 2010), neither FTA has entered into force.

were submitted for importation and sale. In the past 8 years, none of the multinational innovative laboratories has considered manufacturing the latest therapeutic novelties in Colombia; on the contrary, they have chosen to supply the domestic market with imports of the finished product.

5.5 Clinical trials

There has been a significant increase in the number of clinical trials undertaken in Colombia in recent years. Officials of the multinational innovative laboratories that were interviewed during the fieldwork agreed that Colombia has become an important centre in Latin America. According to the officials interviewed, Colombia has started to receive clinical trials that would otherwise have been sent to Mexico or Argentina. The officials agreed that the determining factors to choose Colombia are significantly lower costs and highly trained biomedical researchers.

5.6 Price controls

Since 1968, the Superintendencia Nacional de Precios (National Superintendence of Prices) has controlled the price of medications. The current price control regulatory and institutional schemes were established by Laws No. 81 of 1988 and No. 100 of 1993 (Econometría Consultores, 2005).

Price regulation can be exercised in one of the following ways:

- Direct control: the Comisión Nacional de Precios de los Medicamentos (National Commission of Drug Price Surveillance; CNPM) sets the maximum retail price.
- Regulated freedom: CNPM establishes the criteria and methodology for producers or distributors to set or to modify the maximum retail price.
- Surveilled freedom: producers and distributors may set the price freely, but they are obliged to inform CNPM about any variations in prices and indicate how prices are set (Econometría Consultores, 2005).

In general, until 2006, CNPM regulated the price of medicines, taking into account the number of suppliers per API and on a case-by-case basis CNPM centred its attention on essential medicines, high-priced medicines, and medicines with an impact on public health. Maximum retail prices were set based on the costs declared by the laboratories and on estimations of marketing margins (Econometría Consultores, 2005).

In 2004, a gradual process of liberalization of prices began. The consequences of this process were that no medication was under the regime of direct control and that by 2006, all medications were under the surveilled freedom regime. Thus, laboratories were able to set their prices freely, including for products with patent protection or data protection and for products with the same API that were offered by fewer than three suppliers.

In practice, the Colombian price control system has succeeded only once since 2006 (i.e. entry into force of Circular 04 of 2006 on the general introduction

of the surveilled freedom regime for all medicines on the Colombian market) in lowering the price of a pharmaceutical product. Circular 02 of 2009 set the reference price for Kaletra, an antiretroviral drug, taking into account the average prices in the Brazilian, Peruvian and Ecuadorian markets. CNPM established that the reference price of this medication in the 120 tablets presentation was US$ 1067.35 for the institutional market and US$ 1591.24 for the private market, while the same medication and presentation cost US$ 3443 on the Colombian institutional market and US$ 3296.16 on the private market. Abbott appealed Circular 02 of 2009 and other circulars, but these appeals were rejected by CNPM. Finally, in February 2010, Abbott complied with the CNPM circulars and lowered the price of Kaletra to the level established by the authority of application.

The serious financial situation that the SGSSS was undergoing around 2009 brought about changes in the medications price control policy. As mentioned above, the Colombian Government declared a social emergency in the public health system for 30 days. Under the scope of the social emergency, Decree No. 126 of 2010 was issued, which reversed the trend towards price liberalization. Also, in the context of the public health system regulatory emergency, the Colombian Government established through Decree No. 1313 of 2010 a system of parallel imports for medications not included in the POS (see below, section 5.7).

5.7 Patents

Patent protection in Colombia has been regulated since the 1970s by regional laws taking direct effect in the country because Colombia belongs to the Andean Community. Decision 85 of 1974 was the first regulation on the subject. Decision 85 established the absolute prohibition to patent pharmaceutical products and medical drugs[43] and the obligation to manufacture locally the patented inventions (working requirement), but allowed patents for pharmaceutical or pharmachemical processes.

In November 1991, Decision 85 was replaced by Decision 311, which allowed – with limitations – the patenting of pharmaceutical products except for those included on the WHO list of essential medications.[44] This same decision broadened the working requirement allowing patentees to import as long as this was done in order to meet the demands of the domestic market.[45]

43 Decision 85, Article 5 § c.

44 Decision 311, Article 7, § d.

45 Decision 311, Article 37. One commentator of an earlier version of this study suggested that the Andean Community may have deliberately chosen to phase out the local working requirement, with a view to encouraging multinational companies to abandon their local production sites and leave the latter for purchase by local producers. Information supporting this view is not available to the authors of this study. It should be noted, however, that the process of divestment by multinational pharmaceutical companies concerned Colombia in particular, as opposed to the entire Andean Community. In addition, interviews conducted in Colombia revealed that the main driver for the divestment decision on the part of the multinational companies was related not to the domestic intellectual property framework but to cost-saving considerations and the overall lack of political stability in Colombia (see Section 4).

This process of change consolidated with the harmonization of the Andean norms to the standards established by the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement, which occurred on 1 December 2000, when Decision 486 took effect. This decision eliminated any type of prohibition to patent medications, including those on the WHO list of essential medications, and established the extension of process patent protection to the product obtained through the patented process.[46]

Decision 486 also determines the non-patentability of therapeutic, surgical and diagnostic methods for humans or animals; the international exhaustion of patent rights; an exception for research and educational activities; and compulsory licensing as a remedy for anticompetitive practices.[47] Compulsory licenses are also authorized for reasons of public order or emergencies.[48] Finally, Decision 486 excludes second uses of pharmaceutical products from patentability.[49]

Finally, in the context of the financial crisis of the SGSSS, Decree No. 1313 of 2010 established a system of parallel imports for medications and medical devices not included in the POS. Other products can be added to this regime through a Ministry of Social Protection resolution. Although Decision 486 permits international patent rights exhaustion, including pharmaceutical products, Decree No. 1313 of 2010 establishes the requirement to obtain regulatory authorization for parallel imports of pharmaceuticals.

At the time of writing, the Ministry of Social Protection established that approximately 130 medicines were subject to the regime of parallel imports.[50] However, the Ministry of Social Protection has not laid down the regulations with the requirements and a list of the entities authorized to carry out those imports, which is why these parallel imports have not been carried out.

5.8 Transfer of technology

Decision 291 of the Andean Community of 1991 regulates both the transfer of technology regime and foreign direct investment (FDI). As far as transfer of technology is concerned, Colombia implemented Decision 291 through Decree No. 259 of 1992. This decree established that the registration of transfer

46 Decision 486, Article 52 § b.

47 Decision 486, Articles 20 § d, 54, 53 § b, and 66, respectively.

48 Decision 486, Article 65.

49 Decision 486, Article 21. With reference to this issue, see rulings of the Andean Community Court of Justice regarding the nullity of the sildenafil patent in the cases 89-AI-2000 (Peru), 34-AI-2001 (Ecuador) and 01-AI-2001 (Venezuela); and the prejudicial interpretation in the process 124-IP-2003. In addition, the Colombian Consejo de Estado of Colombia, Sala Administrativa, Sección Primera (Colombian Council of State, Administrative Chamber, Section First) confirmed the denial of a second pharmaceutical use patent in dossier # 1-6480 though the sentence of 2 May 2004.

50Ministry of Social Protection Resolutions Nos 1424, 1499, 1662, 1663 and 1704 of 2010.

of technology contracts will be automatic[51] or if 8 working days have elapsed since the submission and a number of requirements are met.[52]

With regard to the clauses that might constitute an obstacle to the registration of contracts, Decree No. 259 establishes only three: (i) the licensor's right to set sale or resale prices for the products that are manufactured using that technology; (ii) the licensee's duty to transfer to the supplier all such inventions or improvements as may be obtained through use of that technology; and (iii) clauses prohibiting or limiting in any way the export of the products manufactured using the respective technology.[53]

5.9 Foreign direct investment

In the past 10 years, the Colombian Government has carried out an intense policy to attract FDI. Proexport is in charge of promoting Colombian nontraditional exports, international tourism and foreign investment to Colombia.[54] Colombia has signed 15 bilateral investment treaties or free trade agreements with a chapter on investment, 6 of which are in effect.[55]

Andean Decision 291 includes the general framework for FDI for the Andean Community Member Countries. The main principles set forth by Decision 291 are that foreign investors have the same rights and obligations as those to which national investors are subject,[56] and that all direct foreign investments that comply with the conditions established in this Decision and in the respective national legislation must be registered with the competent national agency in freely convertible currency.[57]

With regard to the Colombian legislation, Article 15 of Law No. 9 of 1991 establishes the general principles for the treatment of FDI and empowers the Colombian Government to establish the necessary regulations. In particular, Law No. 9 of 1991 establishes the following rights of the investor, once the investment has been made in agreement with all the legal regulations: (i) remitting the profits of the investment abroad; (ii) reimbursing the capital invested and the profits capital; and (iii) to all intents and purposes, foreign

51 Decree No. 259 of 1992, Article 1.

52 These requirements are (i) identification of the parties and their nationality and residence, (ii) identification of the methods used to transfer the imported technology, (iii) contract prices of each of the elements involved in the transfer of technology, and (iv) establishment of the effective period of the contracts. Decree No. 259 of 1992, Article 2.

53 Decree No. 259 of 1992, Article 2 §§ 1 and 2.

54 Proexport has offices in Colombia (Barranquilla, Bogotá, Bucaramanga, Cali, Cucuta, Medellín, Pereira and Cartagena); and abroad (Beijing, Caracas, México City, Frankfurt, Lima, London, Madrid, Miami, New York, Quito, Ecuador, San José (Costa Rica), Santiago de Chile, São Paulo and Toronto).

55 Conclusion of the author based on information from the Organization of American States' Foreign Trade Information System (http://www.sice.oas.org/tradedata/COL_e.asp).

56 Decision 291, Article 2.

57 Decision 291, Article 3. Furthermore, the Andean regime establishes that the owners of a direct foreign investment have the right to (i) transfer abroad, in freely convertible currency, the proven net profits from their direct foreign investment; and (ii) re-export the proceeds, after payment of the corresponding taxes, from the sale of their shares, equity or rights in the recipient country or when the capital is reduced or the enterprise is liquidated. Decision 291, Articles 4–6.

investment in Colombia should be treated in the same way as that of Colombian nationals.[58]

An interesting policy is Contratos de Estabilidad Jurídica (Legal Stability Agreements) established by Law No. 963 of 2005. The Colombian Government guarantees investors that if, during the life of a contract, legislation is passed that adversely affects any of the rules identified in the agreement as having been a determining factor to make the investment, the investors will be entitled to continue operating under the prior rule during the term of the corresponding agreement. The term of such agreements may vary between 3 and 20 years, and they may cover new investments or increases of existing ones for amounts equal to or above 7500 times the minimum monthly legal wage (approximately US$ 1 700 000). The investor must pay the Colombian Government a premium equal to 1% of the amount of the investment made every year, or 0.5% thereof during nonproductive periods.

Colombia shows low levels of technology-intensive investments. From a regional comparative perspective, Colombia captures 0.62% of FDI with a high technological component directed to manufacturing in Latin America and 0.07% of FDI with a medium to low technological component (Posada Betancourt, 2010).

5.10 Industrial policies

The Ministry of Industry, Trade and Tourism launched the Programa de Transformación Productiva (Productive Transformation Programme) in 2008, with the objective of developing sectors of the Colombian economy so that they would acquire world-class status through the formulation and execution of sectoral business plans in public–private alliances, and with a view to achieving economic growth and job creation. The pharmaceutical industry has not been selected as one of the strategic sectors. Proexport officials mentioned during the field interviews that there are proposals to add the pharmaceutical industry as a ninth strategic sector to the Más y Mejor de lo Bueno subprogramme. Interviewees from the pharmaceutical industry mentioned something similar, but they were sceptical about whether the plan would be realized.

The pharmaceutical industry is the beneficiary of common horizontal promotion policies that benefit all industrial sectors. It is not subject to a special industry policy and it does not receive specific incentives, except income tax exemption for profits resulting from new medications developed in Colombia and protected by patents (see below, section 5.11). As discussed above, there is no difference in the treatment of foreign-owned companies and companies that do not have manufacturing plants in Colombia. Colombia

58 Law No. 9 of 1991, Article 15. FDI does not require authorization and can be carried out in all sectors of the economy, except investments in mining, oil, insurance, television and the financial sector, which requires, in certain cases, previous authorization. In addition, this decree prohibits FDI in activities of national security and defence; private security and surveillance companies; and the processing, handling and disposal of toxic, radioactive or dangerous waste. See Decree No. 2080 of 2000.

does not require, either wholly or partially, that medical drugs or their inputs be manufactured locally.

Regarding tariffs, the pharmaceutical sector is open and often finds itself subject to intense external competition. Imports from the Andean Community (Ecuador, Peru and Bolivia) are exempt from import duties, and also were from Venezuela until 2011. The Common External Tariff (i.e. the Andean Community harmonized tariff system) applies to imports from all other countries.[59] The tariff rate on APIs, excipients and pharmaceutical products varies from zero to 15%, depending on the tariff position. The rate allocation criterion requires a higher tariff for products with higher added value. In line with these criteria, APIs and excipients are, for the most part, charged with a zero or 5% tariff; semi-finished pharmaceutical products pay a tariff of 5% or 10%; and finished pharmaceutical products are subject to a 10% or 15% tariff. In addition, certain raw materials used in the production of the pharmaceutical products included in tariff lines 29.36, 29.41, 30.01, 30.03, 30.04 and 30.06 are exempted from value-added tax (VAT).[60]

5.11 Science and technology policies

The scientific, technological and innovation activities in Colombia have been developed by a large number of players who have been interacting since 1968 under the Sistema Nacional de Ciencia, Tecnología e Innovación (National System of Science, Technology and Innovation; SNCTeI) (CONPES, 2009). The Departamento Administrativo de Ciencia Tecnología e Innovación (Administrative Department of Science, Technology and Innovation; Colciencias), the highest Colombian authority in this area, runs SNCTeI and is responsible for formulating, advising, coordinating, executing and implementing the policies on science, technology and innovation. In the first months of 2009, this institution underwent extensive restructuring.

The current science, technology and innovation policy was approved by Consejo Nacional de Política Económica y Social (National Board of Economic and Social Policy; CONPES[61]) in the document Política nacional de ciencia, tecnología e innovación (National Policy on Science, Technology and Innovation) (CONPES, 2009). This document formulates a diagnosis of the strengths and weaknesses of SNCTeI. For details, see Box 1.

59 See Decision 370 of 1994.

60 For more information on pharmaceutical tariff positions and VAT, see ANDI (2010a).

61 CONPES was created in 1958. It is the highest Colombian national planning authority and its head is the President of the Republic. CONPES has the power to approve policies, strategies, plans, programmes and projects of the Colombian Government.

Box 1 CONPES – strengths and weaknesses of SNCTeI

CONPES affirms that in the past 15 years there has been an increase in highly trained human resources, internationally recognized research groups and centres; an increase in the number of alliances between universities, companies, and research and technology development groups and centres; and an increase in the number of companies that have access to the different innovation and technological development support tools.

The CONPES document, however, affirms that the process of development has been slow and insufficient, due to the fact that scientific activity in Colombia (measured in terms of publications, training of highly qualified staff and patents, among other things) and Colombian corporate dynamics lag behind those of other countries in the region. In addition, CONPES points out six major limitations of the system: (i) low levels of company innovation, (ii) weak institutionalization of the system, (iii) shortage of human resources to carry our research and innovation, (iv) lack of focus on strategic areas, and (v) low appropriation of knowledge and regional disparities in terms of scientific and technological capacities, which, altogether, causes (vi) low capacity to generate and use knowledge. This diagnosis agrees with the conclusions of other studies (Vestergaard, 2006).

CONPES seeks to address these issues in the future and has formulated a number of recommendations to this effect, establishing health as one of the strategic areas on which CONPES should focus future activities.

Source: CONPES (2009).

Colombian science and technology indicators show the following: investment in R&D represented 0.161% of GDP in 2009 (equivalent to US$ 995 million), and expenditure on scientific and technological activities (STA) reached 0.391% (equivalent to US$ 410) (Observatorio Colombiano de Ciencia y Tecnología, 2009). This expenditure on R&D and STA is well below that in other countries in the region.[62] Investment in R&D occurs in both the public and private sectors, at 68.05% and 27.61%, respectively.

With regard to the development of new medicines, Law No. 788 of 2002 established specific tax incentives for technological advances in medication and software. The incentives for medicines consist of an exemption for income tax on revenue generated by new medicines by 31 December 2012. This exemption is subject to a few conditions: (i) that they have been developed after 2003; (ii) that they are manufactured in Colombia; (iii) that a patent has been granted on them; and (iv) that they have a high content of national scientific and technological research (at least 80% of staff).

The experience has been satisfactory in relation to software incentives, with 66 exemptions granted between 2003 and November 2008 (DNP, 2010). However, the experience has not been satisfactory in relation to medicines – not a single

62 Brazil: R&D, 1.09%; STA, 1.43%. Mexico: R&D, 0.38%; STA, 0.81%. Argentina: R&D, 0.51%; STA, 0.61% (2008 data) (RICYT, 2010).

exemption has been granted (DNP, 2010), showing that Colombian authorities overestimated the level of development of the domestic pharmaceutical industry when they established the legal requirements to receive tax incentives.

6. Analysis of Tecnoquímicas

Tecnoquímicas is a locally owned pharmaceutical laboratory that has managed to acquire the necessary knowledge to formulate medications from chemical synthesis and to carry out innovations in terms of processes, new formulations, new associations and release systems. However, its R&D laboratory does not have the capacity to research or develop new molecules. It does not have much experience in the development and formulation of biotechnological medications, or the formulation of antineoplastics, immunomodulators or ARVs, but it has the human resources necessary to receive transfer of technology related to these.

One of the key elements of Tecnoquímicas's relative success is the company's powerful and efficient marketing policy, and the fact that it possesses what might be considered the best distribution network in Colombia. Tecnoquímicas is a key player in the OTC market and is the fifth-ranking company in the prescription market – but if we consider only generic products, the company ranks first with its MK line. Its portfolio of medications is for the treatment of type I diseases exclusively.

The 1990s posed a challenge for Tecnoquímicas: to change its business model due to the loss of important licenses, such as MSD and SmithKline Beecham.[63] The response of Tecnoquímicas was to diversify its range of products (e.g. nappies/diapers, adhesive bandages, agrochemicals), to invest in its own trademarks, and to launch a generic line. Fifteen years later, the reconverted TECNOQUÍMICAS proved to be even more successful and the new lines of business allowed it to continue growing.

The expansion of the coverage and the consolidation of the SGSSS with universal health coverage allowed the emergence and consolidation of a generic market. This segment of the market is becoming more competitive, not only because of the competition from locally owned laboratories but also because some multinational innovative laboratories perceive opportunities there. In addition, in the near future, it is predicted that large laboratories from India, China, Canada, Israel and the United States may attempt to enter this market (Abbott, 2007). Although these companies possess large scales of productions, which might threaten Tecnoquímicas' position, Tecnoquímicas possesses no lesser competitive advantages, such as its large and efficient distribution network, its ability to understand and adapt to the needs of Colombian consumers

63 Although Tecnoquímicas still has some licences, in terms of sales they do not account for more than 7–8% of sales value. Tecnoquímicas's licensors include Angelini Francesco, Pfizer Italia, Recordati and Sigma Tau (Italy); Astellas Pharma and Takeda (Japan); Diffucap Eurand, Elea and Gador (Argentina); Heber Biotec (Cuba); Uriach and Juste (Spain); Medispray Laboratories Pvt. Ltd. (India); and Nutricia (United States).

and patients, and the fact that the supply of APIs in the global market is quite diversified and is thus very competitive in terms of price and quality.

The fierce competition in the Colombian pharmaceutical market of products without patent or data protection (generics and branded generics) and the importance that Tecnoquímicas has taken on may preclude further growth in the domestic market, as a certain level of stagnation in its sales figures shows. The company strategy has been to expand outside Colombia and to try to position itself as one of the large generic products laboratories in the region, with a strong presence in the Andean region and an even stronger position in Central America and the Caribbean. This regional expansion will allow Tecnoquímicas to achieve larger scales of production, thus achieving better competitiveness and efficiency, which will in turn become an advantage for it to operate in all the markets.

It is the small Central American markets that Tecnoquímicas perceives as the best prospects for short-term progress, for a couple of reasons: (i) the large international pharmaceutical laboratories do not pay as much attention to these markets as they do to bigger markets; and (ii) cultural similarities might make the exportation of marketing and distribution know-how easier, thus allowing the swift positioning of Tecnoquímicas in the new markets. The selection of the Salvadorian laboratory Teramed as a stepping stone for the expansion of the company into Central America is an example of Tecnoquímicas's strategy: to start out in the smaller markets to learn about their distinctive traits, and to move on to larger ones later, and then to purchase large strong local laboratories with a good distribution network. The expansion into Central America is facilitated by the fact that, from a regulatory point of view, Tecnoquímicas's Colombian plants meet the standards established by health regulatory authorities of the countries in the region.

The expansion into the Brazilian, Mexican and Argentine markets – the most important pharmaceutical markets in the region – is limited by the fact that Tecnoquímicas's plants do not possess the GMP certification demanded by these countries. If Tecnoquímicas decided to enter these markets, it would have to invest more than what it is currently spending to improve its GMP and other standards and to obtain the required certifications.[64] Some Colombian companies are taking steps in that direction and have hired foreign consultants to advise them.[65]

64 The Brazilian, Mexican and Argentine health regulatory authorities do not recognize INVIMA GMP certifications, which is why these health regulatory authorities must inspect the Colombian plants to authorize the marketing of products manufactured there in the Brazilian, Mexican and Argentine markets, respectively. Colombian businesspeople complain that the Argentine and Brazilian health regulatory authorities delay sending the inspectors, which prevents export to these markets. On the other hand, Colombian businesspeople claim that INVIMA carries out these inspections without delay, which is why Argentine and Brazilian generic laboratories can sell their products on the Colombian market without regulatory obstacles – the reverse is never the case. See also Abbott (2007).

65 Lafrancol is analysing the launch of some products on the Argentine and United States markets, and has hired Argentine and Canadian consultants to give advice on GMPs requested by the Argentine Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (Drugs, Food and Medical Devices National Administration; ANMAT) and the United States Food and Drug Administration (FDA), respectively.

The involvement of the IFC in the company as a shareholder meant that there was fresh money to finance the expansion of Tecnoquímicas. This new shareholder increased Tecnoquímicas's assets by US$ 25 million. IFC also gave Tecnoquímicas a loan of US$ 20 million (IFC, 2010), under such terms and conditions as had never been heard of in the Colombian market. In addition, IFC and Tecnoquímicas agreed that the former would provide a long-term financing package, comprising equity/quasi-equity and a loan for a total of US$ 100 million. At the time of writing, Tecnoquímicas has received US$ 45 million from IFC, which has been used to acquire the Salvadorian laboratory Teramed, to finance working capital, and to improve manufacturing practices and quality assurance.

The involvement of IFC can be valued not only in financial terms but also in terms of corporate organization. Tecnoquímicas opened itself up to corporate investors, albeit one with a public mandate, for the first time. Given the fact that this had been a family company since its foundation, the engagement of a corporate investor has had a very positive impact in terms of strengthening good practices of corporate governance. The participation of IFC can also represent a first step towards a possible opening of the company to the stock market by either going public or issuing bonds. IFC might also fulfil a relevant role to catalyse synergistic linkage opportunities for the company with pharmaceutical companies in other developing countries, such as China and India (IFC, 2008).

It is expected that the alliances with other companies, universities and research centres that Tecnoquímicas has patiently built over the years will turn into strategic assets for the development of the company in the future.

The areas of marketing and R&D have been the company's powerhouse. In R&D, a key role is played by the chemistry-pharmacy professionals. ICESI is meant to play a very important role in the training of the future professionals who will join the Tecnoquímicas ranks to fill positions in the R&D laboratory and in the quality control centre. In addition, close ties between ICESI and Tecnoquímicas will have a beneficial effect on curriculum design and training of professionals, since the training received will be closer to the needs and realities of the Colombian pharmaceutical laboratory.

One of the topics being discussed in Colombia, and in all of Latin America, is the issue of bioequivalence tests. There is considerable pressure from multinational companies to demand bioequivalence in vivo tests for all medications. Colombia does not possess a large infrastructure or the human resources to carry out these studies on a large scale. If INVIMA decides to broaden the list of medications for which bioequivalence tests in vivo are required, the strengthening of Tecnoquímicas's ties with local R&D centres, which will provide Tecnoquímicas with extra human resources and infrastructure to carry out those tests, will be vital for Tecnoquímicas in its search for new markets.

The history of Tecnoquímicas shows that the expansion of the company into markets that were not familiar to it was achieved, in general, through joint

ventures with partners experienced in the new markets; such was the case of Limor and the anti-tick vaccine. One of the possible expansion scenarios for Tecnoquímicas is to become a manufacturer of vaccines for humans. This is a market with high potential not only in Colombia but also elsewhere in Latin America, since there are very few such factories in the region, as the H1N1 pandemic showed. Managing biological products is more complex than formulating medications obtained through chemical synthesis, and the products present other challenges. The joint venture with Limor was successful, and this company might be an ideal partner to penetrate the human vaccines market.

It must be highlighted that the CIDEPRO initiative is perhaps the most important project in Colombia in terms of finding solutions for neglected diseases that affect this country in particular. In Colombia there have not been many successful private–public associations with the aim of generating knowledge and transferring it in the form of technology to the private sector. Although Tecnoquímicas does not have a direct responsibility in CIDEPRO's R&D tasks, its financial support is a key factor. Even though it is premature to predict the results of the different projects that CIDEPRO has under way, Tecnoquímicas could be one of the beneficiaries of the possible transfer of technology for manufacturing medications, vaccines or diagnostic tests that the centre is working on.

7. Implications of local production and technology transfer on access to medicines

Tecnoquímicas's main focus has been on the production of OTC drugs and other nonessential medicines. Although the types of medicine it produces may not necessarily be those that would contribute to greater access to medicines as such, there are a number of important points that ought not to be overlooked when examining this firm, to the extent that it is being examined as a market leader in Colombia.

First, with respect to neglected diseases, its ongoing R&D activities in the area of tropical diseases such as leishmaniasis may provide an important contribution to access to medicines for tropical diseases in the country. These activities do not appear to have resulted, for the time being, in a concrete deliverable cure, but they are an illustration of the considerable potential of public private partnerships such as CIDEPRO for the area of tropical diseases. The lack of capacity to produce many essential drugs is due to the fact that multinational companies ended their licensing agreements for the production of such drugs probably at a point too soon for Tecnoquímicas and other domestic manufacturers to absorb the licensed technology and know-how.

Second, the case study highlights the role that Tecnoquímicas's well-established distribution system plays in providing medicines not only in Colombia but also

in Central America. No foreign company has a comparable network in this area, which may be due in part to its familiarity with the language and culture of the region. At the same time, it was language barriers that were the determining factor in partnering with a Florida-based firm, as opposed to firms from Korea or India.

A related issue affecting access to medicines in Colombia is the high price levels for certain essential medicines, which are in many cases provided through importation by foreign firms and protected under exclusive patent and test data rights (see also Section 8). Comprehensive comparative price data between firms were not available to the study team, but the prices charged by Tecnoquímicas for its products are fairly representative of the prices charged by a market leader in Colombia. The institution of universal health coverage has, however, meant that the majority of the population can have access to medicines without having to pay substantial sums out of their own pocket.

8. Policy-relevant findings

The information gathered on the Colombian pharmaceutical market in general, and on Tecnoquímicas in particular, gives rise to the following principal findings.

1. Due to its size, Tecnoquímicas may not be representative of the Colombian pharmaceutical industry in general. In addition, Tecnoquímicas has shown particular flexibility in terms of its various technology sources, product diversification, use of own brands and export opportunities, as well as the quality of its local distribution network. These elements, which may not be met by the bulk of Colombia's domestic producers, illustrate some general requirements in the pharmaceutical industry, i.e. well-trained staff and specific local advantages that may be used to attract technology partners. On the other hand, the level of Tecnoquímicas's technological capacity does appear typical for the domestic industry, which is characterized by its focus on drugs formulation and adaptation of existing products, and its lack of capacity to develop APIs or new chemical entities. Many Colombian pharmaceutical firms acquired initial technological capacity in pharmaceutical production through licensing agreements with multinational pharmaceutical companies. Local firms such as Tecnoquímicas used this initial expertise to develop other avenues of technological learning after the termination of most of the licensing agreements with multinational companies. The study shows that the purchase of foreign production plants may provide important sources of technology and capacity building for the domestic pharmaceutical sector, provided the latter already has some level of pharmaceutical manufacturing capacity. Tecnoquímicas now receives know-how and technology transfer from foreign suppliers of APIs, consultants, former employees of multinational firms, and a well-developed cooperation network with Colombian universities and research centres. API and equipment suppliers also provide advice on plant design, processes and formulations. With regard to improvements that

allow GMP and other quality standards to be met, the local industry resorts to foreign consultants available on a contract basis.

2. Most Colombian firms are capable of formulating pharmaceutical products that are based on chemical synthesis. However, there is not much experience in the formulation of medications of biotechnological origin, although there are some laboratories that are venturing into this area and into vaccine production (e.g. through collaboration with Cuban institutions). There is little experience in the formulation of cytostatic products, immunomodulators or ARVs, which are supplied through imports. The main determining factor is the lack of investment in special production and development areas, which are required for the production of these products because of their high potency and toxicity (Gallo Castro et al., 2010).

3. In addition to drugs formulation, Colombian firms are usually capable of carrying out incremental pharmaceutical innovation, e.g. the modification of existing products, such as the development of new pharmaceutical forms and combinations of existing ingredients, improvements or adaptations of known products, and improved manufacturing methods. Very few local firms are capable of producing APIs; the large majority depend on imports of APIs from various sources, such as China and Germany.

4. Local producers play an important role in the Colombian health system. Most multinational originator companies left the country for various reasons (inter alia the political instability prevailing in the 1990s and the national health system, which favours affordable generic medicines). They still supply the market with medicines that local producers cannot make, but local producers have taken over the production of many other drugs. Major Indian and Chinese producers of generics are not currently producing in Colombia. This study identifies language and cultural barriers as important reasons for this. Colombian producers prefer collaborations with Spanish-speaking foreigners. In addition, some local producers such as Tecnoquímicas have rejected some API shipments from India and China due to concerns about poor quality. APIs are therefore not only sourced from these countries. For these reasons, Colombian producers in sourcing their APIs are not limited to these countries. Thanks to large and efficient distribution networks of domestic firms such as Tecnoquímicas, and thanks to their ability to adapt products to local needs, Colombian producers seem well prepared to compete with Indian, Chinese and other producers, should these decide to enter the Colombian or Latin American markets. In addition, Colombian producers have benefited from facilitated market access to other Latin America countries on the basis of several free trade agreements to which Colombia is a party (in particular, with Venezuela and the Andean Community). Although these advantages might assist the domestic pharmaceutical producers in becoming economically viable in the long run, more private-sector R&D is needed to increase technological capacity in producing more complex medicines to better compete with foreign imports and to bring down prices.

5. The implementation of a universal health care system has allowed the creation of a public market for generic products that has dramatically expanded access to medicines. The public generic market has been the launching pad for the consolidation of a local pharmaceutical industry. The expansion of the universal health care system, together with the rise of local generic production and the complementary importation of other drugs by multinational firms, has resulted in 86% of the Colombian population having access to medicines. However, intellectual property protection and other issues pose an unresolved problem for price and access to medicines (see below).

6. The high price of medications under patent or data protection is an unresolved issue in Colombia. Under the universal health care system, medicines are provided free of charge by the Colombian Government. The high prices of intellectual property-protected drugs have sparked Government demand for more affordable generic alternatives by domestic producers, where available. However, the social emergency declared by the Colombian Government in December 2009 has exposed long-lasting problems. First, there have been allegations of certain practices in some segments of the pharmaceutical industry to encourage the prescription of certain medications. Furthermore, the fact that some essential ARVs, such as Kaletra, have been sold in Colombia at much higher prices than in comparable markets illustrates the effect of patents and exclusive rights in pharmaceutical test data on medicines prices. The Colombian Government has taken some measures to bring down those prices, but these measures have been insufficient and unsuccessful. The price control system has not resulted in any price reductions, except in one case (Kaletra). The regime of parallel imports has so far not been implemented through regulation and thus is not operational. It would seem that more government determination is required to ensure the success of these measures. In addition, other corrective policy measures may have to be considered, such as anti-trust law and policy. Finally, increased competition through capable local producers could be a promising avenue to address high prices.

7. A strong intellectual property regime and a framework that fosters FDI are not sufficient conditions for encouraging FDI in the pharmaceutical industry. Colombia has an intellectual property regime whose standards of protection are among the highest in the world. There are important incentives for the establishment of FDI and trade agreements that permit export to an important regional market and to industrialized regions, such as the EU and the United States. There is also an interesting domestic market. However, all these conditions that foster investment were not sufficient to prevent the massive closure of plants during the 1990s, or to reverse that trend in the present decade. Insecurity and political violence, the trend in the multinational industry to concentrate production in fewer places, and increased local GMP standards requiring costly upgrades of production sites in Colombia seem to have been more important factors resulting in a withdrawal of foreign investments.

8. The multinational innovative laboratories have not transferred technology to their Colombian branches to synthesize or formulate new chemical entities

in Colombia. Since 2002, all of the marketing approvals for new chemical entities have been for the importation and sale and none have been for manufacturing and sale. The evidence that emerges from the protected NCE registry suggests that, at least since 2002, the multinational innovative pharmaceutical laboratories do no synthesize or formulate new medications in Colombia but supply the market through imports.

9. Colombia's drug regulatory system has contributed to the gradual establishment of local production. The country has to date followed a policy of requiring absolute bioavailability and bioequivalence in vivo tests only for high-risk medications. This selective policy accommodates the industry's limited capacities to carry out such tests on a large scale. It has thereby contributed to keeping the market competitive. The country has at its disposal research centres and human resources to carry out these tests, although not on a large scale. It would be helpful for the preservation of the existing degree of market competition if any tightening of regulatory requirements were preceded by an increase in the capacity to carry out bioavailability and bioequivalence tests and by an active policy regime, e.g. providing for subsidies, transition periods, etc. Finally, the Andean Community, despite legislating on technology transfer, FDI and intellectual property, has so far neglected a regional approach to drug regulation. Unified regulatory standards for medicines would provide an important step towards the realization of economies of scale for local producers by means of regional exports.

10. Even though there is still room for improvement, the Colombian pharmaceutical industry has been gradually raising its GMP levels, especially through the creation and strengthening of INVIMA. This was achieved while preserving a competitive market. The possibility to export to other regional markets has been a stimulus to make some locally owned laboratories improve their GMPs and other quality standards. Plans to export to other nontraditional Latin American markets, such as Argentina and Brazil, will provide incentives to raise GMP capacity even further to comply with higher requirements in these two countries. Technology transfer by foreign consultants is likely to play an important role in this context.

11. Colombia has human resources and minimal infrastructure to carry out R&D regarding type II and III diseases, but investment in R&D is insufficient. The country has at its disposal a significant science and technology system, well-trained human resources and minimal infrastructure in research centres and universities. This is a platform that, although it cannot be compared to those in developed countries, allows the conduct of basic and applied research for the development of medications, vaccines and diagnostic kits for neglected diseases, or for receiving knowledge for such purpose. However, these initiatives are at an embryonic stage and few in number. In addition, public and private investment in R&D is still low, and cooperation between the scientific-technological sector and the pharmaceutical industry is not fully satisfactory. Public–private partnerships between manufacturers and universities, such as the research projects carried out by Tecnoquímicas and others on leishmaniasis, are encouraging examples of such cooperation.

To improve the overall situation, it would be helpful if the government could provide financing for this type of research and establish priorities and coordinate the efforts of the different organizations and existing initiatives. The private sector alone can hardly be expected to take the lead in this context, considering the lack of a market for type II and III diseases.

References

Abbott FM. *Comparative study of selected government policies for promoting transfer of technology and competitiveness in the Colombian pharmaceutical sector*. Washington, DC, US Agency for International Development, 2007.

ANDI. *El mercado de medicamentos en Colombia, 2009*. Bogotá, Asociación Nacional de Empresarios de Colombia, 2009 (http://www.andi.com.co/pages/proyectos_paginas/proyectos_detail.aspx?pro_id=62&Id=12&clase=8&Tipo=2).

ANDI. *Comercio exterior de la industria farmacéutica*. Bogotá, Asociación Nacional de Empresarios de Colombia, 2010a (http://www.andi.com.co/pages/proyectos_paginas/proyectos_detail.aspx?pro_id=62&Id=12&clase=8&Tipo=2).

ANDI. *Indicadores líderes del sector*. Bogotá, Asociación Nacional de Empresarios de Colombia, 2010b (http://www.andi.com.co/pages/proyectos_paginas/proyectos_detail.aspx?pro_id=62&Id=12&clase=8&Tipo=2).

CONPES. *Política nacional de ciencia, tecnología e innovación*. Bogotá, Consejo Nacional de Política Económica y Social, 2009 (http://www.dnp.gov.co/PortalWeb/Portals/0/archivos/documentos/Subdireccion/Conpes/3582.pdf).

Contraloría General de la República. *Inclusión y exclusión social en Colombia: Educación, salud y asistencia social – informe social 2008*. Bogotá, Contraloría General de la República, 2009.

DANE. *Encuesta de calidad de vida*. Bogotá, Departamento Administrativo Nacional de Estadísticas, 2008.

DANE. *Estudios Postcensales*, no. 7. Bogotá, Departamento Administrativo Nacional de Estadísticas, 2010a.

DANE. *Balanza Comercial 1980–2010*. Bogotá, Departamento Administrativo Nacional de Estadísticas, 2010b.

DNP. *Cadenas productivas: estructura, comercio internacional y protección – Cadena Farmacéutica y Medicamentos*. Bogotá, Departamento Nacional de Planeación, 2004 (http://www.dnp.gov.co/PortalWeb/Programas/DesarrolloEmpresarial/CadenasProductivas.aspx).

DNP. *Indicadores de ciencia, tecnología e innovación*. Bogotá, Departamento Nacional de Planeación, 2010 (http://www.dnp.gov.co/PortalWeb/Programas/Comercioindustriadesarrolloempresarial/CienciayTecnolog%C3%ADaeInnovaci%C3%B3n/Estad%C3%ADsticas/tabid/237/Default.aspx).

Econometría Consultores. *Estudio de la política de precio de medicamentos en Colombia: Infome final revisado*. Bogotá, Econometría Consultores, 2005.

Federación Médica Colombiana. *Las verdaderas prácticas perversas del mercado farmacéutico y una propuesta de solución*. Bogotá, Federación Médica Colombiana, 2008 (http://www.observamed.org).

Gallo Castro JJ. *Estudio de la relación proveedor: productor en la gestión de materiales del sector farmacéutico industrial productivo (SFIP) de la ciudad de Bogotá*. Bogotá, Universidad Nacional de Bogotá, Facultad de Ciencias, 2010.

Gallo Castro JJ, et al. La capacidad de manufactura como un indicador de desarrollo tecnológico en el sector farmacéutico industrial. *Ingeniería e Investigación*, 2010, 30:112–117.

Glassman A et al. (eds). *From few to many: Ten years of health insurance expansion in Colombia*. New York, Brookings Institution Press, 2010.

IFARMA. *Comentarios a los decretos de emergencia social en salud*. Bogotá, IFARMA, 2010 (http://www.ifarma.org/web/?p=574#more-574).

IFC. *Tecnoquimicas: Summary of proposed investment*. Washington, DC, International Finance Corporation, 2008 (http://www.ifc.org/ifcext/spiwebsite1.nsf/1ca07340e47a35cd85256efb00700cee/CDAB83AB482E7326852576BA000E2BF2).

IFC. *Summary of IFC investments in life sciences – data as of June 2010*. Washington, DC, International Finance Corporation, 2010 (http://www.ifc.org/ifcext/gms.nsf/AttachmentsByTitle/InvSheetLifeSciencesRegion/$FILE/Life+Sciences+by+region_June+2010.pdf).

Instituto Nacional de Salud. *Estadísticas de la vigilancia en salud pública – Semana 51 de 2009*. Bogotá, Instituto Nacional de Salud, 2009 (http://www.ins.gov.co/?idcategoria=12165#).

INVIMA. *Establecimientos nacionales fabricantes de medicamentos autorizados a 15 de Julio*. Bogotá, Instituto Nacional de Vigilancia de Medicamentos y Alimentos, 2010.

La Nota Económica. *Ranking 2009 laboratorios farmacéuticos de Colombia*. Bogotá, La Nota Económica, 2010 (http://lanota.com/index.php/CONFIDENCIAS/Ranking-2009-laboratorios-farmaceuticos-de-Colombia.html).

Mejía C, Orozco H, Martínez E. *Un estudio de caso de la gestión de la fuerza laboral en la industria farmacéutica del Valle del Cauca: Tecnoquímicas S. A. – informe final de investigación*. Cali, Departamento de Ciencias Sociales, Universidad del Valle, 2009.

Ministerio de Protección Social, PAHO. *Política farmacéutica nacional*. Bogotá, Ministerio de la Protección Social and Pan American Health Organization, 2003 (http://mps.minproteccionsocial.gov.co/VBeContent/Library/documents/DocNewsNo14708DocumentNo1553.pdf).

Ministerio de la Protección Social, PAHO. *Indicadores básicos 08: Situación de Salud en Colombia*. Bogotá, Ministerio de la Protección Social and Pan American Health Organization, 2008 (http://www.minproteccionsocial.gov.co/salud/Paginas/INDICADORESBASICOSSP.aspx).

Observatorio Colombiano de Ciencia y Tecnología. *Indicadores de ciencias y tecnología 2009*. Bogotá, Observatorio Colombiano de Ciencia y Tecnología, 2009 (http://ocyt.org.co/html/archivosProyectos/COLOMBIA_2009_FINAL.pdf).

Posada Betancourt M. *Inward FDI in Colombia and its policy context*. New York, Vale Columbia Center on Sustainable International Investment, 2010 (http://www.vcc.columbia.edu/files/vale/documents/Colombia_IFDI_20_September_2010_Final.pdf).

Proexport. *Estudio de Oferta y Demanda del Sector Farmacéutico, LatinPharma 2008*. Bogotá, Proexport, 2008 http://www.proexport.gov.co/vbecontent/library/documents/DocNewsNo10050DocumentNo7844.pdf.

RICYT. *Gastos en CYT en relación al PBI*. Buenos Aires, Red de Indicadores de Ciencia y Tecnología-Iberoamericana e Interamerican, 2010 http://www.ricyt.edu.ar/index.php?option=com_content&view=article&id=149&Itemid=3.

Roffe P, Vivas-Eugui D. *A shift in intellectual property policy in US FTAs? Bridges Monthly Series*, 2007, 11:15.

Superintendencia de Sociedades. *Ranking de sociedades*. Bogotá, Superintendencia de Sociedades, 2002–2008 (http://www.supersociedades.gov.co/ss/drvisapi.dll?MIval=sec&dir=132).

UNCTAD. *The least developed countries report 2007*. New York and Geneva, United Nations Conference on Trade and Development, 2007.

UNCTAD. *Using intellectual property rights to stimulate pharmaceutical production in developing countries: A reference guide*. Geneva, United Nations Conference on Trade and Development, 2011.

Vallejo Díaz MB et al. Estudio descriptivo de los subsectores productores y comercializadores de medicamentos y fitoterapéuticos en Bogotá. *Revista Colombiana de Ciencias Químico-Farmacéuticas*, 2007, 36:176.

Vestergaard J. *Innovation and university interaction with industry in Colombia: Policies, experiences and future challenges*. Washington, DC, World Bank, 2006.

WHO. *Expert Committee on Specifications for Pharmaceutical Preparations: Thirty-second report*. WHO Technical Report Series no. 823. Geneva, World Health Organization, 1992.

WHO. *Expert Committee on Specifications for Pharmaceutical Preparations: Fortieth report*. Technical Report Series no. 937. Geneva, World Health Organization, 2006.

Annex I: Interviewed individuals and institutions

The following 18 individuals and institutions were interviewed:

Pharmaceutical experts

Rodrigo Arcila Gómez, Executive Director, Cámara de la Industria Farmacéutica, ANDI

Jorge Enrique Ariza B, Operations and Logistics Vice-President, Tecnoquímicas S.A.

Alberto Bravo Borda, Chief Executive Officer, ASINFAR

Claudio Gustavo Cerati, R&D Director, Tecnoquímicas S.A.

John J. Gallo, Technical Manager, ToPharma Consulting

Juan Camilo Palacio, Chief Executive Officer, Lafrancol

Emilio Sardi, Executive Vice-President, Tecnoquímicas S.A.

Roberto M. Ventura, Operations Vice-President, Lafrancol

Eduardo E. Yunis, Industrial Division Manager, Lafrancol

Representatives of the Colombian Government

Jorge Alonso Cano Restrepo, Technological Development and Innovation Director, Colciencias

Cristian de la Hoz, Drugs Area Coordinator, INVIMA

Juan Carlos González, Foreign Investment Vice-President, Proexport

Nancy González Saucedo, Exports Advisor, Proexport

Ximena Montegro, Legal Advisor, Proexport

Mauricio Posada de las Casas, Manufacture and Raw Material Exports Manager, Proexport

Marta Rodríguez, Drugs and Biological Products Deputy Director, INVIMA

Representatives of nongovernmental organizations

Miguel Cortés Gamba, Researcher, IFARMA

Francisco A. Rossi Buenavetura, Director, IFARMA

Annex II: Generics manufactured by Tecnoquímicas

Central nervous system

Amitriptyline	Fluoxetine	Piracetam
Betahistine	Gabapentin	Quetiapine
Biperiden	Imipramine	Sertraline
Caffeine + metamizole + isometheptene	Lorazepam	Trazodone
Carbamazepine	Mefenamic acid	Tramadol
Clozapine	Oxcarbazepine	Zolpidem
Flunarizine	Paroxetine	

Cardiovascular system

Amiodarone	Ezetimibe/simvastatin	Pentoxifylline
Amlodipine	Furosemide	Propranolol
Atenolol	Gemfibrozil	Quinapril
Atorvastatin	Ginkgo biloba	Rosuvastatin
Captopril	Hydrochlorothiazide	Simvastatin
Clonidine	Losartan	Verapamil
Clopidogrel	Lovastatin	Valsartan
Diosmin	Metoprolol	
Enalapril	Nimodipine	

Alimentary tract and metabolism

Aluminium hydroxide	Loperamide	Orlistat
Esomeprazole	Nicotinamide + vitamin B1 + vitamin B2 + vitamin B6	Ranitidine
Glibenclamide	Pancreatine + simeticone	Sibutramine
Glimepiride	Metformin	Thiamine
Lansoprazole	Omeprazole	Trimebutine

Anti-infectives for systemic use

Aciclovir	Clindamycin	Norfloxacin
Amoxicillin	Chloramphenicol	Rifampicin
Ampicillin	Dicloxacillin	Spectinomycin
Azithromycin	Erythromycin	Sulfamethoxazole + trimethoprim

Cefalexin	Fluconazole	Sultamicillin
Cefradine	Gentamicin	Terbinafine
Ciprofloxacin	Ketoconazole	
Clarithromycin	Lincomycin	

Genitourinary system and sex hormones

Algestone acetophenide + estradiol enanthate	Metronidazole	Sildenafil
Clindamycin	Metronidazole/nystatin	Tibolone
Estradiol cypionate	Norethisterone enanthate + estradiol valerate	Tinidazole
Finasteride	Secnidazole	

Respiratory system

Acetylcysteine	Desloratadine	Montelukast
Ambroxol	Ipratropium bromide	Salbutamol
Beclometasone	Ketotifen	
Cetirizine	Loratadine	

Musculoskeletal system

Alendronic acid	Ibuprofen	Nimesulide
Celecoxib	Mefenamic acid	Piroxicam
Diclofenac	Meloxicam	Risedronate
Glucosamine	Methocarbamol	
Glucosamine + chondroitin	Naproxen	

Dermatologicals

Aciclovir	Cyproterone acetate + ethinylestradiol	Finasteride
Betamethasone	Rifamycin	
Betamethasone + gentamicin + tolnaftate + clioquinol	Valsartan	

Sensory organs

Gentamicin	Timolol

Contraceptives

Ethinylestradiol + levonorgestrel	Tibolone	Cyproterone + ethinylestradiol
Drospirenone + ethinylestradiol	Algestone acetophenide + estradiol enanthate	

Blood and blood-forming organs

Clopidogrel

Antiparasitic products, insecticides and repellents

Albendazole	Benzyk benzoate	Pyrantel pamoate
Ivermectin		

Hormonal preparations, excluding sex hormones and insulins

Betamethasone	Prednisolone	Levothyroxine
Deflazacort	Prednisone	

Annex III: Branded generics manufactured or distributed by Tecnoquímicas

Genitourinary system and sex hormones

Bladuril (flavoxate)	OMNIC (tamsulosin)
Erilin (sildenafil)	Uropran (oxybutynin)

Dermatologicals

Hebermin (rEGF)	Locoid (hydrocortisone butyrate)
Iloticina (erythromycin)	Zineryt (erythromycin)

Cardiovascular system

Cardinor (amlodipine)	Lipicare (atorvastatin)	Quinaten (quinapril)
Heberkinasa (recombinant streptokinase)	Triglizil (gemfibrozil)	

Anti-infectives for systemic use

Bactesul (sultamicillin)	Decadron Neomicina (dexamethasone/ neomycin)	Heberon Alfa (recombinant alfa 2a interferon)
Damiclin (clindamycin)	Fixamicin (antipyrine/ benzocaine/neomycin)	Klacina (clarithromycin)
Loxan (quinolone)	Quemicetina (chloramphenicol)	

Central nervous system

Nirvan (alprazolam)	Paxan (paroxetine)	Trittico (trazodone)

Vaccines

Heberbiovac (hepatitis B)

Antiparasitic products, insecticides and repellents

Kitnos (etofamide)

Respiratory system

Aflux (N-acetylcysteine)		

Alimentary tract and metabolism

Cytil (misoprostol)	Laxilose (lactulose)	Pangetan (loperamide)
Eptavis (streptococcus/ lactobacillus)	Dimefor (metformin)	

Antifungals

Micofix (benzoic acid/ salicylic acid)		

Analgesics/anti-inflammatories

Artrofenac Retard (diclofenac sodium)	Benzirin (benzydamine hydrochloride)	
Artroxil (celecoxib)	Decadron (dexamethasone)	

Anti-allergy drugs

Periactin (cyproheptadine)	Trimetabol (cyproheptadine)	Viternum (cyproheptadine pyridoxal phosphate)

Case study 4

Ethiopia

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Abbreviations

AAU	Addis Ababa University
APF	Addis Pharmaceutical Factory
COMESA	Common Market for Eastern and Southern Africa
CPEL	Cadila Pharmaceuticals (Ethiopia) Ltd
DACA	Drug Administration and Control Authority
EHNRI	Ethiopian Health and Nutrition Research Institute
FMHACA	Food, Medicine and Health Care Administration and Control Authority
DBE	Development Bank of Ethiopia
ecbp	Engineering Capacity Building Programme
EHGC	empty hard gelatin capsule
EPHARM	Ethiopian Pharmaceutical manufacturing S.C.
EPMSMA	Ethiopian Pharmaceuticals and Medical Supplies Manufacturers Association
GIZ	Deutsche Gesellschaft für Technische Zusammenarbeit (German Society for Technical Cooperation)
GTP	Growth and Transformation Plan
IV	intravenous fluid
LIDE	List of Drugs for Ethiopia
PFSA	Pharmaceutical Fund and Supply Agency
SEAA	Sino-Ethiop (Africa) Associates Private Limited Company
TFILU	Technology Faculty–Industry Linkage Unit

1. Background and methodology

This case study was designed to examine pharmaceutical production in a least developed country (LDC), namely Ethiopia. Specifically, this case study examines how a small enterprise in an LDC managed to build a strong technological base for one important input needed in pharmaceutical production, the relevance of South–South investment and joint ventures as a vehicle for technology transfer, and the role of North–South technical assistance to support technology transfer to a private-sector initiative in pharmaceutical production in an LDC.

UNCTAD thanks Sino-Ethiop Associate (Africa) Private Limited Company (SEAA) for agreeing to be the subject firm for this case study, and the Engineering Capacity Building Programme (ECBP) and Deutsche Gesellschaft für Internationale Zusammenarbeit (German International Cooperation; GIZ) Ethiopia for assisting UNCTAD for facilitating the arrangement of interviews during the field mission.

The study uses a case study research methodology that consists of collection of data through reviews of relevant regulations and public policy documents and academic literature, and through open-ended, face-to-face interviews in Ethiopia. Interviewees were identified through purposive sampling. During the fact-finding mission to Ethiopia, from 15 to 19 November 2009, the team interviewed representatives and officials of three pharmaceutical companies, one hospital, five government agencies (including two banks and the secretariat of one development programme) and the Ethiopian Pharmaceuticals and Medical Supplies Manufacturers Association (EPMSMA).[1] The interviews with SEAA and two other companies involved the entire senior management of the respective companies and visits of their factories.

In addition, a semi-structured questionnaire designed to capture the dynamics of firm-level activities related to production and technology transfer was administered to the firms, the results of which are included in the case study where relevant.[2]

This case study defines innovation as any new products, processes and organizational changes that are new to the enterprise, context and country in question, although not necessarily to the world at large (UNCTAD, 2007). In keeping with the scope of the project, technology transfer is defined as all components of technology, both codified (in terms of blueprints, hardware, machine parts and plant technologies) and tacit (know-how and skills), that are essential to enhance the capacity of the organizations in the recipient country to produce pharmaceutical products.[3]

1 See Annex: Interviewed individuals and institutions.

2 See Annex: Field questionnaire.

3 A uniform definition of technology transfer was used for all components of the project, including the trends survey, the regional dialogues and the stakeholder analysis.

2. Description of the firm, structure and product

SEAA is a joint venture established in 2001 by an Ethiopian company and two Chinese companies. The Ethiopian company, Zaf Pharmaceuticals Private Limited Company (PLC), holds a 30% share in the joint venture. The two Chinese companies, Dandong JINWAN (Group) Co. Ltd. and China Associates (Group) Co. Ltd., each hold a 35% share of the company.[4] The Chinese partners are producers of pharmaceuticals, gelatin, medical devices, packaging materials, empty hard gelatin capsules (EHGCs), and equipment and machinery for pharmaceutical manufacturing. They also engage in pharmaceutical investment and international marketing.[5] The Ethiopian partner is engaged in import and distribution of pharmaceutical products in Ethiopia. The management board of SEAA consists of representatives of each of the shareholders. The initial capital of the joint venture was 71.4 million birr (approximately US$ 5.2 million at the time of writing) (SEAA, 2009). The joint venture became operational in 2003. The Ethiopian shareholder had been the importer and distributor of the products of the Chinese partners in Ethiopia. The Ethiopian Investment Agency provided services to the investors to facilitate the establishment of the joint venture. In this context, it arranged for the Oromiya Regional Government of Ethiopia to make available the land for the facility at a very low rent with flexible terms.

SEAA's Executive Manager, Ms Zaf Gebretsadik, is also the owner of the Ethiopian partner company. With the exception of the chief engineer, the senior management and the 135 line staff of SEAA are entirely local (Walta Information Centre, 2009).

SEAA is exclusively involved in the manufacturing and marketing of EHGCs, which are considered an excipient. Pharmaceutical substances need to be formulated into specific dosage forms for regular use. EHGCs are used for controlled delivery of drugs routed through the digestive system (Segemann, 2002). Pharmaceutical producers fill EHGCs with powders, granules or pellets containing the drug formulated in a separate process.[6] Drugs contained in hard gelatin capsules provide the advantages of faster formulation, predictable administration, protection of the formulation from light, and increased consumer comfort due to the fact that the capsules render the formulations tasteless and odorless.[7]

SEAA's current capacity is 1.2 billion EHGCs per annum (SEAA, 2009). SEAA is currently running at full capacity, operating four fully automatic hard capsule production lines. It is currently producing EHGCs in standard industry-recognized sizes of 0, 1 and 2, in various colours. It supplies 70% of the EHGCs produced to Ethiopian pharmaceutical companies and exports the rest, mainly

4 Interview with Zaf G/Tsadik and senior management of SEAA, 17 November 2009.

5 See http://www.jinwan.com/eindex1.htm.

6 For oils and for active ingredients that are dissolved or suspended in oil, pharmaceutical companies use soft-gel capsules.

7 Segemann, 3.

to other African countries and, to a lesser extent, the Middle East. The companies that purchase the SEAA product in Ethiopia include Addis Pharmaceutical Factory (APF), Ethiopian Pharmaceuticals Manufacturing Factory (EPHARM), East African Pharmaceuticals PLC (EAP) and Cadila Pharmaceuticals (Ethiopia) Ltd (CPEL). APF is the largest consumer of SEAA products.

In Africa, 18 companies from the Democratic Republic of the Congo, Kenya, Tanzania, Zambia, Zimbabwe and South Africa purchase SEAA's product. The Executive Manager of SEAA considers as one of its biggest successes the fact that SEAA has started supplying bigger companies in South Africa, which is one of the most advanced pharmaceutical producer countries in sub-Saharan Africa. SEAA also supplies two companies in Yemen.

Already operating at full capacity, SEAA is facing difficulty in meeting the increasing demand for EHGCs, especially in Africa. For example, its senior management indicated that SEAA would not match the projected demands received from APF for 2011 without an expansion of its current production capacity. SEAA is also not able to respond to orders from companies in Nigeria due to the high volume of orders and the difficulty of finding insulated thermal containers especially designed to transport products such as EHGCs at competitive rates from shipping lines in the region. This is not surprising, as the total African market for EHGCs is estimated to exceed 30 billion EHGCs per year. In the absence of good-quality EHGCs produced at a reasonable cost in Africa, Africa is mainly supplied by producers from China, India and South Korea.[8]

Both the Chinese and Ethiopian partners are involved in the marketing of EHGCs. The Chinese partners provide the main support for the marketing of SEAA products internationally, while the local partner addresses the supply to the domestic market.

SEAA is not tied to its shareholders with respect to sourcing of raw materials and the distribution of its product. Germany has emerged as its main supplier of raw materials, although the Chinese partners also supply raw materials. Sourcing decisions are made based on price, quality expectations of customers and other business considerations, according to SEAA's senior management.

It is important to understand the business rationale with which the joint venture partners embarked on the production of EHGCs in Ethiopia. It is very difficult to compete on a cost basis alone with the large EHGC factories in China and India. EHGCs come in high volumes but weigh very little. However, the cost of transporting EHGCs over large distances is relatively high, since the volume (i.e. not weight) of the shipment is the main basis for calculating the air or shipping fare using insulated thermal containers. In addition, transportation over long distances puts the quality and safety of the product at risk. EHGCs are relatively sensitive products and can become brittle due to moisture loss during transportation. Location can therefore reduce quality failure during supply. In this regard, SEAA management considers the state-owned local

8 The global demand is well over 240 billion capsule per year (in-Pharma, 2005).

carrier, Ethiopian Airlines, as providing important services for international transportation of its products within the region.

Location provides the further advantage to cater for specific demands from local pharmaceutical companies, allowing short lead times for supply that would have been lost processing import and foreign currency authorization, transportation and handling of the EHGCs over a long distance. It also allows the provision of services such as emergency supply in peak times, easier return of unused supply, deferred payments and other arrangements. With respect to export markets, quality and standards are competitive advantages. The partners believe, therefore, that they could successfully compete with bulk producers of EHGCs by producing in Ethiopia and serving the country and neighbouring regions, given that demand continues to outstrip supply for EHGCs in Ethiopia and the rest of Africa. However, in the long term, the management recognizes the need to scale up production capacity to improve price competitiveness.

In 2009, the company registered a slight profit. SEAA's management estimates that the company's profitability will become sustainable with some cost-saving measures under implementation in relation to energy costs arising from the technology used for air handling, and when a planned expansion is realized. SEAA initiated an expansion project to double its production capacity in 2010.[9] According to interviews with SEAA management, the reasons for the expansion are due to the increased demand for its products since its international good manufacturing practice (GMP) certification. The management first applied for a loan from the International Finance Corporation (IFC). The application for the IFC loan was not successful. Instead, the Development Bank of Ethiopia (DBE) agreed to finance the project. SEAA expects to complete the expansion project and double its output by the second quarter of 2011.

3. Technological capacity of SEAA

The EHGC production technology consists of the gelatin (the ingredient technology)-capsule-making machinery and equipment; a GMP-compliant facility; process, specifications and related know-how for each stage of production; and application of colorant and labelling on the final product. The Chinese partners supplied all of the physical machinery and equipment, and most of the technology and expertise for the production of the EHGCs.

The technology between SEAA and the Chinese partners was supplied through arm's length purchases.[10] During the establishment of SEAA, the founders had the option to contribute in cash or in kind (including technology and know-how) under the Ethiopian investment law. As the valuation of technology contributed in kind would have to be determined by customs officials, however, the Chinese partners decided instead to transfer their investment in United States dollars to SEAA, and arranged for SEAA to purchase in United

9 Interview with Zaf Gebretsadik and senior management of SEAA, 17 November 2009.

10 Interview with Zaf Gebretsadik and senior management of SEAA, 17 November 2009.

States dollars the machinery, equipment and know-how from the businesses of the Chinese partners.

During the start-up phase, at any given time there were 6–12 Chinese engineers working at SEAA, first building the facility and installing the machinery and then, when production started in 2003, training the local staff in handling, operating and mastering the technology and know-how.[11] The joint venture partners consider that there has been full and complete technology transfer of the relevant EHGC technology and that the local staff have mastered the technology.

Finally, the efforts of SEAA to secure international accreditation led to further investment in upgrading the facility. SEAA obtained international GMP certification in accordance with the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) in 2009. To achieve this, experts were brought in from Germany to inspect and advise SEAA on how to upgrade its standards (ecbp, 2009).[12] The GMP PIC/S certificate will help to drive exports, particularly within Africa. It will also help pharmaceutical companies that use SEAA's hard gelatin capsules to secure accreditation of their own products.

The process for GMP certification in accordance with PIC/S took over a year and is one of the key reasons for the company to invest in upgrading its technological capacity and skills for high-quality production. Based on the inspections in 2008, SEAA invested in upgrading its facility and manufacturing practice at a cost of approximately 2.5 million birr (around US$ 200 000). SEAA received certification of PIC/S conformity after the inspection in January 2009 for the manufacturing of EHGCs at its facility. ECBP provided support for SEAA during the inspection and certification process for PIC/S. SEAA became the first Ethiopian company to finalize the process and achieve GMP in accordance with PIC/S. Box 1 explains the importance of GMP certification to manufacturers of drugs in developing countries.

The staff demonstrated the changes during a factory visit that was part of the fact-finding mission. The changes include new laboratory equipment, upgrading of the quality-control system, the introduction of new procedures for handling of raw materials, specifications for each process of production, air control, water treatment and packaging. During the process for GMP certification, the staff also developed standards for each production process through in-house research and development (R&D), for example on the temperature and viscosity of the gelatin before it is released from the feed tanker.

11 Ibid.

12 The Engineering Capacity Building Program (ecbp) is a facility designed by the Ethiopian and German governments to assist the standard and technological upgrading of manufacturing enterprises, including in the pharmaceutical sector. The priority in the pharmaceutical sector is to assist selected local companies in complying with GMP in accordance with PIC/S.

SEAA was under inspection for local GMP by Ethiopia's Food, Medicine and Health Care Administration and Control (FMHACA) of the Federal Ministry of Health during the fact-finding mission on 15 November 2009. SEAA has to keep its certification from FMHACA updated in order to import raw materials and export its products. The first certificate of current good manufacturing practices (cGMP) was confirmed by FMHACA in January 2003, acknowledging the satisfaction and compliance of the SEAA plant with the cGMP requirements. The company has been frequently inspected for cGMP and received feedback in July 2007 and November 2009.

At present, SEAA does not undertake R&D to engineer new products. Its R&D focuses on production processes and the design of EHGCs to meet the demands of each customer, especially by applying trademarks, colours and other identification to the EHGCs. SEAA estimates that 5% of its expenditure goes on R&D, excluding amounts spent on quality control and product stability testing.[13]

Box 1 Good manufacturing practice (GMP) standards – an explanation

GMP is a system for ensuring consistent production and control according to quality standards to minimize the risks involved in pharmaceutical production. GMP covers all aspects of production, from active pharmaceutical ingredients (APIs) and their handling to premises and facilities, the training of staff and detailed documentation showing procedures are followed consistently at each production stage and every time a product is made.

In many countries pharmaceutical and food industries are required to pass certification for GMP. The United States of America, Canada, members of the European Medicines Agency, Switzerland, Norway, Australia, Japan and others are recognized as having highly developed or "stringent" GMP requirements. The World Health Organization (WHO) Medicines Prequalification Programme is also highly recognized internationally; this was set up to provide United Nations (UN) agencies that procure medicines, such as the United Nations Children's Fund (UNICEF), with a range of good-quality products that meet international standards of quality, safety and efficacy. The WHO prequalification programme and the drug regulatory authorities of these countries are also used as reference or "trusted" authorities by other countries that do not have the capacity to make the assessment of each product and facility, and by international funding agencies. The procurement guidelines of the Global Fund to Fight AIDS, Tuberculosis and Malaria, for example, state that grant funds may be used only to procure products that meet WHO prequalification or are authorized for use by a stringent drug regulatory authority.

There are regional cooperation schemes with respect to GMP. The European Union (EU) GMP is used mainly within Europe. The Association of South-East Asian Nations (ASEAN) has harmonized its requirements, and the Gulf Cooperation Council (GCC) is recognized for active regional GMP cooperation.

PIC/S is similar to European GMP but includes membership from authorities from the rest of Europe and countries in the Americas (Argentina and Canada),

13 SEAA's reply to question no. 3 in field questionnaire.

Africa (South Africa) and Australasia (Australia and Singapore), and partners from international organizations such as UNICEF and WHO. Other regulatory authorities can accede to PIC/S. PIC/S GMP certificate is issued by experts from a participating Member State. Although PIC/S is not a trade agreement, some non-PIC/S authorities accept GMP certificates by PIC/S experts.

In terms of harmonization, the WHO c/GMP guidelines are used primarily by regulatory authorities in most developing countries. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) prepares guidelines for use by regulatory bodies of the EU, Japan and United States primarily for new innovative pharmaceuticals.

Source: WHO (2011), PIC/S (see http://www.picscheme.org) and Global Fund (2009).

4. The pharmaceutical market in Ethiopia

With an estimated population of 81 million in 2008, Ethiopia has the potential to become a significant market for pharmaceutical products in sub-Saharan Africa (World Bank, 2009). The main economic activities in the country are services (45.1% of gross domestic product; GDP), agriculture (43% of GDP) and industry (11.3% of GDP) (Access Capital, 2010). Major exports include coffee, gold, leather products, live animals and oilseeds (UNCTAD, 2009). The country's GDP measured in purchasing power parity (PPP) is forecasted to grow from US$ 70 billion in 2008 to US$ 472 billion by 2023 (Negatu, 2009).[14] During interviews, stakeholders highlighted the importance of the opportunities for Ethiopian companies within the Common Market for Eastern and Southern Africa (COMESA).[15]

However, the Ethiopian market for pharmaceuticals is still rather limited. It is currently estimated at around US$ 200 million, due mainly to low per-capita income levels. The per capita GDP at PPP is estimated to reach only US$ 1101 in 2010 (Economist Intelligence Unit, 2009). Ethiopia has more than double the population of Kenya, but in terms of infrastructure and personnel the Ethiopian health care system is about one-third of the size of Kenya's. Currently, there is slightly higher total health expenditure at 4.9% of GDP in Ethiopia than in other countries in Africa, excluding South Africa, but the per-capita expenditure is among the lowest in the region (Wamai, 2009). Ethiopia's health indicators reveal a country with human immunodeficiency virus (HIV) prevalence at 2.1% among inhabitants aged 15–49 years (Wamai, 2009).

The main source of drug expenditure in Ethiopia is household out-of-pocket expenses covering 47% of total drug expenditures. Donor sources,

14 According to Ernst & Young, Ethiopia is expected to become the third-largest sub-Saharan economy by 2023.

15 Article 10 of the Treaty Establishing a Common Market for Eastern and Southern Africa (COMESA) (1993) calls for cooperation in health-related fields, including the production of pharmaceuticals.

governments and nongovernmental organizations (NGOs) cover the rest of expenditure. The Pharmaceutical Fund and Supply Agency (PFSA) of the Federal Ministry of Health undertakes procurement for public health facilities throughout the country. Although recent figures are missing, in 2005–2006 private importers accounted for around 42% of drugs imported into Ethiopia, while the Ethiopian Government and donors imported the rest (Wamai, 2009).

Government procurement and the local market for pharmaceuticals are open to foreign participation, although foreign suppliers cannot engage directly in retail distribution (Ethiopian Investment Agency, 2009). Foreign suppliers can participate in tenders by appointing representatives that register their products locally. Public-sector procurement is done through international and local open tenders, restricted tenders, direct purchasing or negotiation. Public procurement is limited to medicaments on the List of Drugs for Ethiopia (LIDE), revised and supplemented in 2008 (DACA, 2007, 2008a).

Estimates on the share of the market held by local producers of pharmaceuticals vary between 15 and 30% of the market. Ethiopian Pharmaceutical Manufacturing Company S.C. (EPHARM) was the first pharmaceutical company established in the country, having been founded in 1964. It was nationalized in 1975 and is currently being floated for privatization. Following the market reforms of the 1990s, 17 private companies were established, producing a range of pharmaceutical-related products, excipients, medical supplies and veterinary products. These companies were frequently financing acquisition of technology and production of pharmaceuticals through a combination of bank loans and joint venture investments. The local producers engaged in final formulation of drugs combining the API with excipients. There is no API production in Ethiopia (Von Rosenstiel, 2007). According to the President of EPMSMA, the private-sector initiative in the pharmaceutical sector was not matched by government support until 2007. Of the 17 private companies that were producing pharmaceuticals and medical supplies, 4 have gone out of business. One of the companies, ETAB Inter-Medical PLC, which was producing disposable syringes, went bankrupt due to severe competition from imports. The founder attributes the problem to imports that were purportedly sold below production cost.[16] Bethlehem Pharmaceuticals PLC was producing antimalarials and other pharmaceuticals until it closed down in 2006. Former employees attribute the failure to a combination of factors, including lack of knowledge by the investor and the banks, and difficulty in accessing the market. Five of the companies still in operation are joint ventures, including SEAA. The fact-finding mission visited two of these joint ventures to obtain a better understanding of the wider pharmaceutical manufacturing market in which SEAA operates.

EAP was an initiative of British and Sudanese nationals. It had difficulties at the outset when the cost of the investment was driven up because of the decision of FMHACA to order the company to rebuild its plant shortly after the plant started operations, to comply with GMP. In 2003, US$ 4.3 million was invested to get the facilities up and running. In 2009, the factory ran at 30%

16 Interview with Ms Etenesh Abraha W/Giorgis, President, EPMSMA, 16 November 2009.

of its capacity. It produces human and veterinary medicines, which are sold mainly locally, although a small portion is exported to neighbouring Sudan. The company has consistently been running at a break-even level or at a small profit, depending on the year, according to its Sudanese general manager. The management is considering increasing its veterinary medicine production as a strategy for survival. Ethiopia's livestock population is among the largest in Africa (Central Statistical Agency of Ethiopia, 2008). Compared with the market for human medicines, the veterinary medicines market is largely private and is more easily accessible, according to the firm's management. EAP has been coached by FMHACA to meet its GMP requirements for years. The first cGMP certificate was issued to the company in May 2006 after repeated inspections and frequent feedback. The company has been authorized to market more than 50 dosage forms since then. However, the cGMP certificate was suspended in January 2009 since the company failed to keep up with cGMP.

In 2007, Cadila Pharmaceuticals Ltd (India) and Almeta Impex PLC, Ethiopia established CPEL, owning 57% and 43% of the company, respectively. CPEL became operational in 2008. The initial investment to get the factory up and running amounted to US$ 11 million. According to the General Manager of CPEL, Almeta Impex PLC enjoyed a previous working relationship with Cadila India as its distributor in Ethiopia, which was a major factor in the choice of partner to set up a joint venture in Ethiopia. In addition, the market size, including easy access from Ethiopia to other east African countries, motivated the investment. All machines and raw materials are imported from India. Cadila Pharmaceuticals Ltd (India) had registered its products in Ethiopia for export purposes before it established CPEL with the local partner. Since CPEL uses the technology of Cadila Pharmaceuticals Ltd (India), the lead time to register the products to be produced under the new location was very short. This helped CPEL to start production immediately after setting up the production facility. The selection of the products for production is based on first-hand experience from the exports of Cadila Pharmaceuticals Ltd (India) to Ethiopia. CPEL's plant has the capacity to manufacture 390 million tablets, 165 million capsules and 144 million litres per year. It produces 30 products, all of which are also produced by Cadila Pharmaceuticals Ltd (India). The plant is currently running at full capacity. CPEL sells its products in Ethiopia and exports some products to Djibouti, Kenya, Rwanda and the United Republic of Tanzania. Currently, 5% of CPEL staff members are expatriates. The general manager is from India. Although CPEL operated at a loss in 2008, the company expects to be profitable in the near future.

Other examples of Ethiopian-based joint ventures include PharmaCure PLC, a Swedish turnkey in an Ethiopian-Saudi investment, established in 1998, that is currently producing intravenous (IV) fluids. Rx Africa (Ethiopia) PLC is an Ethiopian-United States joint venture established in 2007 through the acquisition of a local company called Sunshine Pharmaceuticals. It launched 36 products in 2009 and plans to roll out further generics in malaria, HIV/acquired immunodeficiency syndrome (AIDS) and tuberculosis (TB) treatment. Another example, APF, is the largest Ethiopian company in terms of production and sales. Established in 1992 with US$ 30 million, APF is 100% locally owned.

It currently produces 92 products with equipment acquired from European suppliers. It is projected to achieve profitability along with above 50% utilization of capacity in 2010.[17] APF is seeking partnerships to fully utilize its capacity and introduce new products to the local market. As a final example, Fäwes Pharmaceuticals PLC is 100% locally owned and produces IV fluids for the Ethiopian market.

As well as its geographical advantage, the presence of multiple joint ventures in pharmaceuticals attests to a certain degree of skilled labour and a manageable regulatory framework for drug manufacture and investment, along with a relatively strong local pharmaceutical manufacturers' association. Other positive factors that have weighed in favour of pharmaceutical production, relative to some other countries in the region, appear to be personal safety and investment security according to the management of CPEL, SEAA and EAP.

At the same time, the pharmaceutical companies in Ethiopia have identified various problems. There is a gap between lists of compounds and other ingredients for tax exemptions compared with what they import; there is a shortage or irregular supply of electricity; and, more recently, there is a hard currency shortage that limits the ability to import raw materials.[18] The President of EPMSMA also stated that many small and medium-sized pharmaceutical producers in Ethiopia cannot cope with the severe competition of the low-cost exports of large-scale Asian producers.

5. The framework for local production and technology transfer

5.1 National drug policy and regulations

Ethiopia adopted its National Drug Policy in 1993. The policy provides for general strategies for supply, distribution and pricing of essential drugs, and support for the development of an effective system of drug administration and control at all levels of production, including by developing the capacity to monitor drug safety, efficacy and quality. It identifies the need to facilitate the integration of traditional medicine with modern medicine. With respect to manufacturing of pharmaceuticals, the policy proposed incentives to public and private industries involved in the production of essential drugs and raw materials, and created favourable conditions for the transfer and further development of appropriate technologies. Furthermore, the policy proposes to conduct coordinated research on modern and traditional drugs in line with the country's medical problems and its capacity, and to strive for the application of their results (Ethiopian Transitional Government, 1993).

To be implemented effectively, the policy needed relevant laws, regulations and institutions for enforcement. The first step was the adoption of rules for

17 Interview with Daniel Ayele, Programme Officer, ecbp, 16 November 2009.

18 Interview with Zaf Gebretsadik and senior management of SEAA, 17 November 2009; and interview with Ms Etenesh Abraha W/Giorgis, President, EPMSMA, 16 November 2009.

the establishment of the Ethiopian Drug Administration and Control Authority in 1999 (FDRE, 1999), replacing the National Drugs Advisory Committee as the country's drug regulatory authority. Soon after the new institution was established, the authority began developing regulations, including those governing the importation and registration of drugs. Additionally, the authority introduced the country's GMP and LIDE, which was revised and supplemented in 2008 (DACA, 2007, 2008a), and the 2008 National Drug Formulary, which introduced the use of nonproprietary names in drug prescription (DACA, 2008b). In June 2009, the mandate and authority of the Ethiopian Drug Administration and Control Authority were strengthened to consolidate all health regulatory issues, including food and nutrition, under one umbrella (DACA, 2009). The organization was re-established as the FMHACA under Proclamation No. 661/2009. The new authority's responsibilities were broadened to include setting standards, and ensuring their implementation and observance, for food safety and quality; safety, efficacy, quality and proper use of medicines; competence and practice of health professionals; hygiene and environmental health; and competence of health and health-related institutions. The new Proclamation also provides for the validity of registration of medicine to last for 4 years, which can be renewed if the requirements of registration continue to be met. Traditional medicine and traditional health practitioners are also required to be registered and licensed. The Proclamation states that an act of "counterfeiting" occurs when using the packaging materials, trademark and trade name of an authentic product and presenting such falsely labelled and packed food or medicine as if the genuine manufacturer has produced it. Adding any foreign ingredient to or substituting the content of a medicine, and storing or manufacturing a medicine under unsanitary conditions that can lead to contamination amounts to acts of "adulteration".

In the interviews conducted, pharmaceutical companies in Ethiopia expressed some frustration that FMHACA is understaffed. Human resource constraints prevalent in many sub-Saharan LDCs may affect FMHACA. Other companies aiming for international accreditation and export, such as SEAA, want to see a stronger FMHACA, as this helps in obtaining international accreditation. If FMHACA were to become a member of the PIC/S, this would help firms in Ethiopia when seeking to export to international markets.[19]

Although the primary responsibility of FMHACA is to enforce regulations, it has been providing technical advice on regulatory aspects of pharmaceuticals. Since 2008, FMHACA has been implementing long-term project plans to provide advanced cGMP training to its inspectors. It has also conducted training for local producers in collaboration with WHO and the United States Agency for International Development (USAID) programme "Promoting the Quality of Medicines". The training covered basic and advanced cGMP, and generic pharmaceuticals dossier preparation and evaluation. According to FMHACA, the basis for this support and follow-up action plan is the study conducted in 2006–2007 that helped to design the 5-year strategic plan for the pharmaceutical subsector. Since 2009, FMHACA has established a team

19 The Ethiopian Quality Standardization Authority has received the international accreditation certificate ISO 9001 (The Reporter, 2009).

of experts to encourage local manufacturing. Inspections oriented primarily towards generating feedback for the companies have been undertaken twice a year for each company.

To enhance its implementation capacity, FMHACA is also completing a new facility and upgrading its laboratory to achieve ISO-17025 certification (The Standards, 2010). Some sources consider FMHACA to have developed one of the more effective regulatory systems compared with many other sub-Saharan African countries (Frost & Sullivan, 2010). Receiving support from various donor agencies, FMHACA is upgrading its overall capacity.

5.2 Intellectual property and technology transfer

Ethiopia's technology transfer regulations lay down the basic norms governing technology transfer agreements involving intellectual property rights. Such agreements must contain provisions on liability, performance guarantees, specification of the technology, the supply of technical services and terms of payment. Technology transfer agreements are valid only when registered. There are several grounds for denial of registration of technology transfer, including restrictions on further R&D or modifications and use of other technologies, unreasonable terms such as grant back clauses, and control on the business of the recipient. Payments made abroad in foreign currency by the recipient of technology can be facilitated only following approval of the National Bank of Ethiopia (FDRE, 1993).

The extent to which the laws governing technology transfer agreements are effective is unclear. The Ethiopian Investment Commission is the designated authority to register and monitor technology transfer agreements. According to Mohammed Seyed, Director of the Research and Promotion Department at the Ethiopian Investment Agency, there are only eight technology transfer agreements registered by the Ethiopian Investment Commission, four of which involve trademarks. Only one company, CPEL, stated that it is processing royalty payments for technology transfer to Cadila Pharmaceuticals Ltd (India). Given the extent to which technology must have been transferred to the pharmaceutical companies in the country, it appears that much technology transfer has been imbedded in ordinary trade and investment transactions, avoiding the periodic royalty payments that are subject to technology transfer regulations. For example, SEAA does not pay any royalties for the technology imported from the Chinese partners.

Ethiopia is not a member of the World Trade Organization (WTO) and therefore the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS Agreement) does not apply at the moment. Ethiopia is, however, seeking to become a WTO Member. In Ethiopia, patents are available for pharmaceutical products for a duration of 15 years from the filing date, with the possibility of renewal for an additional 5 years. Moreover, there is a "patent of introduction", which may be issued to an invention that has been patented abroad and not expired but that has not been patented in Ethiopia. Such a patent is valid for

up to ten years (FDRE, 1996).[20] There is, however, a working requirement for patent rights' holders. An exception to rights conferred by a patent is provided for scientific research and experimentation for noncommercial purposes. Although Ethiopia follows a regime of "national exhaustion" of intellectual property rights, the rights of the patent holders do not include the right to exclude third parties from parallel importation of a patented product obtained at cheaper prices abroad (FDRE, 1996).

Currently fewer than 1000 patent applications have been received by the intellectual property office in all fields. As multinational corporations have so far refrained from filing many patent applications in Ethiopia, this may offer opportunities for the production by local firms of generic equivalents of certain medicaments that are patent-protected elsewhere. Some of the stakeholders nonetheless consider the patent law to be stringent considering the full range of flexibilities that LDCs can avail themselves of under the international minimum standards established by the TRIPS Agreement.[21]

LDCs such as Ethiopia are provided with a transition period lasting until 2013 for the implementation of the TRIPS Agreement and lasting until 2016 to make available or enforce patents and protection of undisclosed information with respect to pharmaceutical products (WTO, 2002a,b). Furthermore, the August 2003 Decision of the General Council of WTO established a system for export of pharmaceutical products, including APIs and diagnostic kits, produced under compulsory licence for the benefit of LDCs and other developing countries with limited or no manufacturing capacity.

Ethiopia has indicated its intention to ratify the Paris Convention in a bid to join WTO (WTO, 2009). LDCs that recently acceded to WTO have asserted their rights for the use of the transition period. Cape Verde, which acceded to WTO in 2008, committed to fully implement the TRIPS Agreement by 2013. However, all LDCs that acceded to WTO were required to ensure that any changes in their laws, regulations and practices made during the transition period do not result in a lesser degree of consistency with the provisions of the TRIPS Agreement (Biadgleng, 2010). Ethiopia is currently considering changes to its patent law in order to fully comply with the TRIPS Agreement.

It should be noted that the decision to establish a joint venture to manufacture EHGCs in Ethiopia is not driven by the TRIPS transition period as such. However, manufacture of pharmaceuticals in Africa may be driven in part by this transition period, as demonstrated by the investment of the Chemical, Industrial and Pharmaceutical Laboratories Limited (CIPLA) in Uganda for the production of drugs for the treatment of HIV and AIDS (UNCTAD, ICTSD, WHO, 2011). In this regard, the TRIPS transition period may have an indirect impact on the demand for locally manufactured high-quality pharmaceutical products.

20 FDRE (1996, Articles 3, 18, 22, 27, 29 and 36).

21 Interview with Daniel Ayele, Programme Officer, ecbp, 16 November 2009. GIZ and UNCTAD undertook a study on the use of TRIPS flexibilities for the local production of pharmaceuticals in Ethiopia (UNCTAD, 2007b).

5.3 Industrial and investment policy

Ethiopia started reform from a centrally planned to a market-oriented economy in the 1990s (Mouton & Boshoff, 2007). The reforms opened up pharmaceutical manufacturing and other industrial sectors for domestic and foreign investment. The focus of the first generation of industrial and investment policies of Ethiopia was on labour-intensive, export-oriented sectors, such as agroprocessing, horticulture, textiles and garments. These sectors received long-term credit with low interest, export incentives, custom duty privileges and provision of land at competitive rents (Ethiopian Investment Agency, 2009). The minimum capital required for investment by foreigners in a joint venture with domestic investors is US$ 50 000. For a sole investor, the minimum is US$ 100 000 (Ethiopian Investment Agency, 2009). Foreign investors cannot participate in retail distribution according to the Ethiopian investment law. The restriction prevents foreign companies from engaging in pharmaceutical distribution in Ethiopia, such as setting up pharmacies and drug stores. Foreign pharmaceutical companies can supply the market by appointing drug representatives and agents under the national drug policy.

A major limitation on the development of the pharmaceutical industry in Ethiopia is the lack of an organized venture capital or capital market from which to raise money for investment.[22] Shares for new investments and expansion projects by the private sector in Ethiopia are sold through commercial banks and public advertisement. Commercial banks currently charge 8.5–9.0% interest rates against loans and are reluctant to finance pharmaceutical production projects. To address this problem, DBE offers up to 70% of the investment capital for new investments or expansion projects in the pharmaceutical sector, with a 7.5% interest rate and a long-term repayment horizon.[23] DBE receives limited loans from the European Investment Bank at a 4.5% interest rate, and then channels these funds to small business in Ethiopia. The financing from the European Investment Bank does not include the pharmaceutical sector. DBE has to date not raised funds from international financial institutions for the pharmaceutical sector and does not have the in-house capacity to evaluate pharmaceutical industry development projects or provide advice to those seeking financing in the sector. Due to the lack of expertise in the pharmaceutical sector, the lead times for obtaining such loans can take over a year.

A related problem concerns the availability of foreign currency for the importation of raw materials for pharmaceutical production. The National Bank of Ethiopia has put in place a system for retaining foreign exchange earnings in a dollar account by exporters for reuse to import raw materials

22 The banking sector is closed for foreign investment and the local currency, the birr, cannot be exchanged on international currency markets. IFC has launched a project for the establishment of the first leasing company in Ethiopia in collaboration with Access Capital, a private investment company. The project will include a comprehensive investment and advisory package in a green-field leasing (Access Leasing, 2008).

23 Interview with Mesenbet Shenkute, Vice President, Credit Services, Development Bank of Ethiopia, 18 November 2009.

and other inputs. The National Bank also gives priority to manufacturers and essential supply importers in the allocation of foreign exchange. However, pharmaceutical companies supplying only the local market have to compete for hard currency with other manufacturers and essential supply importers. Currently, among the pharmaceutical companies, only SEAA, which exports 30% of its products, benefits from the foreign currency earnings retention account system.

The local producers face difficulties in paying for imports of raw materials and operate below their maximum capacity. Pharmaceutical companies faced high tariffs on raw material imports until 2007 and severe competition from imports of final products, which are subject to tariffs that are close to zero.[24] There was also a lack of knowledge about the sector by the managers, investors and banks.[25] Four pharmaceutical companies had closed down by 2006. The rest were operating at a loss or under serious financial stress, with the exception of CPEL and SEAA (World Bank, 2009).[26]

The Ministry of Trade and Industry, Department of Chemicals and Pharmaceuticals has undertaken research to generate adequate information to support investment in basic chemicals (Ohno & Ohno, 2009).[27] Since 2007, direct consultation between EPMSMA and the national taskforce jointly led by the Ministry of Trade and Industry and FMHACA[28] has led to various reforms of the pharmaceutical sector, including tariff reduction for the importation of raw materials, an income tax waiver until 2016, advanced payment for up to 30% of orders, and a higher price tolerance margin in government procurement for locally produced medicines.[29] The reforms are consolidated and adopted under a 5-year strategic plan for the pharmaceutical subsector adopted in 2009. For the fiscal year July 2009 to June 2010, the Ethiopian Government procurement agencies have paid over 650 million birr (approximately US$ 48 million) to local producers. Specific data on the exact impact of price protection in favour of the local producers are lacking, however. The higher price tolerance margin for local producers in government procurement started at 15%, increased to 20% and has now reached 25%. The Ministry of Health also leads a National Forum that involves members of the national taskforce and other institutions, such as the Ethiopian Health and Nutrition Research Institute and PFSA. This Forum has a technical committee to follow up the implementation of the 5-year strategic plan for the pharmaceutical subsector.

24 Interview with Daniel Ayele, Programme Officer, ecbp, 16 November 2009.

25 Interview with Mesenbet Shenkute, Vice President, Credit Services, Development Bank of Ethiopia, 18 November 2009.

26 According to the World Bank, despite the substantially improved business environment, industrial productivity remains very low in Ethiopia, and Ethiopian firms are constrained both by factors at the firm level and by factors that impact allocative efficiency – i.e. the allocation of resources in the economy, especially finance and land.

27 Data also from interview with Shimelis Wolde Birru, Head, Chemical Industry Support and CWC Implementation Department, Ministry of Trade and Industry, Ethiopia.

28 The national taskforce also involve universities, the Customs Authority and the Ministry of Health.

29 Interview with Daniel Ayele, Programme Officer, ecbp, 16 November 2009.

Furthermore, tariff concessions are not comprehensive. SEAA pays a 10% tariff on imports of gelatin (the main input for the production of the EHGCs) due to the classification of gelatin as an input used in a number of other industries. CPEL also indicated that there is a gap between its imports and the tariff concessions for the pharmaceutical sector. With respect to financing investment, the Ethiopian Government is taking measures to make available funds for new start-ups, expansion and the revitalization of the companies that have closed down.[30] ETAP, a company that produced disposable syringes until it was closed down, is negotiating for new financing to relaunch its products. Except for the facility, the founder and the general manger believe that it has to reintroduce all the technology for the production of disposable syringes in order to achieve competitiveness due to severe competition from imported products.

The companies noted in previous sections have received regular training and feedback on their cGMP from FMHACA in collaboration with USAID and WHO. ecbp played a role in advising local manufacturers to obtain GMP certification in accordance with PIC/S and participated in the assistance provided by Ethiopian Government agencies for the establishment of a regional bioequivalence centre (ecbp, 2006). SEAA is the first to receive international GMP as per PIC/S. CPEL, PharmaCure and APF are in the advanced stages of upgrading their facilities and technologies to GMP certification in accordance with PIC/S, and hope to obtain GMP certification. APF received ISO 9001–2008 (Quality Management Standards) certification issued by Deutsche Gesellschaft zur Zertifierung Von Managmentsystemen, an accredited certification body, after a successful audit in 2010.

Table 1 shows the ecbp planned intervention areas for pharmaceutical sector development for implementation by 2012.

30 Efforts for revitalization of companies that were closed down began only in 2009, 6 years after the closure of Lifeline Solutions S.C. (a producer of IV fluids) and ETAB (a producer of disposable syringes), 5 years after the closure of BioSol Pharmaceuticals PLC (a producer of IV fluids) and 3 years after the closure of Bethlehem Pharmaceuticals (a producer of antimalarials and other pharmaceuticals). Despite the determination of the Ethiopian Government, some people in the sector are sceptical about the feasibility of relaunching these companies, except with injection of finance to re-engineer the facilities and technologies (Addis Fortune, 2009).

Table 1 *Engineering Capacity Build Programme (ecbp): planned intervention areas for pharmaceutical sector development for implementation by 2012*

	Intervention	Indicators (by end 2012, compared with 2007)
Standards	Upgrading to GMP standard	Five pharmaceutical producers to be certified by international accepted certification
Marketing	Marketing support	Three human drug products are being exported Local producers' market share reaches 40% Aggregate turnover in the sector has increased by 60%
R&D and technology transfer	Bioequivalence centre School of Pharmacy reform programme Technology transfer Technical skill upgrading	Bioequivalence study centre fully operational More industry-oriented curricula have been developed and implemented by Addis Ababa School of Pharmacy 100 interns placed in companies

Source: ecbp (2006) and Engels (2009).

Many of the reforms implemented by the Ethiopian Government since 2007, however, may have been weakened from 2008 by a high inflation rate and a shortage of hard currency. Inflation led to drastic financial control measures affecting all manufacturing industries, including pharmaceuticals (Access Capital, 2010). Inflation is forecasted to remain below 10% in 2010–2011, from above 40% in 2008 (Economist Intelligence Unit, 2010). The irregular supply of electricity has also been a persistent problem. Despite the reforms, the President of EPMSMA stressed that competition by Asian producers remains strong, and there are few trade remedies available in Ethiopia to help local firms compete.

In August 2010, the Ethiopian Government announced the 5-year Growth and Transformation Plan (GTP), which, among other things, plans to expand infrastructure significantly and increase the role of the manufacturing industry for employment and economic development. The Plan also aims to address the underutilization of capacity (estimated to be at 40%) in the coming 5 years (Walta Information Centre, 2010b). The GTP identifies the pharmaceutical industry as a "priority sector" for the first time in the country's industrial and investment policy (Ministry of Finance and Economic Development, 2010). Moreover, government support for the priority sectors will focus on, among other things, expanding modern systems in the sector by using local

and external technical support and ensuring foreign technical support and investment, focusing on management skills and transformation, technological transfer and capacity building. Special attention is provided to establish institutions to efficiently support the priority sectors (Ministry of Finance and Economic Development, 2010). The market share of local pharmaceutical producers is targeted to reach 50% by 2015.

5.4 Science, technology and innovation policy

Ethiopia adopted its National Science and Technology Policy in 1993. The Policy focuses on sectors prioritized by the industrial and investment policies, but it does not specifically mention pharmaceuticals. Implementation of the policy is constrained by the lack of instruments and action plans for implementation and its focus on the public sector (Amha & Mekuriaw, 2008). The country undertook a review of the policy and upgraded the Science and Technology Commission to ministry level in 2007 (ecbp, 2006). Currently, the Ministry of Science and Technology has developed and submitted a new Science, Innovation and Technology Policy for adoption by the Cabinet. The new policy focuses on technological learning, adaptation and reverse engineering.

Addis Ababa University (AAU) launched the Technology Faculty–Industry Linkage Unit (TFILU) with Ethiopian Government funding in 2000. TFILU is governed by a national advisory body with membership consisting of the Ministry of Trade and Industry, the Ministry of Science and Technology, the Public Enterprises Supervising Authority, the Chamber of Commerce and private companies (Kitaw, 2006). TFILU has, however, always suffered from a lack of consistent financial support. TFILU has focused more on industrial services, including training, consultancies and technology applications (Wasmuth, 2007). Other universities also have various programmes and initiatives that encourage university–industry linkages. Adama University is being developed as a model university and attempts to address the industry–university linkage problem. The Ethiopian Intellectual Property Office provides technology transfer support by collecting and analysing patent information on an ad hoc basis, usually at the request of Ethiopian Government entities.

There is no pharmaceutical R&D cluster in Ethiopia. Overall, the country spends only 0.17% of its GDP on R&D (UIS, 2008). Two noteworthy efforts exist, however, that support the infant generic industry in Ethiopia: EPMSMA and the School of Pharmacy of AAU cooperated for the establishment of a bioequivalence centre under a memorandum of understanding. Ecbp helped EPMSMA and brought together pharmaceutical companies in Ethiopia, Kenya and Tanzania to set up the East African Bioequivalence Centre, in partnership with the School of Pharmacy of AAU.

To secure marketing authorization for generic medicines, pharmaceutical companies must submit data demonstrating the bioequivalence of the generic product with that of the originator's product. Approvals based on bioequivalence were meant to cut the costs of introducing generic medicines. However, there is no local capacity in Ethiopia for such studies,

and pharmaceutical companies have to commission the study to laboratories and clinical research companies abroad, generally at a higher cost. In 2009, a feasibility study was conducted for setting up and maintaining a centre for bioequivalence studies with laboratories and clinical partners in eastern Africa. The cost of bioequivalence studies carried out locally was found to be about 25% or less of the price offered for such studies in the United States, Canada, Europe, India and South Africa (Ali et al., 2009). The East African Bioequivalence Centre is currently recruiting staff to enter into operation.

The GTP has recently listed the establishment of an innovation and technology transfer system as a priority. The implementation strategy includes assisting research activities related to the collection, analysis, protection and distribution of science and technology information, and establishing a centre for the use of information in the protection of intellectual property for economic development. There is also an interest to establish effective linkage between industries and research institutes (Ministry of Finance and Economic Development, 2010).

5.5 Education

The number of graduates per year in science, engineering and manufacturing has increased from a very low base in 2005. Table 2 shows a total of 8412 graduates in engineering, manufacturing and construction and 11 174 graduates in science (including chemistry and biology) between 2005 and 2008. Data on pharmacists and pharmacy technicians show another 533 graduates in 2008, from 8 educational centres (WHO–UNESCO–FIP Pharmacy Education Taskforce). The School of Pharmacy of AAU enrolled 700 students in pharmacology, pharmaceutics, pharmacognosy and pharmaceutical chemistry for an undergraduate degree and 90 students for a postgraduate degree in 2009 (Gedif, 2009). AAU developed new curricula for postgraduate certificates and diplomas in clinical pharmacy, manufacturing and quality control in 2009 to respond to the human resource requirements of the private sector (Gedif, 2009). AAU also launched in 2009 a model drug information centre established in the premises of the medical faculty to provide organized medicine and therapeutics information to meet the drug information needs of practitioners and pharmacy students.

***Table 2** Number of graduates of tertiary education in Ethiopia by field of education, 2005–2008*

Field	Year			
	2005	2006	2007	2008
Social sciences, business and law	13 444	6864	11 881	21 344
Science	2130	2399	2440	4205
Engineering, manufacturing and construction	2396	2235	2813	3128
Health and welfare	2929	2613	2757	3674
Total tertiary graduates	29 581	26 820	32 516	49 244

Source: UIS (2008).

Results from the field interviews and responses to the questionnaire indicate that there is wide use of local skilled and semi-skilled workers. CPEL, EAP and SEAA expressed satisfaction with the ability of their local staff to adjust and manage technology. On the other hand, EAP reported a long delay in replacing its quality control head. Regulations prevent pharmaceutical companies from using chemists for quality control activities in pharmaceutical companies. Local firms have to retrain their employees in the specific industrial application used by the firm, for manufacturing processes, quality assurance and control, or otherwise. Rx Africa (Ethiopia) employs scientists from Germany and India for the formulation of pharmaceuticals.

There is limited information with respect to the nature and number of university centres of excellence and public sector institutes devoted to any aspects of pharmaceutical or medical research (Mouton & Boshoff, 2007). The only national institution of note is the Ethiopian Health and Nutrition Research Institute (EHNRI), at present the main research centre in Ethiopia (Belete, 2009). EHNRI employs around 50 researchers. It covers a wide range of activities, including HIV surveillance, national demographic and health surveys, nutrition surveys, research on infectious and non-infectious diseases, traditional and modern medicine research, vaccine and diagnostics production, and technology transfer and research translation.

5.6 Good governance

Ethiopia performs better in government effectiveness compared with other countries in the region, based on the World Bank governance indicators. However, the general regulatory quality in Ethiopia is still ranked very poor under the World Bank governance indicators. The "regulatory quality" governance indicator captures perceptions of the ability of the government to formulate and implement sound policies and regulations that permit and promote private-sector development in all economic sectors. Results from various governance indicators for Ethiopia and selected countries are shown in Table 3. With respect to governance in the pharmaceutical industry, the private sector has not identified corruption as a problem for its activities in Ethiopia. The implementation of the various reforms since 2007 has been well accepted by pharmaceutical producers. There are still gaps in the implementation of tariff reforms. The pharmaceutical producers, EPMSMA and Ethiopian Government agencies have been meeting since 2006 for consultations and to identify priority areas for action. During interviews, the status of the 5-year strategic programme for the pharmaceutical subsector did not appear to be clear for many stakeholders. The strategic plan was first developed in 2007 and Ethiopian Government agencies have been implementing relevant aspects of the programme. However, its official adoption came only in 2009. There is also a national forum led by the Ministry of Health with technical inter-ministerial coordination committees for the implementation of the industry sector development programmes.

***Table 3** Governance indicators for Ethiopia and other countries*

Country	2009 Global Peace Index	Governance indicator (percentile rank, 0–100), 2008				
		Regulatory quality	Government effectiveness	Rule of law	Control of corruption	Voice and accountability
Eritrea	–	1.9	4.7	8.6	43.5	1.0
Sudan	146	7.2	5.2	4.3	2.4	4.3
Ethiopia	127	19.8	39.8	33.5	30.4	10.6
Kenya	120	50.7	32.2	17.7	13.5	43.3
Uganda	100	50.2	36.0	36.8	23.2	33.2

50–75 percentile
25–50 percentile
10–25 percentile
0–10 percentile

Sources: Institute for Economics and Peace (2010) and World Bank (2008).

6. Analysis of SEAA

SEAA is a good example of a private-sector pharmaceutical firm that has been able to thrive in an otherwise underdeveloped LDC environment. The firm registered its first profitable year in 2009 and is operating at full capacity, one of only two local pharmaceutical firms that are doing so at the time of writing. The information obtained on the firm, and on the pharmaceutical sector in Ethiopia more broadly, indicate, importantly, that there are both sound business reasons and important policy reasons for SEAA being successful so far.

From a business perspective, SEAA was established to concentrate on a single product that serves as an important input in a larger value chain. This product (i.e. EHGCs) is better produced locally, because there are problems with transporting the product over long distances. It made sense for Chinese companies involved in the manufacture of EHGCs to partner with their Ethiopian distributor in the form of a joint venture to establish SEAA.

The Chinese partners are producers of the equipment and machinery used by SEAA. The Chinese partners have the know-how and experience in production and marketing of the EHGCs that SEAA produces. The local partner contributed in marketing the product locally and managing the human resources and the operation of the company. The prior existing business relationship between the Chinese and Ethiopian partners appears to have been important in establishing the trust needed to ensure a successful joint venture. SEAA is the only company in Ethiopia with Chinese participation managed by local staff (Desta, 2009). Also of note is the autonomy SEAA enjoys as a firm in its own right. SEAA sources its raw materials wherever it can find good quality at a lower cost, mostly from Europe, and it is not tied to source exclusively from its Chinese partners.

Furthermore, SEAA was able to protect itself from financial and hard currency problems during 2008 and 2009, because its Chinese shareholders are involved in different value chains of the industry globally and helped generate

additional income through identifying exporting markets for its products. Its strategy of exporting 30% of its products allows it to retain foreign sales proceeds in hard currency and finance the import of raw materials, avoiding complications under Ethiopian foreign exchange regulations.

Despite the business rationale for producing EHGCs in Ethiopia, the actual decision to establish such a joint venture in Ethiopia could not have been made without a number of factors in place, including a market, competitive operating costs, the availability of adequate human resources with ability to absorb and adapt the appropriate technology, and a manageable investment environment with appropriate incentives, which in turn is shaped by enabling policies.[31] For example, although Ethiopia still charges 10% tariffs on gelatin, the tariffs on some other raw materials have been reduced to 0–5%.

The information in this case study shows that SEAA clearly benefited from the technical assistance received through FMHACA and ecbp (for PIC/S). This assistance allowed technology transfer to its facility, which led to GMP certification and meeting a PIC/S standard, the first company from Ethiopia to do so.

SEAA is seeking to become a market leader in the region producing good-quality EHGCs. To achieve this, the company is implementing an expansion project with loans from the DBE to grow its sales and production volume and allow it to cut prices. At present, the firm does not appear to be interested in diversifying to other pharmaceutical products and sees more potential by seeking an increase in its production capacity for EHGCs.

Finally, SEAA's main customer base comprises local manufacturers of pharmaceuticals, which currently purchase 70% of its output. The sustainability of the local pharmaceutical manufacturing industry is crucial for SEAA. In addition, the expansion of productive capacity and export, and of product range (such as softgel and non-animal-product-based capsules, as well as production of gelatin itself), may be relevant for long-term sustainability.

7. Implications of local production and related technology transfer on access to medicines

The health infrastructure of Ethiopia, as demonstrated in Section 4, is underdeveloped and relies heavily on the public sector, including donor agencies and NGOs. The accessibility and affordability of health care, including drugs, is a major issue, especially for the larger rural population accounting for over 80% and the urban poor.

The SEAA joint venture produces only the empty capsules for medicines. In this regard, it is difficult to estimate its impact on access to medicine, as it

31 UNCTAD (2009) has previously advised Ethiopia on how investment-promotion efforts can be better aligned with efforts by Oromia State to develop its pharmaceutical industry.

only supplies local pharmaceutical manufacturers with one of the ingredients in the pharmaceutical value chain. Importation of APIs, excipients and packaging materials is the main driver of costs for the small and medium-sized pharmaceutical manufacturers in Ethiopia. Since capsules and tablets are the most used dosage forms in most therapeutic areas, SEAA supply local manufacturers with one of the excipients they need in the production medicine. Local producers visited during the field mission indicated that they have stopped or are about to stop importing EHGCs. SEAA has not, however, achieved price competitiveness compared with exporters that used to supply EHGCs to Ethiopia.[32]

Due to the role of EHGCs in the production of pharmaceuticals, SEAA's contribution to access to medicine is connected closely with the pharmaceutical producers themselves. The fact that supply cannot keep up with demand indicates a robust market for the local production of pharmaceuticals in sub-Saharan Africa. Although the SEAA joint venture was not driven by the LDC waiver given under the TRIPS Agreement, the high demand for EHGCs in Africa may in part be due to the TRIPS Agreement flexibility.

But SEAA alone cannot provide all that is needed for local pharmaceutical production in Ethiopia to improve access to and availability of medicines. SEAA's contribution could become more visible when investment expands in production of APIs and other excipients in Africa that help local pharmaceutical producers improve their competitiveness.

Beyond the industries, the Ethiopian government is considering implementing a health insurance system (Ministry of Finance and Economic Development, 2010). Depending on the scope and coverage, the introduction of a health insurance system can also play its own role in improving access to medicine.

8. Policy-relevant findings

It is important to note that in the case examined above, it was Chinese pharmaceutical manufacturers who made the decision to manufacture EHGCs in sub-Saharan Africa for reasons based on business and an access-to-medicines perspective. It made sense for the Chinese firms to manufacture EHGCs in Ethiopia, given the risk of spoilage in transporting EHGCs over long

32 Recent initiatives have started to look at measuring the contribution of individual originator companies and generic manufacturers for the access-to-medicine regime of countries. The Access to Medicine Index (funded by the Department for International Development (DFID), the Netherlands Ministry of Foreign Affairs, and the Bill & Melinda Gates Foundation, among others) is one example. In determining the access-to-medicine contribution of companies, the Index looks at the companies' performance with respect to: general access to medicine management; public policy and market influence; research and development for diseases; equitable pricing, manufacturing and distribution; patents and licensing; capability advancement in product development and distribution; and product donations and philanthropic activities. SEAA is not a typical pharmaceutical manufacturing company involved in formulation, and not all of the above apply to it. However, its contribution would be significant in terms of equitable pricing, good-quality manufacturing and distribution, and would advance the capacity of others. SEAA investment improves distribution of the product in the local and regional markets. It has also invested in quality and standards, which also helps the standards of pharmaceutical producers.

distances (i.e. from China) and the demand for EHGCs from the increasing numbers of manufacturers of medicaments across Africa.

An important factor influencing the sustainability of SEAA relative to other pharmaceutical firms in the Ethiopian market seems to be the fact that it has, to date, concentrated on a single product for which there is a high demand and for which a good-quality locally made product can compete successfully with its equivalents manufactured in China and India, even if the firm may not be able to produce at lower costs initially.

The technology involved in the production of EHGCs appears to have matched the skills available in the local labour market to absorb and adapt that technology, i.e. to a level that can compete with other firms, both in the local market and in the wider sub-Saharan African markets. Although some studies have been critical of the economics of engaging in local pharmaceutical production (Kaplan & Laing, 2005), the example of SEAA shows that firms can be viable with the right investment decision and if given the right opportunity. Moreover, although the firm currently focuses on just one input, its success can provide a sound basis for the development of future local pharmaceutical production initiatives, particularly for the upstream firms that rely on SEAA's excipients.

Targeted technical assistance was critical in ensuring the development and competitiveness of SEAA. The government has addressed some of the problems of Ethiopian pharmaceutical producers since 2007 working with EPMSMA. Measures introduced include lowering tariffs on a large number of raw materials, acceptance of higher-priced bids from local manufacturers in Ethiopian Government procurements, advance payments to alleviate working capital problems, and facilitating supplier credit. Pharmaceutical companies are receiving technical support to upgrade their facilities, with a view to helping local firms obtain quality certification in export markets. A notable success in this regard is the GMP accreditation of SEAA, the establishment of a regional bioequivalence centre, and curriculum reform at the AAU School of Pharmacy. The technical support has been provided by various Ethiopian Government agencies, including FMHACA, the Ministry of Health, the Ministry of Industry the and Ministry of Capacity Building.

The apparent success to date of SEAA is very much more an exception than the rule. Despite having a critical mass of chemists, pharmacists and other human resources needed for pharmaceutical production, many firms have failed, as noted above. The inability of many Ethiopian companies to penetrate the existing Ethiopian market itself – where 85% of the residents live in rural areas – and utilize their full capacity suggests that many improvements are still necessary to support pharmaceutical production in Ethiopia.[33] In general, the Ethiopian pharmaceutical manufacturers lack working capital, experience difficulty in securing loans and equity investments, and therefore lack the hard currency required to import raw materials and pay for regular upgrades. Policy reforms will certainly help to address some of these deficiencies, and

33 Similar findings were made by von Rosenstiel (2007) and World Bank (2009).

the Strategic Plan for the Pharmaceutical Subsector adopted in June 2009 is a good start. Previous studies by the United Nations Industrial Development Organization (UNIDO) (Von Rosenstiel, 2007)) and UNCTAD (2009) have highlighted the problem of market information and communication increasing the transaction cost and creating uncertainty. Additionally, the current regulation of technology transfer agreements is clearly inadequate to form the basis for any policy-making in this sector, as most deals in the pharmaceutical sector appear to be avoiding registering technology transfer agreements involving royalty payments.

Nevertheless, Ethiopia has high potential among LDCs in the region in pharmaceutical production initiatives, due to the efforts to date in improving absorptive capacity and, with SEAA, a base in Africa where an important excipient is produced. The potential to serve not only a large local population but also a wider region from an Ethiopian hub will no doubt continue to be attractive to foreign firms such as Dandong JINWAN (Group) Co. Ltd and China Associates (Group) Co. Ltd.

References

Access Capital. *The Ethiopia macroeconomic handbook: 2010*. Addis Ababa, Access Capital, 2010.

Access Leasing. *Summary of proposed investment*. Project Number 27071. Washington, DC, International Finance Cooperation, 2008 (http://www.ifc.org/ifcext/spiwebsite1.nsf/c9aba76ed1df1938852571c400727d66/526372f9c344c913852577f80059fbf2?opendocument).

Addis Fortune. Gov't to salvage troubled drug manufacturers. *Addis Fortune*, 2009, 11, no. 568.

Ali SL, Vilbel B, Scheidel B. Study on the feasibility of conducting bioequivalence studies in east Africa: Setting up and maintaining a centre for bioequivalence studies with bioequivalence laboratories and clinical partners in eastern Africa. Eschborn, GIZ, 2009.

Amha M, Mekuriaw A. Preliminary review of the S&T policy of Ethiopia in the framework of the national system of innovation. In: Etzkowitz H, Roest M, eds. *Transforming university–industry–government relations in Ethiopia*. Malmo, International Organisation for Knowledge Economy and Enterprise Development, 2008.

Belete W. *The patent system and innovation performance in Ethiopia*. Presented at the WIPO Regional Forum on the Role of Patents and the Patent Cooperation Treaty (PCT) in Research in Developing Countries, Nairobi, 30 March to 1 April 2009. WIPO/PCT/NBO/09. Geneva, World Intellectual Property Organization, 2009.

Biadgleng TE. Accession to the WTO, IPRs and domestic institutions. In: Correa CM, ed. *Research handbook on the interpretation and enforcement of intellectual property under WTO rules*. Cheltenham and Northampton, MA, Edward Elgar, 2010.

Central Statistical Agency of Ethiopia. *Livestock sample survey 2007–2008*. Addis Ababa, Central Statistical Agency of Ethiopia, 2008.

DACA. *List of drugs for Ethiopia (LIDE)*, 5th edn. Addis Ababa, Drug Administration and Control Authority, 2007.

DACA. *Supplement to NDL*. Addis Ababa, Drug Administration and Control Authority, 2008a.

DACA. Ethiopian national drug formulary. Addis Ababa, Drug Administration and Control Authority, 2008b.

DACA. *DACA Bulletin*, 1. Addis Ababa, Drug Administration and Control Authority, 2009.

Desta A. Chinese investment in Ethiopia: Developmental opportunity or deepening China's new mercantilism? San Rafael, CA, Dominican University of California, 2009.

ecbp. The engineering capacity building program: five year strategic plan, 2006–2010. Addis Ababa, Engineering Capacity Building Program, 2006.

ecbp. *Meeting standards increases safety and export potential*. Addis Ababa, Engineering Capacity Building Program, 2009.

Economist Intelligence Unit. *Country report: Ethiopia*. London, Economist Intelligence Unit, 2009.

Economist Intelligence Unit. *Country report: Ethiopia*. London, Economist Intelligence Unit, 2010.

Engels R. *Examples for GIZ experience in promoting pharmaceutical manufacturing: Ethiopia and BE center*. Presented at the IPC Informal Subgroup Meeting on the Local Production of Essential Generic Medicines, 30 September 2009. Geneva, World Health Organization, 2009.

Ethiopian Investment Agency. *Invest in Ethiopia: the land of your real business*. Addis Ababa, Ethiopian Investment Agency, 2009.

Ethiopian Transitional Government. *National drug policy of the transitional government of Ethiopia*. Addis Ababa, Ethiopian Transitional Government, 1993.

FDRE. *Transfer of technology*. Council of Ministers Regulations No. 121/1993. Addis Ababa, Council of Ministers, 1993.

FDRE. *The proclamation concerning inventions minor inventions and industrial designs*. Proclamation No. 123/1995. Addis Ababa, The House of Peoples' Representatives of the Federal Democratic Republic of Ethiopia, 1996.

FDRE. *Drug administration and control*. Proclamation No. 176/99. Addis Ababa, The House of Peoples' Representatives of the Federal Democratic Republic of Ethiopia, 1999.

Frost & Sullivan. *Healthcare industry overview in Ethiopia*. Dublin, Frost & Sullivan, 2010.

Gedif T. *Partnership's effort to shape pharmacy education in Ethiopia*. Presented at the American Association of Colleges Pharmacy (AACP) 2009 Annual Meeting, 18–22 July 2009, Boston, MA.

Global Fund. *Guide to the Global Fund's policies on procurement and supply management*. Geneva, Global Fund to Fight AIDS, Tuberculosis and Malaria, 2009 (http://www.theglobalfund.org/documents/psm/pp_guidelines_procurement_supplymanagement_en.pdf).

In-Pharma. *Shionogi Qualicaps sold to private equity firm*. In-Pharma, 2005 (http://www.in-pharmatechnologist.com/Materials-Formulation/Shionogi-Qualicaps-sold-to-private-equity-firm).

Institute for Economics and Peace. *Global peace index*. Sydney, Institute for Economics and Peace, 2010 (http://www.visionofhumanity.org/).

Kaplan W, Laing R. Local production: Industrial policy and access to medicines – an overview of key concepts, issues, and opportunities for future research. Health, Nutrition and Population (HNP) Discussion Paper. Washington, DC, World Bank, 2005.

Kitaw D. *Higher education – industry resource integration center: Towards solving existing Industrial Problems*. Paper presented at the Conference on Launching a Program to Transforming University–Industry–Government Relations in Ethiopia, Addis Ababa, United Nations Conference Centre, 29–31 May 2006.

Ministry of Finance and Economic Development. *Growth and Transformation Plan (GTP), 2010/11–2014/15: Draft*. Addis Ababa, Ministry of Finance and Economic Development, Federal Democratic Republic of Ethiopia, 2010.

Mouton J, Boshoff N. The Federal Democratic Republic Of Ethiopia. In: Mouton J, Waast R, eds. *Science in Africa: Country reviews*. Paris, UNESCO, 2007.

Negatu Z. *Investing in Ethiopia: The global business advisors' perspective, 2009*. Washington, DC, Ernst & Young, 2009.

Ohno I, Ohno K. Cross-cutting issues and organizational arrangements for industrialization in the context of broadening the policy scope in Ethiopia. Tokyo, National Graduate Institute for Policy Studies, 2009.

SEAA. *Expert in capsule engineering*. SEAA information booklet. Sino-Ethiop (Africa) Associates Private Limited Company, 2009.

Segemann S. *Hard gelatin capsules today – and tomorrow*, 2nd edn. Capsugel Library, 2002.

The Reporter. Standardization authority receives accreditation from German body. *The Reporter*, 28 February 2009 (http://en.ethiopianreporter.com/index.php?option=com_content&task=view&id=749&Itemid=1).

The Standards. Ethiopia works to improve medicine quality control in collaboration with USP–USAID PQM program. *The Standards*, 2010, 7:17.

UIS. *Customs table: Ethiopia – education*. Montreal, UNESCO Institute for Statistics, 2008 (http://stats.uis.unesco.org/unesco/TableViewer/document.aspx?ReportId=136&IF_Language=eng&BR_Topic=0).

UNCTAD. The least developed countries report: Knowledge, technological learning and innovation for development. Geneva, United Nations Conference on Trade and Development, 2007a.

UNCTAD. Intellectual property rights, investment and access to medicines: The Federal Democratic Republic of Ethiopia. Geneva, United Nations Conference on Trade and Development, 2007b.

UNCTAD. *Oromia: investment opportunities report*. Geneva, United Nations Conference on Trade and Development, 2009.

UNCTAD, WHO, TCTSD. *The local production of pharmaceuticals and related technology transfer: Country case studies*. Geneva, United Nations Conference on Trade and Development, World Health Organization, International Centre for Trade and Sustainable Development, 2011.

Von Rosenstiel I. *Study on the economic competitiveness of the pharmaceutical manufacturing sector in Ethiopia*. United Nations Industrial Development Organization, 2007.

Walta Information Centre. *Factory saves over 10mln birr foreign currency*. Addis Ababa, Walta Information Centre, 2009 (http://www.waltainfo.com/index.php?option=com_content&task=view&id=2200&Itemid=141).

Walta Information Centre. *Discussion on GTP concludes in 3 towns*. Addis Ababa, Walta Information Centre, 2010 (http://www.waltainfo.com/index.php?option=com_content&task=view&id=22952&Itemid=134).

Wamai RG. Reviewing Ethiopia's health system development. *International Medical Community Journal*, 2009, 52:279–286.

Wasmuth N. *Proposal for the implementation of a technology transfer system in Ethiopia*. Addis Ababa, Engineering Capacity Building Program, 2007.

WHO, UNESCO, FIP Pharmacy Education Taskforce. *Global pharmacy workforce report, 2009*. Geneva, World Health Organization, United Nations Educational, Scientific and Cultural Organization, and International Pharmaceutical Federation, 2009.

WHO. *GMP question and answers*. Geneva, World Health Organization, 2011 (http://www.who.int/medicines/areas/quality_safety/quality_assurance/gmp/en/index.html).

World Bank. *Governance indicators*. Washington, DC, World Bank, 2008.

World Bank. *World development indicators database*. Washington, DC, World Bank, 2009.

WTO. Extension of the transition period under Article 66.1 of the TRIPS Agreement for Least-developed country Members for certain obligations with respect to pharmaceutical products. Decision of the Council for TRIPS, 27 June 2002. IP/C/25. Geneva, World Trade Organization, 2002a.

WTO. Least-developed country members: Obligations under Article 70.9 of the TRIPS Agreement with respect to pharmaceutical products. Decision of the Council for TRIPS, 8 July 2002. WT/L/478. Geneva, World Trade Organization, 2002b.

WTO. Working party on the accession of Ethiopia: Legislative action plan – accession of Ethiopia. 19 June 2009. WT/ACC/ETH/6. Geneva, World Trade Organization, 2009.

Annex: Interviewed individuals and institutions

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Case study 5

Indonesia

This study on Indonesia was carried out by Kiyoshi Adachi, Legal Officer and Chief of the Intellectual Property Unit at UNCTAD, and Brian Tempest, UNCTAD Consultant and Partner at Hale & Tempest. Inputs for the study were collected during a field mission to Jakarta, Indonesia from 7 to 12 March 2010. The case study report was finalized under the overall responsibility of Mr James Zhan, Director of the Division on Investment and Enterprise, and Mrs Nazha Benabbes Taarji, Officer-in-Charge, Investment Capacity-Building Branch.

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Abbreviations

APL	PT Anugerah Pharmindo Lestari
CAFTA	China–ASEAN Free Trade Area
IMS	Intercontinental Marketing Services
IPMG	International Pharmaceutical Manufacturers Group
PTEI	PT Eisai Indonesia

1. Background and methodology

This case study was designed to investigate the high prevalence of Japanese pharmaceutical companies setting up manufacturing factories in Indonesia since the 1970s and the source of their technology, and to better understand both the reasons behind their sustainability over this period and issues that their subsidiaries currently face. Specifically, the case study examines intra-firm technology transfer in the context of a relationship between a parent research and development (R&D)-based pharmaceutical firm with headquarters in a developed country and one of its subsidiary factories based in a developing country.

UNCTAD thanks PT Eisai Indonesia (PTEI) for agreeing to be the subject firm for this case study and for the International Federation of Pharmaceutical Manufacturers Association (IFPMA) for assisting UNCTAD in facilitating the arrangement of interviews with Japanese manufacturers in Indonesia.

A case study research methodology was used in the study. Data were collected through reviews of academic literature and policy documents, and through open-ended face-to-face interviews in Indonesia. Interviewees were identified through purposive sampling. During the fact-finding mission to Jakarta from 7 to 12 March 2010, 28 people and institutions were interviewed, including 12 pharmaceutical experts (from Eisai, PTEI, PT Tanabe Indonesia, PT Ferron Par Pharmaceuticals and PT Kalbe Farma), 8 representatives of government (from the National Agency of Drug and Food Control, the Investment Coordinating Board, the State Ministry of Research and Technology, the Agency for the Assessment and Application of Technology, and the Directorate of Intellectual Property Rights), 5 members of the pharmaceutical distribution network (PT Anugerah Pharmindo Lestari (APL) and visits to 3 independent pharmacies), 2 representatives of nongovernmental organizations (NGOs; including Hilfswerk Austria and an independent logistician formerly with Médecins du Monde) and 1 investment banker (Batavia Investment Management Ltd.).[1]

In addition, a semi-structured questionnaire designed to capture the dynamics of firm-level activities related to production and technology transfer was administered to the firms, the results of which are included in the case study where relevant.[2]

This case study construes innovation as any new products, processes and organisational changes that are new to the enterprise, context and country in question, although not necessarily to the world at large (UNCTAD, 2007). In keeping with the scope of the project, technology transfer was defined as all components of technology, both codified (in terms of blueprints, hardware, machine parts and plant technologies) and tacit (know-how and skills), that are essential to enhance the capacity of the organizations in the recipient country to produce pharmaceutical products.[3]

1 See Annex: Interviewed individuals and institutions.

2 See Annex: Field questionnaire.

3 A uniform definition of technology transfer was used for all components of the project, including the trends survey, the regional dialogues and the stakeholder analysis.

2. Description of the firm, structure and range of products

Established in 1970, PTEI is a subsidiary company of Eisai Co., Ltd (hereafter Eisai), one of Japan's leading R&D-based pharmaceutical firms. Typical of subsidiaries of Japanese pharmaceutical firms, PTEI enjoys a very tight relationship with its parent Eisai, which holds the controlling stake of the firm's shares. Eisai chooses the President Director of PTEI. The current President Director is Mr Philip Tan, who was formerly the Chief Executive Officer of Eisai's subsidiary in the Philippines. Before that, the President Directors of PTEI were appointed from Eisai's headquarters in Tokyo. All of the staff of PTEI are otherwise locally recruited. Staff at PTEI currently number 96 in manufacturing, including 18 contract workers, in addition to a number of staff involved in administrative work in the Jakarta office.

PTEI established its first factory in 1971 at Puncak. The current factory was established in 1987 in Bogor, a suburb of Jakarta, to replace the Puncak factory, and sits on a patch of land that extends over 4500 square metres. This factory has received regular upgrades and investments. Government certificates for good manufacturing practice (GMP) and analyses of environmental impacts were issued in 1994. In 2001, the packing warehouse and formulation area was expanded and renovated. In 2003, the workshops were expanded. In 2004, the quality assurance and quality control operations were expanded and renovated. The factory received the highest regulatory approval rating in 2005, at the A level, after being inspected by the National Agency of Drug and Food Control. In 2006, further renovation took place, including a rainwater-harvesting facility. In 2007, the warehouse was expanded further so that it could hold 2 months' inventory, and in 2009 the Bogor factory received additional environmental approvals. At present, the Bogor factory is one of ten Eisai factories worldwide. The others are in China, India, Japan, Taiwan Province of China, the United Kingdom of Great Britain and Northern Ireland, and the United States of America.

The Bogor factory produces 22 products and is involved in 30 packaging operations. These include 14 products in 18 packs that are manufactured for the local market and 3 granule products that are manufactured for export to the Philippines and Thailand. At present, Eisai does not use the Bogor factory as a regional base for export to South-East Asia but instead uses its China (Province of Taiwan) factory for drug formulation product exports to Association of South-East Asian Nations (ASEAN) countries. In addition, four products in seven packs are locally packaged (but not manufactured) in Indonesia, including Eisai's leading products Aricept (donepezil) for Alzheimer's disease and Pariet (rabeprazole) for gastrointestinal disorders. Products manufactured by PTEI are generally outside of those contained on the National Essential Medicines List for Indonesia.

Also, Eisai has carried out contract manufacture for the Indonesian subsidiary of Takeda, another Japanese R&D-based pharmaceutical manufacturer, since 2005. In turn, Eisai has outsourced some cosmetic products to another local

factory since 2006. All active pharmaceutical ingredients (APIs) are procured from Eisai, and excipients are purchased from the same source as those used by Eisai in Japan, since recipes provided by the parent are followed precisely. Factory capacity usage is relatively low, at 65% on a daily shift of 8 hours per day.

PTEI products are distributed in Indonesia through an exclusive distributor, APL. In this regard, Indonesia has one of the most complicated distribution markets in the world. The difficulties begin with the country's geography, comprising 17 508 islands, which lie between the Indian and Pacific Oceans. Indonesia is a large country, with an area reaching 1.9 million km2, and its length from west to east spanning around 5000 km and from north to south 1700 km. Indonesia has a characteristic of geographical imbalance in population distribution: 9% of the country's population is located on Java, which covers only 7% of the total area. There is also a tropical climate, with high humidity and blazing sunlight, which is a challenge for pharmaceutical companies. The country's poor infrastructure complicates this difficult task further. APL is the largest independent distributor, with 28 branch offices and a national distribution centre in Jakarta. It operates in 65 cities and delivers 3–4 times a day to its customers. The company has 2400 staff and uses SAP in its management systems. It is majority owned by Zuellig Pharma, the largest distributor in Asia. APL has also used technology to enhance its services by creating new tools such as information databases covering medical representative doctor visits. It runs a specialized programme for delivering expensive life-saving drugs to patients and doctors 24 hours a day, 7 days a week.

In 2009, PTEI had a turnover of 108 billion Indonesian rupiah (Rp) (about US$ 12 million), and it is expected to have a turnover of about 95 billion Rp in 2010. Although some of the firm's profits are repatriated in the form of purchase transactions for inputs and final products, PTEI generates its own revenue as well with, for example, its toll manufacturing for Takeda. PTEI is subject to corporate income taxes under Indonesian law.

Intercontinental Marketing Services (IMS), a global pharmaceutical intelligence company, valued the Indonesian pharmaceutical industry in the retail sector at the end of 2009 at 6205 billion Rp, growing at 5.8%, and in the hospital sector at 4581 billion Rp, growing at 10.4%. In the retail sector, the local companies are strong, with Sanbe ranked first, Kalbe second and Dexa Medica fourth. The strongest foreign companies are Pfizer (third) and Sanofi Aventis (fifth). By comparison, the subsidiaries of Japanese companies are ranked 25th (Takeda), 33rd (Otsuka), 37th (Tanabe) and 38th (Eisai). Meiji (62nd) and Astellas (63rd) are much smaller. In the hospital sector, the local companies rank first (Kalbe), second (Sanbe), third (Dexa Medica) and fifth (Dankos). The strongest foreign company in this category is Japanese (Otsuka, which is strong in intravenous fluids). In this category, the other Japanese companies rank 21st (Takeda), 43rd (Tanabe), 45th (Eisai) and joint 52nd (Meiji and Astellas).

3. PTEI's technological capacity

The state-of-the-art facilities in Bogor are appropriate for the formulation of a wide range of pharmaceutical products. The PTEI staff with whom the fact-finding mission had discussions all appeared to be well-trained professionals and technicians. Discussions with the management of PTEI revealed that they had relatively few problems in recruiting competent pharmacists, chemists and engineers locally (other firms did, however, mention a problem with a lack of PhD scientists and pharmacists, as well as a shortage of doctors in the country). Efforts are made by management to offer attractive conditions of work as a means to avoid staff turnover.

Technology transfer takes place at PTEI along a single axis, i.e. from the parent Eisai to its subsidiary PTEI. The entire Bogor plant was built to detailed specifications of Eisai. Quality assurance and quality control procedures, and manufacturing recipes, are carried out in accordance with instructions and standards spelt out in volumes of manuals supplied by Eisai, and regularly updated through communications from Eisai. Some aspects of GMP in Eisai's Indonesian factory are stricter than those often seen in plants in Japan and the United States. Standard operating procedures such as those related to hygiene are established by Eisai and are strictly adhered to by PTEI. From time to time, Indonesian staff visit Japan for training. Also, Japanese-based experts from Eisai visit Indonesia to advise the workforce on new technology. According to the semi-structured survey responses, staff of both the parent company and the subsidiary consider technology transfer projects to have been completed successfully.

Apart from the contract manufacturing arrangement with Takeda's Indonesian subsidiary, all products manufactured by PTEI are Eisai products. At present, no independent R&D activity takes place at PTEI. Eisai's R&D activity for new chemical entities (NCEs) generally takes place in its laboratories in Japan, the United Kingdom and the United States, and in India since 2009, while clinical trials for NCEs take place in Eisai's target markets.

Previously, Eisai had invested in an R&D facility in Indonesia dedicated to developing local tropical plant-based medicines. Difficulties in commercializing products led to the decision by Eisai to close this facility in 2006. All samples collected by the laboratory were given to the Indonesian government at the time of closure.

A limited number of adaptive activities take place at PTEI. Basic facilities exist at the Bogor factory to undertake tests to ensure that various local requirements are met, such as tests on the heat stability of their pharmaceutical products given the hot and humid climate in Indonesia. Extra hygiene measures at the factory were adapted, for instance in light of the threat of avian flu as and the threat of insect contamination given the factory's tropical location.

4. The pharmaceutical market in Indonesia

Indonesia is the fourth most populous country in the world. The Indonesian Government has said that it aims to offer universal health coverage by 2012, although this may be delayed. Indonesia has 0.66 hospital beds per 1000 population, the lowest rate among the ASEAN countries. There are 16 physicians, 50 nurses and 26 midwives per 100 000 population. Both traditional and modern health practices are employed. Human immunodeficiency virus (HIV) has posed a major public health threat since the early 1990s; in terms of the prevalence of HIV, Indonesia ranks behind Myanmar and Thailand among the ASEAN countries. Other health hazards facing Indonesia are dengue fever, malaria, haemorrhagic fever and avian flu.

Despite sustaining double-digit economic growth in recent years, Indonesia's pharmaceutical industry is relatively modest in size, at approximately US$ 2.5 billion in a country with a population of over 240 million people. The pharmaceutical industry in Indonesia has undergone a series of transformations in its history since its formation in the late 1960s, when the R&D-based multinational firms began to enter the market, including the Japanese pharmaceutical manufacturers. Six R&D-based Japanese pharmaceutical companies have operations in Indonesia, which include Astellas, Eisai, Meiji, Otsuka, Takeda and Tanabe, indicating a relatively large presence of Japanese firms compared with the size of the market. Of these, only Astellas has no local factory. Most of these companies entered the Indonesian market in the late 1960s, apparently driven by a combination of a history of Japanese presence in Indonesia since the immediate post-Dutch colonial period, the potential size of the market and the regulatory environment (see below). By 1991, multinationals controlled over 70% of the total market share for pharmaceuticals in Indonesia.

In the early 1990s, however, the Indonesian Government started to support the local companies, which began chipping away at the dominance of the multinational firms, so that today the local companies have over 70% of total market share and the multinationals hold only 25%. The results of field interviews tend to show that this is a result of local industry moving rapidly along the learning curve, improving manufacturing in tandem with weak multinational NCE pipelines, along with flanking policies that support local industry.

At present, the retail market is composed of the top earners in the middle class and the wealthy. The rest of the population relies on the Indonesian Government-subsidized nonbranded generics from the state-owned pharmaceutical companies and from the local private industry. The four state companies are Kimia Farma, Indofarma, Biofarma and Phapros, which are run as profit-seeking enterprises and can be deployed as instruments of Indonesian Government policy when necessary. In 2009, two of the Indonesian Government companies agreed to merge. In 2008, Indofarma had a loss of US$ 1.5 million and Kimia Farma had a loss of US$ 0.4 million due to high costs associated with the import of raw materials. The plan was that these

companies would enter the API market and the market of pharmaceutical manufacturing equipment. However, in March 2010 the merger was delayed. Further merge and acquisition activity is likely in this generic pharmaceutical sector in Indonesia in the search for greater efficiencies.

The Indonesian Government runs a public medical insurance programme for the poorest people, who live on less than US$ 1 a day. The insurance scheme was restructured in 2008 under the name *jamkesmas* and comprises 15% of Indonesia's health expenses, covering an estimated 76 million people. The poorest part of the population (who live on less than US$ 1 a day) has shrunk significantly in recent years, leaving 70% of health expenses coming directly from the pocket of patients and the rest from corporate health insurance paid by employers.

In recent times, some of the multinationals have tried to regain their position in the local market. Interviews confirmed that these multinationals appear to be attracted by the new wealth of some Indonesians and the potential size of the Indonesian market if the country continues to become more prosperous (the Jakarta stock market grew by 150% in 2009 and appears minimally affected by the economic downturn). Pfizer leads this effort and has recently offered an "E-card", which enables medicines to be bought at a discount; it now has 25 000 patients signed up. Some companies are focusing on over-the-counter (OTC) drugs, such as Bayer, and others are using Indonesia as a central hub for regional manufacturing because of the low cost of labour. Of the Japanese firms, only Otsuka has made inroads into the top ten firms in the country in the hospital market, because of its strength in intravenous fluids. Tanabe uses its subsidiary as a hub for exporting its products across South-East Asia.

The most vibrant segment of the pharmaceutical market in Indonesia appears to be that for branded generics. Branded generics refer to off-patent pharmaceutical products that carry the trademark of a known pharmaceutical manufacturer. The branded generic market can generate significant mark-ups on pharmaceutical products, which is attractive for the local companies involved in this business.

To take an example, the fact-finding mission visited three pharmacies and asked for the same product over the counter – a strip of ciprofloxacin 500 mg (Figure 1). The same products varied in price from pharmacy to pharmacy: 3500 Rp, 5000 Rp and 143 250 Rp. The first two products were nonbranded generics and were supplied by independent pharmacies. The product that cost 5000 Rp displayed the price "4000 Rp" on the strip, indicating an overcharge of 1000 Rp compared with the regulated price set by the Indonesian Government. However, the prices of the nonbranded generics are estimated to be at the likely cost of manufacture of the strip. The expensive strip was branded Baquinor Forte from the local company Sanbe and was supplied by the Century chain of pharmacies; it carried a price on the strip of 145 750 Rp, representing a slight undercharge compared with the regulated price set by the Indonesian Government, albeit at a price 40 times that of the unbranded versions. The mission received the product each time with no request for a doctor's prescription.

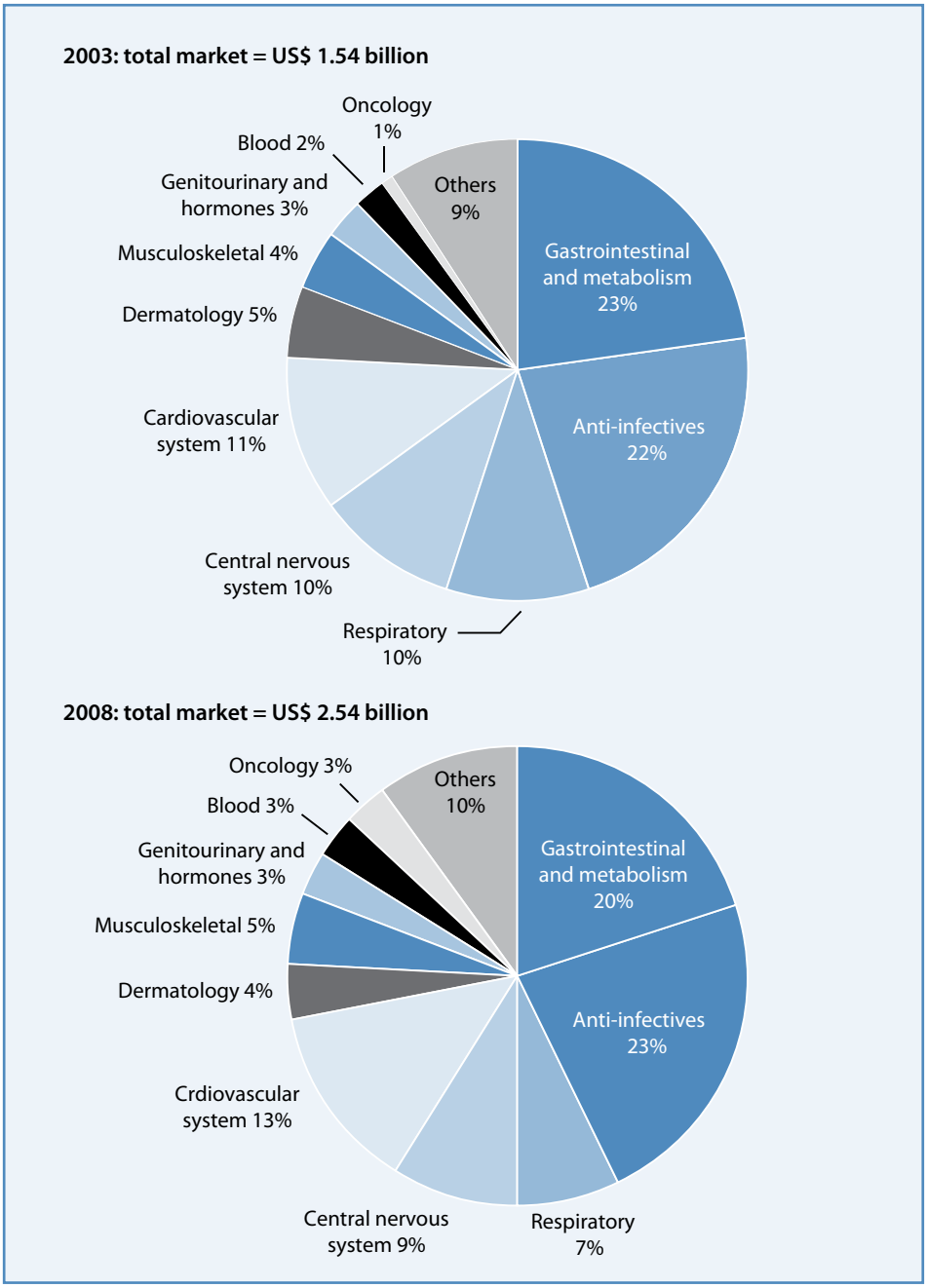
Figure 1 *Branded and nonbranded versions of the same medicine are sold at significantly different prices in Indonesia*

When tabulated by composition of the market (Figure 2), Indonesia is typical of evolving markets, with high local generic activity in low-value therapeutic areas. The top local manufacturers, such as Kalbe Farma (the largest pharmaceutical firm in South-East Asia), Sanbe and Dexa, typically have large portfolios and are present across many therapeutic areas. The leading area continues to be anti-infectives (23% by value), with gastrointestinal drugs second (20% by value) and cardiovascular drugs third (13% by value). However, not many of the Japanese companies are present in the antibiotic segment.

The Indonesian OTC market has double-digit growth owing to prevalent self-medication. The expansion of the fast-growing pharmacy sector with chains such as Century and Apotek K-24 also aids the OTC market by increasing consumers' knowledge of medicines. There is also a "grey" resale market for pharmaceuticals; for example, at the Pasar Pramuka market in Jakarta, one can exchange half-used strips of medicines for cash.

Indonesia depends on imports for 85–90% of its pharmaceutical basic materials (APIs). The multinationals generally source their APIs from Europe, the United States and Japan, while the local pharmaceutical companies use China and India. This supply routing has been in existence for many years, and clearly documented sales are available attesting to these purchases. The main market for Indonesian firms appears to be domestic, with a limited amount of exports. Such exports in the main have gone to the ASEAN, Middle East and African markets. Kalbe has, for example, established branches in Cambodia,

***Figure 2** Indonesia pharmaceutical market: top therapeutic areas*



Source: Presentation "Entering the Indonesian Pharmaceutical Market" by Sharma Abhishek of Mergers, Acquisitions, Private Equity (MAPE), Mumbai, India, January 2010.

India, Malaysia, Myanmar, Nigeria, the Philippines, Singapore, Sri Lanka, South Africa and Viet Nam.

At one time there were 350 local pharmaceutical factories, and each factory distributed its own products across Indonesia. Nowadays, the top five local manufacturers own their own distribution business, and other pharmaceutical companies rely on distributor firms such as APL to ensure that their products reach their customers. With respect to the top five local manufacturers, the guaranteed business of the parent pharmaceutical company means that

they can subsidize distributor costs and attract external clients relatively inexpensively. Dos Ni Roha has the most extensive distribution network in Indonesia. This includes 48 branches with over 200 000 outlets served. Each branch has a sales force, fleet operation and finance operation. The distributors deal with chain pharmacies, hospital groups and modern outlets such as Carrefour, Hypermarket, Hero, Makro, Indomart and Alfamart. There are currently about 2100 distributors/wholesalers, 8200 retail pharmacies, 6400 licensed drug stores and 1300 hospitals in Indonesia.

Investments into the pharmaceutical sector in Indonesia are robust, indicating that investors see potential, despite the small size of the industry. Overall, the investment in Indonesia from both domestic sources and foreigners has continued to grow, even in 2009, which was a global recession year. According to the Investment Coordination Board, the pharmaceutical/chemical sector was the leading sector for domestic investment in 2008 (the latest year for which full statistics were available) and ranked second in terms of foreign direct investment (FDI), with 15 and 17 projects accounting for 17.4% (5850 billion Rp) and 10.7% (1111 billion Rp), respectively, of total investment for that year. Early indications are that these robust figures have continued in 2009.

Japan has been a consistent investor in Indonesia over the years. For FDI in 2008, Investment Coordination Board statistics show that the most important country sources were Singapore and Japan. In terms of employment generated by FDI, the Republic of Korea takes the lead position, with investments leading to 53 025 new jobs in 2008. Japan comes third, with 26 728 new jobs, and Singapore second, with 32 392 jobs. A large Japanese expatriate community exists in Jakarta, comprised mostly of Japanese staff and their families stationed in the capital and working in the Indonesian subsidiaries of Japanese multinationals. Japan is thus well placed in most statistics, and it is not surprising that Japanese pharmaceutical companies are so prevalent in Indonesia.

5. The framework for local production and technology transfer

5.1 Drug regulation

The local drug regulatory authority, the National Agency of Drug and Food Control, employs 1000 staff, who inspect the 200 manufacturing facilities in Indonesia. There are usually 60 inspections each year, and at any one time there will be 2 or 3 problem factories. Regular inspections award a label of A, B, C or D. A-rated factories (such as PT Eisai Indonesia) are the best. D-rated factories are not wanted in Indonesia. The industry would prefer more factories to be closed after defective inspection reports.

Generic product approvals often take 150 days, or 80 days if they are due to be exported. The regulatory approval requires a bioequivalence study showing the equivalence of the generic to the innovator. Indonesian law permits the use of generic companies to rely on test data submitted by originator companies. Local firms are aware of this and make use of the possibility to file for marketing authorization based on bioequivalence. Frequency companies, however, only begin the process of bringing a generic equivalent to market after the patent term has expired (see discussion below on the Bolar exception).

NCEs take 300 days for approval, or 150 days if they have a life-saving property. The multinationals take their global master file from their headquarters and "top and tail" the document for the Indonesian authorities. ASEAN drug registration harmonization started in 2008, and Indonesia is well placed to take advantage of this process. Indonesia has Pharmaceutical Inspection Convention (PIC) membership and Indonesian facilities have applied for World Health Organization (WHO) prequalification. The only toxicology facility is established in one of the universities. Phase 2 and 3 clinical trials are also carried out.

In Indonesia, prices of medicines are not regulated, except for about 150 nonbranded generics. These 150 medicines are part of a list of 369 essential drugs for Indonesia. The remainder of the essential drugs list is price-controlled for the purchases by the Indonesian Government, the military and other public institutions.

Clinical trial activity takes place in Indonesia and is overseen by the National Agency of Drug and Food Control. The contract research organization (CRO) industry is driven by the huge number of unsaturated clinical sites. Some CROs claim they can find 10 000 patients for a trial if necessary. Gleneagles CRC is a Singapore-based CRO, and Quintiles, the leading global CRO, is also present in Indonesia. In order to deal with issues of corruption, these CROs have set up a track record of heavily scrutinized and carefully audited clinical studies. The CROs are also looking towards the regulators to align more quickly with global standards and processes. Quintile is looking to build its local operation in the next 6 years to 100 employees and 70–80 clinical trials per year.

5.2 Intellectual property rights

As a developing country Member of the World Trade Organization (WTO), Indonesia was obliged to fully implement the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) by 2005. The current patent law was introduced in 2001 and extends patent terms to 20 years, but with the possibility of a 2-year extension period (which would be beyond the required TRIPS minimum of 20 years). Compulsory licence provisions have been retained in the law. In 2006, two Government-use compulsory licenses for HIV products were issued by the Indonesian Government in favour of Kimia Farma, a state-owned pharmaceutical company, at a minimal royalty payment to the

patent owner. Kimia Farma produced one order of the antiretrovirals (ARVs) for the Indonesian Government but then discontinued production because of the high cost of manufacture, citing the price it paid for imported APIs.[4]

Overall, about 5000 patents are issued each year, at a cost of US$ 60 each, predominantly to foreign applicants. Although exact figures are not available, R&D-based pharmaceutical firms generally seek patent protection for new chemical entities in Indonesia due to the potential of the large domestic market. Indonesia is a member of the Patent Cooperation Treaty.

With respect to TRIPS Agreement flexibilities relevant to public health, the Indonesian Patent Law has not incorporated the so-called Paragraph 6 system,[5] whereby compulsory licenses may be issued and notified to the WTO to facilitate exports to countries with little or no manufacturing capacity, notwithstanding the existence of a robust generic industry that could potentially export to LDCs in ASEAN or to nearby small-island nations in the Pacific that have limited production capacity. A Bolar exception is available under the patent law but is hardly used. There is also a research exception in the patent law, but this does not appear to be well understood. A major deterrent to use in this regard is that the text of both exceptions appears to be that, notwithstanding the understanding of health and intellectual property authorities to the contrary, the text of the patent law seems to exclude those who may use these exceptions from criminal liability only (and it remains unclear whether the exception covers civil liability). The result is that generics generally come on the market later than they would otherwise.

5.3 Foreign investment and industrial policies

There is a formal legal limit of foreign ownership defined for various business sectors. For example, pharmaceutical companies have a foreign ownership limit of 75% shareholding.[6] Independent pharmacies have a foreign limit of 0%, while educational facilities are at 49%, private hospitals 65% and financial services 80%. The latest version of this regulation was introduced in 2007, when restrictions on foreign ownership were introduced into 23 sectors. The Indonesian Government is, however, currently revisiting its "negative" list.

The Ministry of Health issued Decree No. 1010 in late 2008, as part of its efforts at technical reform. The 1010 regulation requires every company to manufacture every one of its pharmaceutical products in Indonesia. If companies do not agree, then their product licences will be withdrawn and they will not be able to sell drugs that are not manufactured in Indonesia. Existing foreign firms that are importing drugs will be classified as pharmaceutical wholesalers and lose their registration rights for their products 2 years following the promulgation of the Decree. Imported pharmaceuticals can be registered by local pharmaceutical companies with

4 Statement by Kimia Farma staff during an UNCTAD workshop in Jakarta, 11 November 2010.

5 See the 30 August 2003 Decision on the Implementation of Paragraph 6 of the Doha Declaration.

6 A grandfather clause allows Eisai's shareholding in PTEI to be higher than 75%.

written consent by a foreign company. The written consent must include technology transfer to allow local manufacturing within 5 years.

The 1010 Decree is, quite understandably, controversial. Although it aims to secure greater technology transfer to Indonesia in a strategic industry that the government is trying to strengthen, a factory of a multinational firm manufactures only a handful of products and the rest are imported from other factories around the world because of the need to be globally efficient. Some of the fiercest criticisms of the Decree therefore come from the trade association of multinational pharmaceutical firms in Indonesia, the International Pharmaceutical Manufacturers Group (IPMG), which has 29 members, 12 of whom are strongly opposed to the new policy and may have to withdraw as they do not have a factory in Indonesia. These companies include Merck, Novartis, Eli Lilly, Novo Nordisk, Astra Zeneca and the Japanese company Astellas, although Astra Zeneca is said to be setting up a new facility in Indonesia (while it is closing its plants in Europe). The 1010 Decree will also be an issue for Malaysian and Thai pharmaceutical companies that want to export to Indonesia as part of ASEAN trade, who will find that they now need a local factory in order to register a drug for distribution. It remains to be seen whether any countries will legally challenge the Decree.

For its part, the National Agency of Drug and Food Control appears to recognize that it might be problematic to require that all pharmaceuticals be produced locally, and that a rigid implementation of the Decree could have potentially negative consequences for access to medicines. It has indicated that the Indonesian Government is prepared to be flexible in the interpretation of the Decree. In this regard, it should be noted that even before the issuance of the 1010 Decree in 2008, the Indonesian Government was encouraging foreign firms to establish local factories to manufacture pharmaceuticals. Before the 1010 Decree, however, companies wanting to distribute any of their products (including those manufactured abroad) could hold a distributor's licence, which would not necessarily require a factory in Indonesia.

Free trade agreements with China and India are seen as threats to the domestic industry. For example, the China–ASEAN Free Trade Area (CAFTA) will open Indonesia's health sector to competition from abroad. It took effect on 1 January 2010, but its impact is yet to be seen.

In the early 1980s, there was a 5-year tax holiday for new investments in the pharmaceutical sector, but this programme ended in 1984. Now there are few incentives offered by the Indonesian Government specific to the pharmaceutical industry. There is, for example, no tax relief on pharmaceutical exports or on R&D expenditure. At present, there is no particular Government policy in place to lower the cost of APIs. This is unusual in the light of the significance of the pharmaceutical industry to Indonesian inward investments.

5.4 Science and technology policies

The Indonesian Government has a Tropical Diseases Centre and the Indonesian Center for Agricultural Biotechnology and Genetic Resources Research and Development. The major focus of research seems to be on herbal products and vaccines, which appears in part to be driven by the concerns in the country over avian flu. It should be noted that in 2007 Indonesia, in a controversial move, had restricted access to H5N1 virus samples to parties who agreed to use them for noncommercial purposes. More recently, and with the adoption of the Nagoya Protocol to the Convention on Biodiversity in November 2010, a Japanese non-profit-making organization, announced technology transfer and joint development of a vaccine for avian flu with the state-owned enterprise Biofarma. Biofarma is also part of a WHO project to respond to the need for stepped-up vaccine production in the event of a pandemic.

Apart from the exceptions mentioned above, there appear to be few incentive schemes to encourage science, technology and innovation in Indonesia. Discussions with the State Ministry of Research and Technology revealed that there are neither special economic zones nor R&D grants or soft loans for new technology. Overall, there appears to be little coordination of science and technology policies with industrial and economic policies. Apart from the opportunities presented by the Nagoya Protocol and biodiversity-based products, there appears to be little interest in developing indigenous R&D capacity beyond the generics market.

As far as private-sector initiatives are concerned, medium-sized Indonesian companies (such as Pyridam) are focusing on expanding their contract manufacturing business. The biggest pharmaceutical company in South-East Asia is Indonesia's Kalbe, which is also developing its own innovative products. Kalbe owns a research coordination and licensing entity based in Singapore called Kalbiotech. Most of the other R&D in Indonesia is based on licensing in products and carrying out additional development. It will take some time for research to come close to replacing manufacturing as a growth driver in Indonesia.

5.5 Education

While Indonesia spends 5% of Government expenditure on health, it spends 17% of total Government expenditure on education – compared with 25% in Thailand. Indonesia has, nonetheless, undergone a major improvement in the area of education. The literacy rate among people aged 10 years and over has increased from 62% in 1971 to 91% in 2002. The adult literacy rate is now 92% (WHO, 2007). Indonesia is probably doing better with its Millennium Development Goals (MDGs) in terms of primary education and enrolment in secondary education facilities than in areas of health. However, the focus on higher education is weaker, and scientific and medical education in particular needs strengthening. The graduate programmes en masse started in the mid-1980s, but the brightest students preferred to go overseas to study. Quality appears to be the main issue. The Times Higher Education

(2008) World university rankings 2008 report ranks the leading university of Indonesia at 287th and Bandung Institute of Technology at 315th. This comes after Singapore (77th), Taiwan Province of China (124th), Mexico (150th), India (154th), Thailand (166th), South Africa (179th), Malaysia (230th), Brazil (249th) and the Philippines (276th). However, both Indonesian universities have improved their ranking on the previous year in the same report. The Indonesian President is encouraging the Indonesian universities to take up business school subjects such as entrepreneurship.

5.6 Good governance

The Corruption Perceptions Index of Transparency International (2009) places Indonesia at 111th, ahead of other ASEAN countries, with Viet Nam ranked 120th, Laos 158th and Myanmar 178th, but behind Singapore at 3rd, Malaysia 56th and Thailand 84th. The Political & Economic Risk Consultancy (PERC, 2010) put Indonesia at the bottom of its Asia Pacific corruption perception ranking in March 2010.

The multinationals often blame the local industry for controversial marketing activities. Local firms deny engaging in unethical marketing, and some firms, such as Kalbe, conduct public relations to explain their marketing policies to the outside world.

5.7 Competition policy

The Law Concerning the Prohibition of Monopolistic Practices and Unfair Business Competition (Law No. 5 of 1999, hereafter the Competition Law) is administered by the Commission for the Supervision of Business Competition. The authority has to date not addressed any case on excessive pricing of pharmaceuticals, although it is apparently aware of significant price differentials between nonbranded and branded generics (see above). The Competition Law excludes the consideration of any cases dealing with intellectual property; it therefore would not act as a check on excessive pricing or abuse of a dominant position deriving from exclusive rights that may emanate from patents or other protected intellectual property.

6. Analysis of PTEI

The situation of PTEI within the overall pharmaceutical market in Indonesia and its policy environment appears to be relatively typical of Japanese pharmaceutical firms with a factory in the country. PTEI entered the market early, in the 1970s, along with other Japanese multinationals and has remained in the country ever since. The decision to set up its own factory in the country appears to have been driven by a number of factors. The size of the market was, and continues to be, attractive, perhaps even more so now given Indonesia's growing affluence. The policy environment clearly favoured local production, as even before the 1010 Decree Indonesia made sure that preferential treatment was given to companies that established manufacturing facilities

in the country. The policy environment for local production also appears to have been bolstered by various reforms undertaken to open the economy to investment in the 1970s. Finally, Japan has had a history of good relations with Indonesia, dating back to Indonesia's immediate post-Dutch colonial era.

The transfer of technology to PTEI follows a very typical model of such transfer between a parent multinational and a subsidiary and involves dissemination of manuals, training and frequent communication between PTEI and Eisai. Strong efforts are made to keep the technology in-house, including making sure that conditions of employment are attractive so that staff are not tempted to take acquired knowledge to other firms. Most products manufactured by PTEI are off-patent, although a number of patented products are produced as well. The manuals and recipes followed offer little room for deviation but ensure that the quality of the products manufactured is exactly the same as if they had been made in any of its factories located in a developed country (i.e. Japan, the United Kingdom or the United States). The experiments undertaken locally are basically to adapt to the local environment, i.e. to ensure greater heat and humidity resistance.

What perhaps distinguishes Eisai from other Japanese multinationals in the country is (i) that Eisai feels confident about its technology transfer, to the extent that it no longer feels the need for any Japanese expatriates to be stationed in Indonesia; and (ii) that, although unsuccessful, it did briefly attempt to set up an R&D facility in Indonesia for plant-based herbal medicines.

That PTEI as well as other foreign multinationals have continued to operate factories in Indonesia despite a tough operating environment is perhaps more surprising. Where multinationals once controlled 70% of the market, they now have only a 25% share. Most of the Japanese companies are working at a capacity utilization of only about 50%. The factories are thus clearly underutilized. Caps on shareholding in the industry and requirements to manufacture locally make the market even more difficult for the R&D-based pharmaceutical firms with headquarters in developed countries. The drug regulatory environment does not appear to be particularly strong either. Local companies are aggressive in their pursuit of market share. Kalbe announced in November 2009 that it will spend up to US$ 53 million on acquisitions in 2010 to accelerate growth and bring new technologies and skills to Indonesia. It is believed that such merger and acquisition activity to bring new technology to the local industry will expand in the future. Finally, there is little in the way of incentives offered for FDI in the pharmaceutical industry. The operating environment is thus a difficult one, not only for the Japanese R&D-based pharmaceuticals but also for all foreign pharmaceutical companies seeking to do business in Indonesia.

Both the surveys and face-to-face interviews indicate, however, that the large majority of Japanese pharmaceutical firms already present intend on staying in Indonesia, particularly in the lucrative branded generics market. The pharmaceutical market in Indonesia is predicted to grow to US$ 3.9 billion by the end of 2011 (Sudharta et al., 2010), with 250 companies – 33 being

multinational companies and the rest local companies (Kulkarni, 2009). It remains to be seen what will happen with patented products that are currently manufactured abroad and imported to Indonesia, given the 1010 Decree.

Ironically, the Japanese companies have helped to spawn growth of the local industry. In terms of human resources, the local industry representative indicated that many of the local firms hired staff away from the multinationals. When the employees moved jobs, they often took the knowledge, experience and technology with them. On the formal side, in-licensing from Japanese firms is also prevalent, and this is also a form of technology transfer. Kalbe was initially started up from inward technology from a Japanese licence. Finally, Japan provides regular training in intellectual property to Indonesian Government stakeholders, mainly on technical subjects such as patent examination, as a part of its official development assistance.

7. Implications of local production and related technology transfer on access to medicines

The selection of PTEI for a case study represents one model of pharmaceutical production that takes place in developing countries. The choice of Eisai to locate and maintain a factory in Indonesia appears to have been driven by a number of factors, including the size of the market and its history. It should also be underlined that the PTEI model is a typical model of local production and technology transfer between a parent company transnational corporation (TNC) and its subsidiary, where the main driver of local production in this case is not access to medicines but is very much market-driven. Accordingly, the range of products manufactured by PTEI has little correlation with the Indonesian National Essential Medicines List.

PTEI is probably too small a player in the Indonesian market to have made a significant impact on prices or access alone. Moreover, the prices it charges are generally what the market will bear in the absence of price regulation for the bulk of its products.

This is not to say that the factories of large developed-country-based pharmaceutical TNCs have not had any impact on access to medicines in Indonesia. As the original providers of technology to Indonesia, Japanese firms were among the first to train locals and bring in quality control and assurance methodologies, and PTEI is no exception. Without this basis, the local industry would not exist. The technology transfer and local production provided by the multinationals were not, however, designed with public health/access to medicines as the primary driver. It should also be borne in mind that other developing countries with promising pharmaceutical industries, such as Bangladesh and Colombia, have followed a similar development path, with multinationals first entering the market and establishing factories, and then eventually yielding the market to local firms after a number of years.

Some of the more interesting findings from an access-to-medicines perspective stem from the policy environment in which PTEI operates. The 1010 Decree is a source of heated debate, as although it attempts to encourage technology transfer and increase health security by mandating the local production of all pharmaceuticals, its strict application could result in blocking availability by Indonesians to some high-cost, low-volume drugs manufactured abroad and could thus potentially be problematic. It remains to be seen how the country will actually implement the 1010 Decree and how it will affect firms such as PTEI, but there will be a need to reach an agreement with foreign pharmaceutical companies to guarantee access to medicines that would be difficult, for one reason or another, to manufacture in Indonesia.

The 1010 Decree should, however, also be seen in the context of the wider policy by the Indonesian Government to encourage local production of pharmaceuticals and vaccines. A number of important decisions have been taken by the Indonesian Government in this regard, including the use of Government-use licences to enable Kimia Farma to manufacture ARVs in 2006, and the decision to restrict access to avian flu pathogens to noncommercial researchers in the absence of a better-access regime for any vaccine developed from the source material. These decisions, although controversial, reflect a government that uses available means to secure lower-priced, high-quality medicaments and vaccines. In this regard, the former decision (Government-use licences) appears to have been less successful than the latter (Kimia Farma soon discontinued production as it could not cope with the high cost of imported raw materials, but Indonesia successfully negotiated important projects with donors to develop avian flu and other vaccines with BioFarma). It should be noted, however, that there is no evidence from the interviews to point to a conscious effort to induce divestiture by foreign firms. Rather, the emphasis has been on technology transfer to build local capacity, with a view to improving security of supply at lower cost.

Finally, the resulting market structure for medicines is perhaps what one would expect from a middle-income country. Locally produced nonbranded generics, branded generics and imported pharmaceuticals (both generic and non-generic) are generally available on the market. People tend to use medicaments based on their income levels, with locally manufactured nonbranded generics being the most affordable. Access is supported by price controls on some essential medicines and on a medical insurance scheme that guarantees that the poorest people do not pay for medicaments out of pocket. The long-standing policy of the country to encourage local production has no doubt been a major factor in the development of a local pharmaceutical industry, and has certainly had an effect on how the market is structured today.

8. Policy-relevant findings

Indonesia has had a relatively successful experience in encouraging the local production of pharmaceuticals and reaping the benefits of technology

transfer. Local firms became the beneficiaries of early technology transfer by the R&D-based multinational pharmaceutical firms, who once controlled the Indonesian market. This happened when staff who worked at these subsidiaries subsequently moved to local firms that, due to a favourable policy environment that supported local pharmaceutical manufacturing, offered growth potential or commensurate salaries. It is thus not surprising that PTEI tries to offer competitive terms of employment for its staff, in order to minimize turnover. Also, local firms became more comfortable with in-licensed technology and know-how, and they were able to manufacture medicaments (mostly generic) on their own.

This examination of PTEI presents a case study on local production of pharmaceuticals and related technology transfer between a parent and its subsidiary. At PTEI, technology transfer occurs on a north–south axis; some positive points from a development perspective include that Eisai was confident early on about the ability of Indonesia to produce high-quality medicaments, that Eisai continues to be committed to regularly upgrading its facilities for manufacture in Indonesia to very high standards, and that no Japanese expatriate staff are seen as needed to run its operations in the country, which is still uncommon for many Japanese pharmaceutical companies. Generalized to the wider industry, the early presence of multinationals appears to have had a positive impact on improving the quality control and quality assurance required to support a robust pharmaceutical industry, and to upgrade the skills of the pharmaceutical sector. The approach of Eisai is, nonetheless, very top-down, with Eisai senior management determining the product range for PTEI and trying to ensure that the transferred technology remains in-house. The benefits from a technology transfer perspective therefore derive mainly from spillover effects, such as when staff decide to change firms, and are difficult to quantify.

There do not appear to have been many obstacles to technology transfer between Eisai and PTEI. The technology and know-how transferred to PTEI were systematically reduced to detailed manuals developed by Eisai, which continue to be consistently updated through briefs from headquarters in Japan. Eisai diligently supported the transfer process, making available its staff as necessary. Although there is room for improvement in the local education system, management at Eisai and PTEI considered local universities sufficient to attract qualified pharmacists, chemists, engineers and other professionals.

That Eisai, along with other multinationals from Japan and elsewhere, continues to operate in Indonesia despite having lost significant market share since the early 1990s and a difficult operating environment for foreign firms is perhaps more a reflection about the market prospects of the country than anything else. For the most part, Indonesia never offered the types of incentive that typically form part of a coherent investment promotion strategy, such as tax holidays. The size of the market also appears to have contributed to preventing established investors from becoming "footloose".

In this case study, it was found that of all the strengths of the Japanese pharmaceutical companies, the most outstanding example of good practice was by PT Mitsubishi Tanabe Indonesia, which used its operations in Indonesia as a regional base for ASEAN markets. In the Eisai group, the choice appears to have been to deploy its Taiwan Province of China facility to reach ASEAN markets. Also, one Japanese company has an API facility and is exporting API to other ASEAN countries. From the non-Japanese multinationals, Bayer locates its regional manufacturing hub for South-East Asia in Indonesia. From the generic companies, Actavis has also located its manufacturing hub for South-East Asia in Indonesia.

References

Kulkarni N. Indonesia insists on local pharma production. *BioSpectrum Asia Edition*, 2009, 1 February (http://www.biospectrumasia.com/content/280109IDN8410.asp).

PERC. *Asian risk prospects*. Hong Kong, Political & Economic Risk Consultancy, 2010 (http://www.asiarisk.com/subscribe/dataindx.html).

Sudharta J et al. *Position paper for sector working group on medical and pharmaceutical*. Presented at EU-Indonesia Business Dialogue, Jakarta, 28 September 2010.

Times Higher Education. *World university rankings 2008*. London, Times Higher Education, 2008 (http://www.timeshighereducation.co.uk/hybrid.asp?typeCode=243, 2008).

Transparency International. *Corruption perceptions index 2009*. Berlin, Transparency International, 2009 (http://www.transparency.org/policy_research/surveys_indices/cpi/2009/cpi_2009_table).

UNCTAD. *The least developed countries report 2007: Knowledge, technological learning and innovation for development*. Geneva, United Nations Conference on Trade and Development, 2007.

WHO. *Country profile: Indonesia*. Geneva, World Health Organization, 2004 (http://memory.loc.gov/frd/cs/profiles/Indonesia.pdf).

WHO. *Indonesia: National health system profile*. Geneva, World Health Organization, 2007 (http://www.searo.who.int/LinkFiles/Indonesia_CHP-Indonesia.pdf).

Annex: Interviewed individuals and institutions

Pharmaceutical experts

Estiyasa H, Manager, QC Department, Production Division, PT Eisai Indonesia

Harjono, Manager, Manufacturing Department, Production Division, PT Eisai Indonesia

Rosalina Haryadi, Deputy Director, QA, PT Kalbe Farma, Indonesia

Tita Miawati, QA Manager, QA Department, Production Division, PT Eisai Indonesia

Iwan Agung Pribadi, Manager, Administration Department, Production Division, PT Eisai Indonesia

Sudjati Prihartono, Vice Director, Production Division, PT Eisai Indonesia

Karta Sadana, Deputy Director, Medical and Business Development, PT Kalbe Farma, Indonesia

Djoko Sujono, Managing Director, PT Ferron Par Pharmaceuticals; Member, Dexa Medica Group, Indonesia; Head, Pharmaceutical Affairs and Regulatory Committee, National Board Indonesian Pharmaceutical Association, GP Farmasi Indonesia

Toshifumi Tada, Director, Corporate Planning Division, PT Tanabe Indonesia

Toru Takekawa, Executive Director, Demand Chain Coordination Department, Demand Chain Headquarters, Eisai Co. Ltd, Tokyo

Philip Tan, President Director, PT Eisai Indonesia

Mimi Yosiani, Regulatory Manager, PT Kalbe Farma, Indonesia

Representatives of the Indonesian Government

Hari Baktio, Deputy Chair, Investment Coordinating Board, Indonesia

Nada DS Marsudi, Director for International Research, State Ministry of Research and Technology, Indonesia

Eka Saswita, Patent Examiner, Directorate of IP Rights, Ministry of Law and Human Rights, Indonesia

A Retno Tyas Utami, Director for Control of Production of Therapeutic Products and Household Products, National Agency of Drug and Food Control, Indonesia

Erni Widhyastari, Head of Division 3, Chemicals, Biotech and Pharmaceuticals, Directorate of IP Rights, Ministry of Law and Human Rights, Indonesia

Rifatul Widjhati, Agency for the Assessment and Application of Technology, Centre of Medical and Pharmaceutical Technology, Indonesia

Listyani Wijayanti, Advisor for Food and Health Technology, State Ministry of Research and Technology, Indonesia

Dede Mia Yusanti, Head, International Cooperation Division, Directorate of IP Rights, Ministry of Law and Human Rights, Indonesia

Members of the Pharmaceutical Distribution Network

Santiago Garcia, President Director, PT Anugerah Pharmindo Lestari, Indonesia

Nyoman Sukertha, Vice President – Sales, PT Anugerah Pharmindo Lestari, Indonesia

Pharmacies

Three independent pharmacies, including Apotek Cerme, Wahid Hasyim No. 64, Jakarta, Indonesia, and pharmacy chains, including Century Healthcare.

Representatives of nongovernmental organizations

Nurfadliah Abdillah, ex-country logistician, Médecins du Monde, Indonesia

Tutut Sri Purwanti, Hilfswerk Austria International, Indonesia

Investment banker

Patrick Alexander, Managing Partner, Batavia Investment Management Ltd, Indonesia

Case study 6

Jordan

This study on Jordan was carried out by Ermias Biadgleng, Legal Expert at UNCTAD's Intellectual Property Unit, and Brian Tempest, UNCTAD Consultant and partner at the consulting firm of Hale & Tempest. Inputs for the study were collected during a field mission to Amman, Jordan from 7 to 11 February 2010. The case study report was finalized by Kiyoshi Adachi, Chief of the Intellectual Property Unit, under the overall responsibility of Mr James Zhan, Director of the Division on Investment and Enterprise, and Mrs Nazha Benabbes Taarji, Officer-in-Charge, Investment Capacity-Building Branch.

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Abbreviations

HPLC	high-performance liquid chromatography
IPRC	International Pharmaceutical Research Centre
JAPM	Jordanian Association of Pharmaceutical Manufacturers
JFDA	Jordan Food and Drug Administration
JIEC	Jordan Industrial Estates Corporation
JPM	Jordanian Pharmaceutical Manufacturing Co. PLC

1. Background and methodology

This case study is designed to examine the Jordanian pharmaceutical industry, looking at one particular firm and the wider domestic pharmaceutical manufacturing industry in which it is located. Local firms in Jordan have become exporters of high-quality pharmaceutical products. Indeed, Jordan has become a major supplier of medicaments to the wider Middle East/ North Africa (MENA) region and is considered a major success story for local industry. This study examines the original sources of technology used in the Jordanian pharmaceutical industry, the technology transfer that currently occurs between Jordan and other countries, the innovation environment, and the issues that the particular firm and the larger Jordanian pharmaceutical industry are presently facing.

UNCTAD thanks the Jordanian Pharmaceutical Manufacturing Co. PLC (JPM) for agreeing to be the subject firm for this case study, as well as the Jordanian Association of Pharmaceutical Manufacturers and Medical Appliances (JAPM) and the World Health Organization (WHO) office in Jordan for assisting UNCTAD in facilitating the arrangement of interviews with Jordanian manufacturers and relevant government offices.

A case study research methodology was used in the study. Data were collected from academic literature and policy documents, and through open-ended face-to-face interviews with individuals involved in the Jordanian pharmaceutical industry. Interviewees were identified through purposive sampling. During the fact-finding mission to Amman from 7 to 11 February 2010, 18 people from across the local pharmaceutical innovation system were interviewed, including 7 pharmaceutical experts (from JPM, Hayat Pharmaceutical Industries, Hikma Pharmaceuticals and JAPM), 2 leaders of contract research organizations (from the International Pharmaceutical Research Centre (IPRC) and Triumpharma), 5 government representatives (from the Jordan Food and Drug Administration (JFDA), the Jordan Investment Board, the Jordan Joint Procurement Department and the Jordan University of Science and Technology), 1 employee of the Jordan Specialty Hospital, 1 employee of Pharmacy1 and 2 WHO staff members.[1] The case study team also visited a pharmacy owned by Nairoukh Pharma.

In addition, a semi-structured questionnaire designed to capture the dynamics of firm-level activities relating to production and technology transfer was administered to the firms, the results of which are included in the case study where relevant.[2]

This case study defines innovation as any new product, process or organizational change that is new to the enterprise, context or country in question. The innovation need not be novel to the world at large (UNCTAD, 2007). In keeping with the scope of the project, technology transfer was defined as all components of technology, both codified (such as blueprints,

1 See Annex: List of interviewed individuals and institutions.

2 See Annex: Field questionnaire.

hardware, machine parts and plant technologies) and tacit (such as know-how and skills), that are essential to enhance the capacity of the organizations in the recipient country to produce pharmaceutical products.[3]

2. Description of the firm, structure and range of products

JPM is located in Amman, Jordan. It is one of 257 pharmaceutical companies headquartered in the MENA region, and one of 17 located in Jordan. JPM has the third highest sales of the local companies, ranking only behind Hikma Pharmaceuticals and Dar Al-Dawa, according to JAPM. JPM was established in 1978 as a private limited joint stock company. Production commenced in 1980. In 2004, JPM completed merger negotiations with Al-Razi Pharmaceuticals; at this point the newly expanded company became a public joint stock company and was listed on the Jordan Stock Exchange Market. Production capacity and capital both increased significantly at this point (Business Monitor International, 2010a). The company's paid-up capital reached JD 20 million (approximately US$ 14 million) in 2010 (Zawya, 2010).

As JPM is a publicly traded company, its ownership structure is diverse. Institutional investors include the Islamic Corporation for the Development of the Private Sector of Saudi Arabia (28.32%), the Islamic Bank of Jordan (26.00%), the Altawfeek Company for Investment Funds of Saudi Arabia (4.44%) and Jordan Dubai Properties (1.04%). Two Jordanian and one Saudi private investor hold 19% of the shares. The rest of the shares of JPM are held by the public (Zawya, 2010).

Sales grew from JD 10.3 million (US$ 14.5 million) in 2004 to JD 18.5 million (US$ 26 million) in 2008. Exports currently represent two-thirds of this amount. The remaining one-third is sold on the domestic market, of which 71% is sold to the private sector and 29% to the public sector. In 2008, 1.3% of total sales were reinvested into research and development (R&D). Year-by-year sales data and the percentages invested into R&D are provided in Table 1.

***Table 1** Jordanian Pharmaceutical Manufacturing Company sales (JD, thousands)*

Year	Local			Export	Total	R&D
	Private	Public	Total			
2004	1012	296	1308	9027	10 335	0.0002%
2005	2863	403	3266	7658	10 924	0.003%
2006	4645	319	4964	9107	14 071	0.003%
2007	4294	439	4733	13 199	17 932	1.9%
2008	4479	1773	6252	12 209	18 461	1.3%

Source: JAPM (2010, p. 23).

3 A uniform definition of technology transfer was used for all components of the project, including the trends survey, the regional dialogues and the stakeholder analysis.

JPM produces 184 products that span 40 therapeutic classes, including cardiovascular, endocrine, musculoskeletal, gastrointestinal, respiratory, central nervous system and anti-infective drugs, according to JPM's current product list. The company has manufacturing contracts with other third-party companies for the production of 58 additional products. JPM's product line compares favourably with the other leading Jordanian pharmaceutical firms. For example, the leading company by sales, Hikma Pharmaceuticals, produces 174 products; JPM's product line is, however, larger and encompasses a wider range of therapeutic classes, including molecular diagnostic kits, blood-grouping reagents and latex kits for routine laboratory testing.

All of JPM's products are branded generics, meaning that the company uses its brand name for its generics, a practice that is probably caused in part by the tendency of doctors in the MENA region to prescribe drugs by a brand name. For example, Bactall is the JPM brand name for ciprofloxacin tablets. JPM is also working to bring to market five new chemical entities (NCEs) that have been identified but not yet developed fully, owing to cost limitations.

***Table 2** Subsidiaries, alliances/partnerships*

Company	Country	Holding by JPM
Algerian Jordanian Pharmaceutical Manufacturing Co. (AJPM)	Algeria	98.00%
Delass Company	Jordan	93.33%
Suwagh Company	Jordan	93.33%
Aragen Company	Jordan	56.67%
Final Farma Factory	Mozambique	45.00%
Azel Pharma	Eritrea	42.00%
El-Obour Modern Pharmaceutical Co. (Opi-Pharma)	Egypt	15.5%*
Tassili Arab Pharmaceutical Co. (TAPHCO)	Algeria	10%*
Shifaco	Yemen	10%*
Société Arabe Des Industries Pharmaceutiques (SAIPH)	Tunisia	8%*
Sewar	Sudan	–**

Sources: Zawya (2010). See also LESI (2008) and JPM (2011a).

As indicated in Table 2, JPM has a considerable number of subsidiaries and participates as a shareholder in a number of companies in Jordan and the MENA region for manufacturing and marketing pharmaceuticals and related products. Three of the subsidiaries are established within Jordan.

The Delass Natural Products subsidiary produces more than 50 natural and herbal products in all dosage forms. The subsidiary undertakes toxicological and clinical research in developing and producing its products.

The Suwagh Company focuses on R&D of proprietary specialized drug delivery systems and pharmaceutical additives.

AraGen Biotechnology is an innovative biotechnology company focusing on the development and distribution of innovative rapid diagnostic test kits and laboratory devices. The innovation capacity of AraGen is discussed in detail in Section 3.

JPM currently employs 478 individuals, 226 of whom hold tertiary education degrees. The workforce is proportionally represented in terms of gender. JPM managerial policy attempts to encourage long-term commitment to the company and a number of human resource policies contribute to this goal, including a programme that provides university tuition support to qualified employees. The management operates with an "open door" policy: there is no secretary outside the managing director's office, thereby increasing accessibility and encouraging open communication, feedback and discussion between the management and the staff. The company contributes to an employee health insurance scheme. The company indicates its commitment to the community through a social programme that supports two local schools. Overall, these policies seem to be successful, as staff turnover is modest, according to the management. The management's primary human resource concern at the moment is how to increase salaries on par with inflation without raising the company's product prices.

The General Director of JPM, Dr Adnan Badwan, provides both leadership and the main scientific vision for the company. He devotes much of his time to the R&D deprtment. The mission team felt that Dr Badwan's expertise has had a significant impact on the results the company has attained since its founding.

To give a better idea of the extent to which JPM is representative of some of the more advanced pharmaceutical firms in Jordan, this section briefly examines two of its competitors, namely Hikma Pharmaceuticals and Hayat Pharmaceuticals.

Hikma Pharmaceuticals was established in 1977 as a private shareholding company with paid-up capital of JD 22.3 million (US$ 31.5 million) and became a public company in 2005 with paid-up capital of JD 29.8 million (US$ 42.1 million). Hikma Pharmaceuticals is listed on the London Stock Exchange, and the International Finance Corporation (IFC) is a shareholder. Hikma Pharmaceuticals is certified by the United States of America Food and Drug Administration (FDA), the European Medicines Agency (EMEA) and the United Kingdom Medicines and Healthcare Products Regulatory Agency (MHRA). Sales have grown formidably, from JD 68 million (US$ 96 million) in 2004 to JD 216 million (US$ 305.2 million) in 2008. The majority of sales (88%) are international; the remaining 12% are consumed domestically. Of the domestic sales, 85% are in the private sector and 15% are in the public sector. Hikma Pharmaceuticals reinvests 3.4% of sales (JD 7 million) in R&D. The company employs 1004 members of staff, of whom 83% are male. Other Jordanian pharmaceutical industry executives believe that Hikma Pharmaceuticals is strong in the management of its finances – a reputation that is probably due to the fact that it is listed as public company and is regularly followed by financial analysts. Hikma Pharmaceuticals has manufacturing factories in Algeria, Egypt, Italy,

Germany, Portugal, Saudi Arabia and the United States. The company conducts business in 40 countries. Although the company has its origins in Jordan, Hikma Pharmaceuticals' headquarters are located in London, United Kingdom. Hikma Pharmaceuticals has in its portfolio 28 originator products sold under licence from 19 foreign pharmaceutical companies, according to its list of products in April 2007. Table 3 shows sales data for Hikma Pharmaceuticals.

***Table 3** Hikma Pharmaceuticals sales (JD, thousands)*

Year	Local			Export	Total	R&D
	Private	Public	Total			
2004	8098	1389	9487	58 546	68 033	6.6%
2005	9535	1776	11 311	78 427	89 738	6.4%
2006	12 331	2176	14 507	100 478	114 985	6.3%
2007	17 534	1061	18 595	146 852	165 447	5.0%
2008	22 815	3835	26 668	189 548	216 216	3.4%

Source: JAPM (2010, p. 20).

Hayat Pharmaceuticals is a mid-sized Jordanian pharmaceutical company that was established as a private company in 1994 with an issued share capital of JD 9.5 million (US$ 13.4 million). The company started production in 1997 and became a public company in 2005. Hayat Pharmaceuticals employs 166 people. It produces 87 products, some of which are produced under licence for R&D-based multinational corporations. Some products are also manufactured under a contract. The company is certified by the Ministries of Health in Algeria, Bahrain, Iraq, the Libyan Arab Jamahiriya, Oman, Qatar, Saudi Arabia, the Sudan, the United Arab Emirates, Yemen and EMEA. Sales doubled between 2004 (JD 2 million) and 2008 (JD 4.4 million). Exports represent 56% of sales. Of the remaining domestic sales, 80% are sold into the private sector. R&D investment is 3.5% of total sales and constitutes 8% of the company's workforce. Table 4 gives sales data for Hayat Pharmaceuticals.

***Table 4** Hayat Pharmaceuticals sales (JD, thousands)*

Year	Local			Export	Total	R&D
	Private	Public	Total			
2004	1231	0	1231	783	2014	4.7%
2005	1158	0	1158	1401	2559	3.7%
2006	1537	283	1820	1422	3242	3.8%
2007	1597	326	1923	1878	3801	3.5%
2008	1532	391	1923	2454	4377	3.5%

Source: JAPM (2010, p. 31).

Comparison of JPM with both Hikma Pharmaceuticals and Hayat Pharmaceuticals shows that JPM appears to be fairly representative of the top-tier local pharmaceutical firms in Jordan.

3. JPM's technological capacity

JPM three main facilities are in and near Amman. The facility at Ibn Sina complex is newly renovated and is the centre of research and operations for its Suwagh, Delass and AraGen subsidiaries (LESI, 2008). The Al Razi facility is the flagship facility for JPM, operating with current good manufacturing practices (cGMP) and regularly inspected by different international regulatory bodies. AraGen operates much of its production activity from the Ibn Hian facility in the Sahab Free Industrial Zone near Amman. The Ministries of Health of Bosnia and Herzegovina (2004), Uganda (2005), Turkey (2006), Saudi Arabia (2007) and the Gulf Cooperative Council (2009) have certified the facilities for exports. The company markets its products to Algeria, Armenia, Azerbaijan, Bahrain, Egypt, Iraq, Kazakhstan, Kuwait, Lebanon, the Libyan Arab Jamahiriya, Oman, Qatar, the Russian Federation, Saudi Arabia, Sudan, the Syrian Arab Republic, Tunisia, Ukraine, the United Arab Emirates and Yemen. There are ten licensees of the company located in Algeria, Bosnia and Herzegovina, Iraq, Oman, the Syrian Arab Republic and Tunisia.

There are approximately 862 pharmaceutical patents currently held by entities in the Middle East, of which 75 are held by JPM, according to the interview with the General Director of JAPM.

The top seven Jordanian pharmaceutical companies on aggregate spent 3% of sales in 2008 on R&D (JAPM, 2010, p. 66). The R&D department of JPM has 25 employees focusing on product development and another 12 employees focusing on discovery; for a company of JPM's size, this is a small team. As noted above, the amount of sales reinvested into R&D remains somewhat limited, although JPM has five potential NCEs in the pipeline.

JPM's first bioequivalence clinical studies were conducted in 1983. The JPM research programme is not guided by an advisory board, due to the cost of maintaining such a group, but its scientific papers are sent to peer-reviewed journals as a method of obtaining free technical advice.

JPM has formed research alliances with multiple British universities, including Lancaster University, King's College London and Greenwich London College. The company is working with one of the United Kingdom biotechnology companies in the Cambridge Cluster.[4] JPM is also undertaking R&D on NCEs, including oral insulin.

From a domestic innovation perspective, JPM's subsidiary for diagnostics, AraGen, may be of particular interest. AraGen Biotechnology was established in 1998 and specializes in the development and manufacture of diagnostic test kits of various types, including molecular diagnostic kits, blood-grouping reagents and latex kits for routine laboratory testing. Its manufacturing location in the Saheb Free Zone of Jordan is certified ISO9001 and ISO13485. All of the

4 The Cambridge Cluster, also known as the "Cambridge Technopole", is a geographical area of intense high-technology innovation activity encompassing the city of Cambridge, MA at its heart and the subregional Greater Cambridge hinterland of approximately 25 miles radius.

technologies produced by AraGen are the result of in-house R&D. The company has 121 patent applications in Jordan at various stages of approval, and its products are at the cutting edge of development in this field. AraGen's products are currently being co-developed with two German companies. The tools and kits are in two main areas: the first is rapid diagnostics for both consumers and health workers, including identification of fertility issues, cardiology markers, infectious agents and cancer markers. The second area is DNA technology testing, which has a wide range of applications, including early detection of cancer and infectious diseases such as human immunodeficiency virus (HIV) infection and hepatitis B and C. Altogether there are 276 types of testing kit available from AraGen. The platform technology for AraGen's products was developed in Jordan. Registration for the kits is also being sought in Brazil and South Africa.

JPM has established five joint venture entities located in Eritrea, Mozambique, Egypt, Tunisia and Algeria. These entities have been established by capital investments and selling services, including technology. The ventures have been quite successful, and there are predictions that JPM may gradually move away from pharmaceutical manufacturing to focus on technology transfer as its core business (Business Monitor International, 2010a). JPM is responsible for the technical oversight of all five entities. JPM also has licensed its own developed formulations to a number of manufacturers throughout the Arab world (JPM, 2011b).

In this regard, JPM officials appeared to be particularly proud of its Eritrean joint venture, Azel Pharma, which was established in a very difficult operating environment. Azel Pharma employs 150 individuals. All Azel Pharma employees are initially trained in Jordan for 3 months. Exports from Azel Pharma are now exported to Sudan after 6 years and the joint venture is breaking even. JPM holds a minority interest in Azel Pharma of around 30–40%.

4. The pharmaceutical market in Jordan

Jordan is a small country in the MENA region, with a population of approximately 6.5 million. The population growth rate from 2005 to 2010 has been approximately 3.0% annually.[5] In 2008, the gross domestic product (GDP) was US$ 21.2 billion, the GDP per capita was US$ 3596 and the real annual growth was 7.9%. There is a significant rural/urban divide, with 78.4% of the population living in urban localities (World Bank, 2011). The average family size in 2006 was estimated at 5.4 (JAPM, 2010, p. 72), with an age dependency ratio of 63.2%. The current unemployment rate is 12.7%. In 2008, 13.3% of the population lived below the national poverty line (UNDP, 2010). There are 106 males per 100 females in Jordan. Adult male literacy is 96% and adult female literacy is 90% (World Bank, 2011).

In 2008, the birth rate was 25.7 per 1000, and the death rate was 4.2 per 1000. The infant mortality rate was 17 per 1000 live births. In 2007, the health

5 Source: UNCTAD GlobStat Database).

expenditure per capita was US$ 248 and the total expenditure represented 8.9% of the GDP. The life expectancy at birth is 73 years (World Bank, 2011). Overall, these statistics indicate that the Jordanian economy is growing.[6]

The pharmaceutical industry in Jordan is considered to be one of the strongest in the MENA region. The first pharmaceutical factory in Jordan was built in 1962. As noted above, there are now 17 local pharmaceutical companies in Jordan (Business Monitor International, 2010a). As indicated by the data for JPM, Hikma Pharmaceuticals and Hayat Pharmaceuticals, pharmaceutical production in Jordan is mainly generic and covers a wide range of therapeutic products. Active pharmaceutical ingredients (APIs) are sourced mainly from Europe, China and India. More than half of the Jordanian companies were established in the past two decades and therefore have state-of-the-art facilities equipped with the latest machinery and technology. Jordanian factories also tend to have large capacities, which enable them to be contracted by foreign companies for production.

Pharmaceuticals represented 8.2% of Jordan's exported goods in 2009 (UN comtrade, 2010). Indeed, the pharmaceutical market is extremely export-focused: According to JAPM, 70% of the sales of the pharmaceutical industry are of exports, positioning the pharmaceutical industry as the second highest exporter in Jordan (Amwal Invest, 2010). Fertilizers (12.4%) and clothing (11.4%) are the other major exported commodities (UN comtrade, 2010).

Most (88%) of the Jordanian pharmaceutical exports go to the MENA region. Between 2004 and 2008, Jordanian exports of pharmaceuticals had an average annual growth of 20% (UN comtrade, 2010). There was a slight decline of exports in 2009 compared with 2008 (Amwal Invest, 2010). The Saudi Arabian market is the largest destination for Jordanian pharmaceuticals and was worth US$ 354 million in 2006 (Economist Intelligence Unit, 2008). The next largest national market for Jordanian pharmaceutical exports is Algeria, which receives 21% of all exports, followed by Sudan (8%), Lebanon (6%) and the United Arab Emirates (6%) (JAPM, 2010). Responses to the field questionnaire indicate that this growth can be attributed to the reputed high quality of Jordanian products, and the industry's success in actively marketing abroad. The market's international reputation for quality is also reflected in the fact that many of the regional firms' products have earned certification in the United States and Europe. Efforts to obtain certification in export markets appear to have been an incentive for investing in regular upgrading of equipment, technologies and skills. Although the local industry consider tariffs in the export market to be generally low, the Greater Arab Free Trade Area (GAFTA) in 2005 instituted full exemption of customs duties and charges for all members, except Sudan, Yemen and the Occupied Palestinian Territories (US Department of State, 2009).

The penetration of foreign markets is one of the greatest achievements of the industry, particularly as the local industry's share of the domestic market is still quite modest, at an estimated 25% in 2009, according to JPMA. Domestically,

6 Jordan appears in the "emerging market" list of Dow Jones. See Dow Jones (2010).

per-capita drug expenditure is expected to reach US$ 73.70 by 2014, meaning that approximately 1.7% of the GDP will be spent on pharmaceuticals (Business Monitor International, 2010b). This situation may be the result of the fact that foreign medicines, for people who can afford them, are perceived by the public to be superior in quality to those produced domestically (Business Monitor International, 2009).

Medicaments are dispensed through pharmacies and hospitals. At the retail level, there are 1883 pharmacies in Jordan. In general there are two classes of pharmacy: large modern chain pharmacies, and older local pharmacies, which may or may not be part of a larger chain. The case study team visited both types of pharmacy.

Pharmacy1 is a chain store with 43 modern pharmacies where the pharmacist fulfils the role of a health-care adviser. There is also a distribution centre where 4 weeks' inventory of fast-moving stock is held. The JFDA regularly inspects this chain. The company offers a free delivery service 24 hours a day, 7 days a week for telephone and online orders. When the case study team visited one store, the pharmacy was staffed by a number of qualified pharmacists; the prescription medications, many of which appeared to be originator products, were kept separate from the over-the-counter (OTC) products. After receiving security clearance, the case study team was chaperoned into the prescription products area of the pharmacy, an indication that safety and security procedures are maintained and followed. Pharmacy1 was established with private funds.

In comparison with Pharmacy1, Nairoukh Pharma is an older pharmacy chain. When the case study team visited a branch of Nairoukh Pharma, the team found both OTC and prescription medicines on display on shelves. The case study team picked up a box of generic ciprofloxacin 500 mg tablets and purchased it with relative ease, without any prescription.

There are 103 hospitals in Jordan, with a total of 11 200 beds. Two of the hospitals are university teaching hospitals, 60 are in the private sector, 30 are managed by the Ministry of Health in the public sector, and 11 are affiliated with the Royal Medical Services. There are 1415 Ministry of Health clinics, 30% of which are mother and child health centres. The major hospitals report an average occupancy rate of 64% and an average length of stay of 3 days.

The budget of the Jordan Ministry of Health was US$ 544 million in 2008, which represented 7% of the US$ 7.4 billion total national budget (JAPM, 2010). In 2007, there were 26.7 physicians, 14.1 pharmacists, 8.5 dentists, 18 hospital beds and 2.4 primary health care units per 10 000 Jordanian citizens (WHO, 2011).

Jordan boasts some of the leading hospitals in the MENA region. Of particular note is the Jordan Specialty Hospital, which is located in Amman. The Specialty Hospital is a world-class private hospital with 250 beds and 40 clinics, according to the Deputy Director of the hospital's pharmacy. The hospital has achieved

international accreditation with the Joint Commission International (Chicago, USA), which ranks it alongside the hospital elite of the world. The hospital is equipped with the latest technology available and is the first in the Middle East to introduce 3-tesla magnetic resonance imaging, the most advanced system for detecting cancerous tumours.

Most of the population (approximately 87%) is covered under private or public insurance, with the remainder paying for medical expenses out of pocket.[7] The main insurance companies are the Social Security Corporation, Jordan Insurance Federation, Jordanian Trade Unions, Jordanian Society of Health Insurance and the Consumer Protection Society. Additionally, the Jordanian Social Security Corporation has 800 000 active contributors and 100 000 retirees (Jordan Social Security Corporation, 2009). In cases of hardship, any Jordanian can apply to the Royal Court for financial assistance with their health-care costs; well-justified requests are almost always granted.[8] Thus, although the cost of pharmaceuticals in Jordan is not inexpensive relative to that in many other developing countries, efforts are made to ensure that medicaments are accessible to the wider population. Prices of locally made medicaments are, nonetheless, still cheaper as a whole than similar imported products offered by European and United States originator companies (Table 5) in the local market. However, previous studies have demonstrated that medicine prices in Jordan are high in comparison with international reference prices for the country's level of development and average income (WHO, 2007).

7 Source: JPM data gathered during field visit.

8 Source: interview with Director General, JFDA, 9 February 2009.

***Table 5** Price comparison of selected JPM products and imported drugs in the Jordanian market*

Active ingredient, dosage, pack size	Drug trade name/ dosage form	Country of manufacturer/ market authorization holder (MAH)	Public taxed price (JD)	Manufacturer/MAH
Fluconazole capsule,150 mg, 1 capsule	Funzol 150/capsule	Jordan/Jordan	5.2	JPM
	Flucozal/capsule	Cyprus/Cyprus	5.87	Aegis
	Diflucan/capsule	France/France	8.22	Pfizer (MAH)
Metronidazole tablet, 250 mg, 20 tablets	Metrozole 250 mg/ tablet	Jordan/Jordan	1.07	JPM
	Supplin/tablet	Austria/Austria	1.53	Merck Spittal KgaA & Co./Sandoz GmbH (MAH)
	Metrolag/tablet	Switzerland/ Switzerland	1.73	Labatec/Lagap SA (MAH)
	Flagyl Oral/tablet	France/France	1.99	Famar-Lyon/Aventis Pharma SA (MAH)
Mebendazole tablets, 100 mg, 6 tablets	Bendazole 100 mg/ tablet	Jordan/Jordan	1.22	JPM
	Vermox/tablet	Portugal/ Belgium	1.88	Lusomedicamenta-Sociedade Tecnica Faraceutica SA/Janssen Cilag (MAH holder)

Source: Based on current prices available from the Jordan Food and Drug Administration at http://www.jfda.jo/barcode_java/index.jsp. The price comparison is limited to drugs produced by JPM and with a foreign equivalent. Equivalent foreign products are selected by considering the formulation (e.g. tablet, syrup, injection), concentration (strength) and pack size. The three drugs are part of the WHO Model List of Essential Medicines, 2010.

One interesting finding is that there appears to be a poor success rate for local firms in Jordanian Government drug procurement. Jordanian companies are provided with a 10% price advantage, provided that they are competitive in terms of standardized specifications of drugs and medical supplies. But the Jordanian firms perform poorly in public tenders. In 2009, a new Joint Procurement Directorate was designed to improve the situation, although some medical sectors still perceive imported medicines to be of a better quality than domestic medicines.

As part of its accession to the World Trade Organization (WTO), Jordan has made a commitment to initiate negotiations for membership to the Agreement on Government Procurement (WTO, 1999a). The Agreement applies only to a small number of WTO Members, largely from developed countries that voluntarily agreed to negotiation discipline on government procurement. The Agreement does not apply to all government procurements but only to those sectors that each Member agreed after negotiation with the rest of the Members of the Agreement and above certain threshold values. The main principle of the Agreement is non-discrimination and as such, without an exclusion for the sector, may threaten existing preferential arrangements in Jordan for local suppliers.

The main pharmaceutical association is JAPM, which was established in 1996 (Business Monitor International, 2010a). Currently, JAPM is working with the United States Agency for International Development (USAID) "to make the Jordanian pharmaceutical industry more internationally competitive" (Business Monitor International, 2010c).

Additionally, the global future of generics is particularly relevant for the Jordanian pharmaceutical market. Governments around the world are encouraging the use of generics in order to reduce the cost of health care, a trend that bodes well for generic manufacturers such as those in the Jordanian industry, which export much of their output. There has recently been a considerable amount of consolidation in the local generics sector, due at least in part to intense domestic competition (Business Monitor International, 2010a).

5. The framework for local production and technology transfer

5.1 Drug and clinical trial regulation

JFDA is the main body in Jordan responsible for the registration and marketing approval of drugs, inspection and certification of pharmaceutical producers. The drug department of JFDA deals with the authorization, registration and quality control of raw materials and finished pharmaceuticals, production and storage facilities, laboratories, documentation according to quality control standards, standard operational procedures, and water and air units in the production facilities of pharmaceuticals. The Drug Directorate is also responsible for pricing of drugs, export and import permits, and following up clinical trials. The various committees implementing the responsibilities of the Drug Directorate include the following:

- Medical Devices, Including Disinfectants And Detergents Committee
- Re-registration of Registered Products Committee
- Technical Committee for the Registration of New Drugs (Originators)
- Medicinal Plants and Natural Extracts Committee
- Clinical Studies Committee
- Pricing Committee
- Pharmaceutical Preparations Containing Vitamins and Minerals Committee
- Bioequivalence Studies Committee
- Infant Milk Formula, Special Formula and Food Supplement Committee
- Vaccines and Sera Committee
- Accreditation of Pharmaceutical Sites Committee
- Cosmetics Committee
- Biological Products Committee.

The Drug and Pharmacy Law of 2001 and its amendments govern the establishment and operation of pharmaceutical production facilities, drugstores and pharmacies (JFDA, 2001). The law is supported by specific

regulations on accreditation of manufacturing sites, cGMP guidelines, criteria for registration of drugs, vaccines and biological materials, including bioequivalence requirements, and collection, analysis and evaluation of adverse drug reaction reports. Approval of the manufacturing site is required, and site inspections are often carried out. The technical dossier in the regulatory submission requires a bioequivalence study, which may take up to 4 months. In 2009, 170 bioequivalence studies and 19 clinical trials were approved, including some phase I and II trials. JFDA carried out 70 inspections of manufacturing sites during 2009. JFDA has 530 employees and in 2009 saw only 5 staff members leave.[9]

Jordan maintains pharmaceutical price regulation, a process that is managed by JFDA. End-user prices for generics are determined by applying different calculation methods and choosing the lowest price (USAID, 2009). For imported medicines, the various options to determine the price of the product use as a reference the price of the product offered in the home country, taking into account the cost of production and profit margins. The price control may discourage many foreign branded generic companies that sell at lower prices in their home country from exporting to Jordan. The local pharmaceutical producers complain that the pricing system is not flexible to adjust for inflation and the prevailing market situation and does not take into account the cost of energy in Jordan (USAID, 2009).

Clinical trial activity takes place in Jordan and is overseen by the JFDA Clinical Studies Committee. The Law on Clinical Studies, 2001, regulates authorization for research organizations, including university academic institutions, consent, insurance and liability, study protocol, and supervision of entities undertaking such study. Novartis, Sanofi Aventis and Organon from the big pharmaceutical industries have used Jordanian contract research organizations (CROs). The CROs discussed below are adding to the positive reputation of the Jordanian health care sector and improving the rigour of the technical climate within Jordan.

One Jordanian CRO, Triumpharma, was founded in 2002 with a paid-up capital of JD 100 000 (US$ 140 000) and currently employs 38 people. The company is now a leading regional CRO that offers services covering all aspects related to clinical research, including phase I, II, III and IV clinical trials. The company has 100 beds and 4 mass spectrometer/high-performance liquid chromatography (HPLC) instruments. It is certified by Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS) in 2009 and the United States FDA in 2008 and has GMP, good laboratory practice and good clinical practice approvals. Triumpharma's clinical trial business is generating a positive cash flow that is partly being invested in a drug delivery development programme for which some international patent applications have now been filed, according to the Chief Executive Officer.

Another successful Jordanian CRO, IPRC, was founded in 1994 as a private company with a paid-up capital of JD 100 000 (US$ 141 000) and currently

9 Source: interview with General Director, JFDA, 9 February 2009.

employs 100 people. IPRC offers services that cover most aspects of clinical research. It is certified by the United Kingdom MHRA. Sales reached JD 2.6 million (US$ 3.6 million) in 2008, of which 60% was from exports.

The Jordan University of Science and Technology (JUST) also runs another CRO called the Pharmaceutical Research Centre (PRC-JUST) established in 2004 to meet the growing needs of Jordanian pharmaceutical manufacturing companies in drug discovery, development and evaluation.

5.2 Intellectual property rights

Jordan has been a WTO Member since 2000 and has had a bilateral free trade agreement (FTA) with the United States since 2001. When Jordan acceded to the WTO, it agreed to make patents available for pharmaceutical products, sacrificing the transition period until 1 January 2005 that was available for developing countries such as Jordan. This was followed immediately by the entry into force of the FTA with the United States that significantly changed the standard for pharmaceutical-related intellectual property rights. For example, the data exclusivity provisions of the Jordan–United States FTA provide 5 years of data exclusivity for NCEs and 3 years of data exclusivity for new indications.[10] Exclusivity provisions such as these can delay the introduction of generics by not allowing the generic company regulatory submission to refer to the submitted toxicology data in the innovator's initial drug submission already held by JFDA. The FTA also requires Jordan to extend the patent term to compensate the patent owner for unreasonable curtailment of the effective patent term as a result of the marketing approval process. Jordan is a Member of the Paris Convention for the Protection of Industrial Property, and of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (both administered by the World Intellectual Property Organization, WIPO). Jordan has also indicated to WTO Members its interest to accede to the Patent Cooperation Treaty (PCT) (WTO, 1999a).[11]

Countries such as Algeria, the Islamic Republic of Iran, Iraq, Lebanon, the Libyan Arab Jamahiriya, the Syrian Arab Republic and Yemen in the MENA region are still in the accession process to the WTO. However, many other MENA countries, such as Bahrain, Morocco, Oman and Israel, have an FTA with the United States as well (USTR, 2011). The FTAs, and

10 Since Jordan was negotiating access to the WTO and the FTA with the United States during the same period, the source of Jordanian law on pharmaceutical data exclusivity may appear controversial. However, Jordan has not entered into commitment under its Protocol of Accession to the WTO to provide for pharmaceutical data exclusivity. As a result, the only source of binding commitment on data exclusivity is its FTA with the United States. See WTO (1999b).

11 The expression of interest by Jordan to accede to the PCT does not amount to a commitment to do so, and Jordan has not acceded to the PCT to date. In 2008 Jordan reported that it is in the process of accession to the PCT (WTO, 2008).

subsequent legislation in these countries,[12] similarly require protection of pharmaceutical data and extension of the patent term to compensate the patent owner for unreasonable curtailment of the effective patent term as a result of the marketing approval process. Saudi Arabia also provides exclusivity of pharmaceutical data submitted for regulatory purposes (WTO, 2005). Jordanian generic manufacturers are operating in an environment that provides a higher protection of patent.

The patent and data exclusivity provision of the United States–Jordan FTA was controversial in Jordan due to its implication for generic manufacturing of pharmaceuticals. The FTA restricts the grounds for issuing compulsory licences to cases of public anticompetitive practices, noncommercial public use, national emergency and failure to meet working requirements, provided that importation is considered specifically to constitute working. Marketing exclusivity and data protection extend to data submitted in third countries if Jordan relies on foreign marketing approvals. The protection covers not only data related to NCEs but also data related to new use of products previously approved. The data exclusivity requirement restricts regulatory authorities and generic manufactures from relying on the data to approve the marketing of the generic version of the product. Oxfam (2007) has argued that the provisions of the FTA have led to an increase in the Jordanian market in the share of products with no generic alternative produced by Jordanian pharmaceutical companies. Others claim that multinational companies may be choosing to rely on data exclusivity by registering their medicines instead of filing for patents (Grover, 2009).

JAPM and pharmaceutical manufacturers expressed the problem they had with the scope of NCEs protected by data exclusivity and other changes introduced by the Jordan–United States FTA. The term "new" was used in practice to describe a chemical entity that was not marketed in Jordan despite being marketed elsewhere. JAPM and the local industry succeeded in convincing the Jordanian Government to adopt an appropriate definition for NCEs to avoid extensive barriers to the early introduction of generic versions of medicines. Data exclusivity protection for NCEs applies only when the originator of the data seeks marketing approval of the product within Jordan within 18 months of the product being approved in any market. The term "new use" is also defined to describe new therapeutic indication in a manner that excludes new dosage forms and new combinations (Cullen, 2007). During the interview, JAPM officials and pharmaceutical companies appeared satisfied with the delineation of the scope of "new chemical entities" but recognized the challenge of pharmaceutical data exclusivity compared with other competitors in the region that do not provide such protection.

12 The Israel–United States FTA does not require pharmaceutical data exclusivity. In 2005 Israel adopted legislation amending the Pharmacists Ordinance to increase protection for confidential test data submitted to the Ministry of Health in connection with an application seeking regulatory approval for medicines that contain a "new chemical entity". Israel has agreed to address the United States' demands on intellectual property rights, including pharmaceutical related data protection in 2009. See USTR (2010).

By September 2010, non-resident (international) filing of patents in Jordan in all fields of technologies had reached 3081, of which 352 were finally granted. Patent filing by residents remains at 535, of which 116 were granted (Jordan Ministry of Industry & Trade, 2011).[13] There were 55 NCEs registered by JFDA between 2005 and 2009.[14] Of these, three were by local producer Hikma Pharmaceuticals and one was by a Saudi company, Tabuk. According to a Jordanian Government report in 2008, 7% of all pharmaceuticals produced in the country are patent-protected products produced under licence (WTO, 2008).

5.3 Investment and industrial policies

With respect to the investment environment, the marketplace is open to investment, and foreigners are permitted to own any amount of local firms, including in the pharmaceutical sector (Business Monitor International, 2010d). There are, however, certain regulatory hurdles that must be overcome. Since 2008, the minimum capital requirement for registering a pharmaceutical company by a Jordanian national is JD 1000 (US$ 1410) (down from JD 30 000 (US$ 42 313) and for foreign investors with the option for full ownership JD 50 000 (US$ 70 522). However, the minimum capital requirement is JD 30 000 (US$ 42 313) for Jordanian investors and JD 150 000 (US$ 211 566) for foreign investors if the investors wish to benefit from various investment incentives. In addition, if the investment is a joint venture or syndicate of more than one foreign investor, then each investor should contribute JD 50 000 (US$ 70 522) (Amwal Invest, 2010).

The Jordan Investment Board is the Jordanian Government organization dedicated to assisting and guiding investments in Jordan. A variety of services are provided to familiarize investors with the investment environment, potential opportunities and available tax exemptions provided under the Investment Promotion Law. The Jordan Investment Board is a single office staffed by representatives from key ministries of relevance to investors (a "one-stop shop"), a set-up that ensures a high level of efficiency. As part of its mandate, the Jordan Investment Board provides investors with an insight into currently available opportunities in many sectors, including pharmaceuticals. Marginal financial assistance is often given on relieving the import duty on equipment and packaging materials, and grants are not available. The Jordan Investment Board can only make introductions to commercial banks for those parties interested in investing in the pharmaceutical sector. Tax incentives exist to encourage exports, which explains in part why the sector is focused more on exports than on the domestic market.

The Jordan Investment Board implements the "Investment Map Project" scheme, an initiative that undertakes pre-feasibility studies for project concepts

13 A total of 40 patents were granted in 2009. Official Gazette No. 409 of 2009 published 29 patents granted in the year, which covers 16 patents that concern inventions in the filed of pharmaceuticals.

14 See http://www.jfda.jo/Download/News/105_168.doc. These were registered by multinational companies such as Abbott, Bayer AG, Bristol Myers, Eli Lilly, Novartis, Roche and Pfizer. The definition of "new chemical entities" since 2009 is expected to reduce the number of NCEs being registered in Jordan.

in different sectors in order to help investors assess investment opportunities in Jordan and raise the required capital. Of the existing 150 Investment Map Projects, 15 concern the pharmaceutical sector. These include a project for expansion of generic manufacturing (valued at JD 10–25 million), expansion of insulin injectables and non-injectables (valued at JD 20 million and JD 21 million, respectively), and a clinical trials laboratory (valued at JD 21 million). These projects indicate the keen interest of the Jordanian Government to encourage investment in the field of pharmaceuticals.

As noted above, the Jordanian Government does not supply the pharmaceutical industry with soft loans or direct grants, a practice that is common in other developing countries. The Jordan Investment Board is, however, working to position Jordan as a competitive location for manufacturing pharmaceuticals and completing clinical trials. A message that is being emphasized is that clinical trials performed in Jordan cost approximately half of what they would in western Europe,[15] making this an attractive direction in which to expand the market. The Jordan Investment Board and other Jordanian Government officials are hopeful that Jordan could increasingly attract medical tourists from other Arabic-speaking countries, particularly Saudi Arabia. The Jordanian Government is encouraging this trend, and 25% of the patients at Jordan's Specialty Hospital are from outside Jordan.[16] It is predicted that medical tourism may lead to an increase in the demand for better facilities, which could lead medical device makers of advanced technologies to consider producing in Jordan (Business Monitor International, 2010b).

The Jordan Industrial Estates Corporation (JIEC) is engaged in establishing and developing industrial estates that include infrastructure development. JIEC is a financially and administratively autonomous corporation responsible for managing, marketing and developing industrial estates. The two industrial estates, namely the Amman Industrial Estates at Sahab (Abdullah II Ibn Al-Hussein Industrial Estate) and Al-Hassan Industrial Estates at Irbid, host pharmaceutical manufacturers among hundreds of other small and medium-sized enterprises. In addition to infrastructure and land development, incentives available for industries established within the industrial estates include the following:

- full and permanent exemption from land and building taxes and exemption or reduction on most municipalities' fees;
- full exemption from taxes and fees on fixed assets of the project, fixed assets necessary for expanding purposes, and spare parts needed for the project;
- streamlined investment and business procedures through the investors' one-stop service shop;
- no foreign equity restrictions on investments, and the use of foreign labour is permitted;
- full repatriation of profits and capital.

15 Source: interview with chief executive officers of Triumpharma and IPRC, 10 February 2009.

16 Source: interview with Pharmacy Deputy Director, Jordan Specialty Hospital.

There are 17 pharmaceutical manufacturers with operations in Jordan, 6 of which are listed on the American Stock Exchange. Multinationals such as Sanofi-Aventis and Pfizer have strong presences in Jordan (Business Monitor International, 2010a). The presence of multinationals is expected to continue to increase given the prevailing perceptions of higher quality of originator drugs and due to the pervasive practice in Jordan of prescribing by brand name, despite a restrictive pricing policy and a strong domestic generic manufacturing sector (Business Monitor International, 2010d). Multinational companies have established marketing operations in Jordan. This has not, however, prevented local firms from in-licensing technology from these large R&D-based pharmaceutical companies; nor has it prevented multinationals from using local firms for contract manufacturing.

From the case study interviews, it became clear that Jordanian pharmaceutical technology was originally imported from two sources: early alliances with a number of Japanese R&D-based pharmaceutical companies (e.g. Fujisawa) resulted in technology importation, and many Jordanian scientists went overseas for training and returned with new skills and technical knowledge (see Section 5.5).

5.4 Science and technology policies

Jordan does not have a formalized national innovation policy (EC & OECD, 2008). It has recently signed an agreement with the United Nations Education, Science and Culture Organization (UNESCO, 2010) to develop the country's science, technology and innovation policy for 2011–2015, with the support of the Japanese government.

Currently, the Jordanian science and technology structure involves public institutions, universities and research centres, and the private sector. Formed in 1988, the Higher Council for Science and Technology, a Jordanian Government organ, coordinates the development of research and the administration of science and technology in Jordan, with a view to coordinating national policy and creating a national scientific and technological base for the country. The goal of the Higher Council for Science and Technology is to make science and technology a major element in the overall development of Jordan. The Council's administrative secretariat has a department dedicated to health and the environment, which is actively seeking to encourage domestic capacity in the health sciences, medical care and biotechnology.

Among the public institutions, the Industrial Research Fund was established in 1994 to improve the standards of industry by providing technical assistance and financing for joint research projects between industry, universities and research centres. The National Fund for Enterprise Support, established in 2001, provides technical support for small and medium-sized business to improve their competitiveness locally and internationally. iPark Jordan Technology Incubator, established in 2003, supports the development of the information and communication technology industry in Jordan (Higher

Council for Science and Technology, 2009). The Jordan Innovation Centre is also building a network of innovation centres and incubators.

The Royal Scientific Society, a non-profit-making nongovernmental organization established in 1970, promotes technological change through its research, value-added services and technology transfer. It relies on revenues generated from its technical services, studies and research contracts. It also receives some government grants, grants and donations from local institutions, and technical assistance from other governments and regional and international organizations. With more than 600 staff, the Royal Scientific Society operates 7 technical centres and 38 specialized laboratories, including the Industrial Chemistry Centre and Technology Transfer Centre. The Royal Scientific Society operates the Jordan Innovation Centre for Engineers and Industrial Enterprises together with the Jordanian Engineers Association and the Amman Chamber of Industry. This centre provides space and services for business incubation and financial support.

Jordanian universities maintain schools, departments and research centres covering pharmacy, medicine, engineering, applied chemistry, biotechnology and genetics. The Faculty of Pharmacy of the Jordan University of Science and Technology is the first in Jordan and currently offers higher degrees, including at the PhD level. The faculty has a specialized programme in pharmaceutical technology covering the development of pharmaceutical products and quality control. The Pharmaceutical Research Centre of the university was established in 2004, as an independent unit that was to become one of the first CROs of Jordan. The CROs demonstrate an example of the linkage between universities and pharmaceutical industries in Jordan. The Pharmaceutical Research Centre undertakes clinical trials, including bioavailability and bioequivalence studies, preclinical studies covering drug efficacy studies on animals, product preformulation, formulation and other aspects of product development, and medicinal plant studies.

Overall, Jordan is has one of the highest numbers of researchers per million inhabitants in the MENA region and among the Members of the Organization of Islamic Conference (SESRIC, 2010). Jordan has 8060 researchers per million inhabitants. The university gross enrolment rate of people aged 18–25 years has increased from 18.5% in 2001 to 22% in 2006, among the highest in the Arab world (World Bank, 2009).

The Jordanian Government is reviewing a potential technology transfer policy for the first time. In its current form the policy seems to be mainly a protocol on how to approve products from Asia for which the development work has already been completed overseas. This policy will specify what needs to be done locally in Jordan for regulatory approval to be forthcoming for imported medicines.

5.5 Education and human capital

The case study team felt that human capital is the most significant factor contributing to the success of the pharmaceutical industry in Jordan. Despite the relatively small number of companies based in Jordan, the skill and scientific ability of the Jordanian pharmaceutical companies is generally regarded as superior to those in other Arab countries. Jordanian scientists are often recruited by other Arab counties, according to interviews with some pharmaceutical company chief executive officers in Jordan. The Jordanian companies have sales networks in the rest of the Arab world, and in Africa, Asia, Europe and the United States.

The domestic industry directly employs approximately 4500 people, with the industry as a whole employing over 8000 individuals. The sector accounts for around 3.5% of the total workforce employed in Jordan's industrial sector (Business Monitor International, 2010a). Thirty-seven per cent of pharmaceutical sector employees are female. Forty-one per cent of employees hold a university degree. There are a total of 255 employees in the R&D sector, who represent 5% of the total R&D sector. Of the R&D employees, 87% hold university degrees and 13% hold high school diplomas. The average expenditure on R&D represented on average 3% of each company's budget in 2008. Worker productivity (defined as Jordanian pharmaceutical sales per head of pharmaceutical company employees) increased from US$ 63 000 in 2005 to US$ 110 000 in 2008, with annual increments of 24% (JAPM, 2010).

Human capital will likely remain a strong asset to the Jordan pharmaceutical market. There are currently 7374 undergraduates enrolled at the 8 pharmacy colleges at Jordanian universities, and it is expected that 1475 pharmacists will graduate in 2010. The number of undergraduate students in pharmacy colleges has increased annually by an average of 7% from 2005 to 2009. Furthermore, 11 universities in Jordan are now offering degrees in paramedical sciences; the number of undergraduate students enrolled in these programmes has increased 12% over the past 5 years, resulting in 13 624 students enrolled in 2009. Additionally, there are 5824 students enrolled in similar programmes at community colleges (JAPM, 2010).

There are currently 20 111 doctors in Jordan, of which 68% are general practitioners. The remainder are hospital consultants and specialists; the largest specialist groups are gynaecologists and obstetricians (4.5%) and paediatricians (4.2%) (JAPM, 2010).

6. Analysis of JPM

JPM has benefited significantly, as has its competitors such as Hikma Pharmaceuticals, from the high level of education and expertise investments made by Jordan compared with other MENA countries. This has allowed JPM to build a solid technical base with the capacity to absorb technologies, produce at high quality and service both domestic and export markets. In-licensed

Japanese technology appears to have provided the initial technology transfer needed to initiate operations.

The policy environment has had a significant impact on JPM's markets in so far as it has a tax-free incentive to export more than to serve the domestic market. The success of JPM is bolstered by the solid reputation of JFDA, which ensures that medicaments meet high-quality standards. High-quality standards required for certification in export markets have been a driver for continued upgrades of JPM's facilities.

Through its investments in diagnostics and other areas, JPM has become an exporter of technical expertise to many neighbouring states. There are also plans to expand these services further to Asia and eastern Europe.

The case study team found that of all the strengths of the JPM, the most outstanding example of a model that facilitates access to health product innovations in developing countries is its joint venture in Eritrea. The fact that a pharmaceutical company in a small Middle Eastern country can seed a successful joint venture in a poor, post-conflict African state is groundbreaking. The Azel joint venture has achieved good product flow, exports, employment and financial break-even and is a model worth examining further. It should be noted that it is unlikely that any large multinational corporation would build a manufacturing presence in a post-conflict least developed country (LDC) such as Eritrea that faces a chronic undersupply of medicaments.

Potential weaknesses of JPM identified by the case study team include the low amount of reinvestment into R&D activities. From an innovation perspective, this could limit the firm's potential, especially since it appears that it is starting to develop NCEs. This is also surprising given the emphasis of the General Director on R&D activities. Another potential weakness for the firm are the clinical data protection provisions emanating from Jordan's obligations under its FTA with the United States, which potentially prevent its generic products from reaching market soon after the expiration of an underlying patent.

JPM is successfully marketing its know-how and expertise for the generic manufacturing of pharmaceuticals. However, JPM is facing problems with commercializing its research results. The risks of failure to commercialize R&D results are inherent to R&D activities in all fields of technologies. But for JPM, such risks tend to be higher due to the fact that it finances its R&D activities without any government subsidy or grants, unlike many medical R&D projects in the developed world. Moreover, JPM is a small/medium-sized business with limited resources. With more visibility, including journal publications and profiling the work in investment promotion, JPM may attract partners for product development, or may develop new R&D strategies.

7. Implications of local production and related technology transfer on access to medicines

From an access-to-medicines point of view, there are little or no data available on the question of whether JPM's operations have helped reduce prices of pharmaceuticals in Jordan. There is some evidence that JPM offers prices lower than R&D-based pharmaceutical originators, but prices of medicaments tend to be relatively high in Jordan, despite price controls.

Pharmaceutical expenditure in Jordan is considered to be the main out-of-pocket payment for health services. Although local producers are competitive in price in the local market, the Jordanian pharmaceutical prices are found to be higher compared with international reference prices. The price of pharmaceuticals is one of the reasons for such high out-of-pocket expenditure (Saad, 2010). There is a large difference in prices of originator products and generics. However, prescription practices tend to favour the use of originator products. In 2007 one-third of total health expenditure in Jordan was on pharmaceuticals. The National Health Account of Jordan for 2007 identifies poor prescription policy, preferences of physicians and consumers, promotional activity by pharmaceutical suppliers, OTC purchases, and inadequate availability of pharmaceuticals in the public sector as the main reasons contributing to high expenditure on drugs (High Health Council & National Secretariat, 2009). Public sector prices, such as those purchased and distributed by the Joint Procurement Department and the Ministry of Health, are cheaper than public prices and even international reference prices.

The high prices are not necessarily borne by the general population, however. Health insurance coverage reaches around 87% of the people. The figure was only 70% in 2007 but is expected to reach 100% in 2011, according to the plan of the Jordanian Government (High Health Council & National Secretariat, 2007). The depth and converge of insurance varies depending on the insurance provider. The Ministry of Health is the largest health insurance provider, covering 40% of the population with the broadest coverage, followed by the Royal Medical Services (27%) and private companies, including employers such as JPM, covering the remaining population (Bader, 2010).[17] The Jordan University Hospital and King Abdullah the Second Hospital provide health insurance and services for their employees and serve as educating and referral centres for other health sectors. The Royal Court currently provides medical costs for poor and uninsured Jordanians.

Domestically, local firms and imports provide the population with a wide range of high-quality medicaments. Demand for originator products remains high, despite the robust domestic production of generic medicaments. JPM produces a wide range of pharmaceuticals, including those on the essential medicines. It is interesting to note that JPM has used its expertise in

17 The United Nations Relief and Welfare Agency for Palestinian Refugees (UNRWA) also provides health insurance support.

pharmaceuticals to try to expand into additional areas, including biologicals (medicinal preparations made from living organisms and their products, such as serums and vaccines) and diagnostics, and has become very much an innovator firm with respect to the latter.

It is noteworthy that JPM concentrates its efforts on exports rather than on the domestic market. Having earned a reputation for making high-quality medical products (both pharmaceuticals and devices), Jordan exports its products to many other MENA and African countries. These are also the regions where Jordanian firms have entered into joint ventures, creating a multiplier effect and contributing to a wider diffusion of pharmaceutical technologies. JPM was able to establish a manufacturing facility in Eritrea that operates as a going concern, and contributes to providing access to a country that otherwise has limited access to medicines, is a major achievement.

For these reasons, one can infer that JPM and the other local pharmaceutical producers in general have a limited role in contributing to access to medicines in Jordan. Estimated figures on the share of local producers in the local market, as indicated earlier, is around 25%. Although their share is limited in the local market, Jordanian producers contribute in terms of local availability of medicines and providing competition based on both quality and price. Furthermore, companies such as JPM undertake R&D with global partners but also focus on cheaper and rapid diagnostics that can benefit developing countries. In this sense, JPM has used its pharmaceutical manufacturing base to expand to new areas that could contribute to other important public health objectives, both in Jordan and elsewhere.

JPM's out-licensing and technology transfer activities can also be considered as a contribution to accessing medicine in the long term.[18] JPM is also gaining experience in post-conflict countries in sub-Saharan Africa with chronic problems with availability of medicines, especially Eritrea, Mozambique and Sudan, all LDCs. Few organizations in the private sector, especially multinational companies, are willing to take the risks taken by JPM in investing in poor countries.

8. Policy-relevant findings

In general, the Jordanian pharmaceutical industry has become successful for a variety of reasons:

There has been large-scale investment in the education of pharmacists, doctors and scientists to improve and develop the technical expertise of the industry, which is essential to preserving current markets and to penetrating new ones. The strategic goal is to make Jordan a regional centre of advanced pharmaceutical technology.

18 See Access to Medicine Foundation (2010) for further benchmarks measuring the contribution of individual companies to access to medicine.

JFDA enforces its regulations with efficiency and thoroughness, as explained in Section 5.1.

The Jordanian Government offers tax-free incentives on exports (which additionally explains why so many Jordanian pharmaceutical companies' sales are so export-focused).

The Jordanian trade industry has a strong rapport with the Jordanian Government, which has helped to resolve difficult technical issues.

Local prices have enabled the local industry to thrive. (This is the same factor that has allowed the Indian pharmaceutical industry to expand around the world, while the progress of the Chinese and Japanese pharmaceutical industries has been stilted. The Indian industry has used the Indian domestic market for cash flow for its international expansion, while China and Japan have carried out regular price cuts of domestic pharmaceutical prices and have not allowed their local pharmaceutical companies sufficient cash flow to expand overseas.)

The export market has also provided an opportunity for the Jordanian pharmaceutical sector to develop.

In addition to the strength of its human capital, the Jordanian pharmaceutical industry has other advantages. First, more than half of the Jordanian companies were established in the past two decades and therefore have state-of-the-art facilities equipped with the latest machinery and technology. Jordanian companies also tend to have large capacities, which enables them to be contracted by foreign companies for production. Second, the Jordanian industry has accumulated good manufacturing and technical experiences. Jordan has become a centre of GMP in the region, which has led to alliances with many foreign companies.[19] Third, Jordan has seven CROs. These companies perform clinical trials for regulatory submissions to health authorities to fulfil registration requirements of pharmaceutical products for Jordan and for other countries. A few years ago, clinical testing legislation was passed to allow for clinical testing in humans, i.e. for phase I, II, III and IV trials. This has encouraged multinational pharmaceutical companies to conduct more clinical research in Jordan.

The educated scientific human capital of Jordan will likely ensure the future success of the Jordanian pharmaceutical industry. As with JPM, one potential limitation is the relatively low reinvestment on R&D as a percentage of overall sales. Additionally, the Jordanian Government's lack of targeted incentives, in particular for inward investment, is also a potentially limiting factor for continued success.

However, the operating environment has been changing for the pharmaceutical producers. Iraq and Saudi Arabia have been the bigger

19 In September 2008, the United States FDA announced office postings in Amman, Jordan, to focus on Jordan as a centre for regulatory practices in food and drugs in the MENA region (FDA, 2009).

markets for the Jordanian producers. Iraq's pharmaceutical market changed when it started to import products certified by the United States FDA. Saudi Arabia is actively seeking to establish its own local pharmaceutical industrial base, which includes recruiting Jordanian pharmacists and managers. In the rest of the MENA region, the Jordanian pharmaceutical industry is facing regulatory problems, including local facility requirements, price control and drug registration restrictions. Responding to these challenges, companies such as Hikma Pharmaceuticals and JPM are establishing subsidiaries and partnerships throughout the region and beyond. Furthermore, JPM is establishing its presence in the sub-Saharan market, especially in LDCs such as Eritrea, Mozambique and Sudan. JPM has also been expanding its business to include R&D and technical and know-how services.

It is perhaps no coincidence that the main markets to which JPM and similar companies export tend to be in the MENA region. The package offered by Jordan is increasingly a full range of health-related goods and services, starting with pharmaceuticals offered by a neighbouring country that shares the region's religious and cultural affinities, thus catering to a regional market-driven demand.

References

Access to Medicine Foundation. *The index 2010*. Haarlem, Access to Medicine Foundation, 2010 (http://www.accesstomedicineindex.org/content/index-2010-0).

Amwal Invest. *Pharmaceutical sector*. Amman, Amwal Invest, 2010 (http://www.amwalinvest.com/sites/default/files/Pharmacuetical_Report.pdf).

Bader R. *MeTA Jordan case study on CSOs in Jordan*. London, Medicines Transparency Alliance, 2010 (http://www.medicinestransparency.org/fileadmin/uploads/Documents/Global_Forum/Global_Forum__-_case_studies/MeTA_Jordan_-_CSO.pdf).

Business Monitor International. *Jordan: First quarter pharmaceuticals and healthcare report*. London, Business Monitor International, 2009.

Business Monitor International. *Jordan: Third quarter competitive landscape*. London, Business Monitor International, 2010a.

Business Monitor International. *Jordan: Third quarter industry forecast for pharma and healthcare*. London, Business Monitor International, 2010b.

Business Monitor International. *Jordan: First quarter pharmaceuticals and healthcare report*. London, Business Monitor International, 2010c.

Business Monitor International. *Jordan: Third quarter market overview*. London, Business Monitor International, 2010d.

Cullen D. Data protection: the new IP frontier – an overview of existing laws and regulations. *Journal of Generic Medicines*, 2007, 5:9–25.

Dow Jones. *Dow Jones Total Stock Market Indexes*. Princeton, NJ, CME Group, 2010 (http://www.djindexes.com/mdsidx/downloads/brochure_info/Dow_Jones_Total_Stock_Market_Indexes_Brochure.pdf).

EC, OECD. *Report on the implementation of the Euro-Mediterranean Charter for Enterprise: 2008 enterprise policy assessment*. Luxembourg: European Communities and Organisation for Economic Co-operation and Development (http://www.oecd.org/dataoecd/39/22/41779100.pdf).

Economist Intelligence Unit. *Jordan: Country profile*. London, Economist Intelligence Unit, 2008.

FDA. *FDA's action plan for import safety*. Washington, DC, United States Food and Drug Administration, 2009 (http://www.fda.gov/downloads/ICECI/EnforcementActions/EnforcementStory/UCM129822.pdf).

Grover A. *Report of the Special Rapporteur on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health*. A/HRC/11/12. Geneva, Office of the United Nations High Commissioner for Human Rights, 2009 (http://daccess-dds-ny.un.org/doc/UNDOC/GEN/G09/127/11/PDF/G0912711.pdf?OpenElement).

High Health Council, National Secretariat. *National health strategy for the years 2008–2012*. Amman, High Health Council and National Secretariat, 2007.

High Health Council, National Secretariat. *National health accounts 2007*. Amman, High Health Council and National Secretariat, 2009 (http://www.who.int/nha/country/jor/jordan_nha_2007.pdf).

Higher Council for Science and Technology. *Recommending strategy*. Amman, Higher Council for Science and Technology, 2009 (http://www.medinnov.com/doc/medinnov07/panel/Walid_El_Turk_HCST_Presentation_Marseille.ppt#256,1).

JAPM. *Pharmaceutical industry data bank 2010*. Amman, Jordanian Association of Pharmaceutical Manufacturers, 2010.

JFDA. *Provisional law no. 80 of the year 2001: Drug and pharmacy law*. Amman, Jordan Food and Drug Administration, 2001 (http://www.jfda.jo/custom/law/24.doc).

JFDA. *The criteria and standards related to drugs pricing, repricing and objections to pricing decisions*. Amman, Jordan Food and Drug Administration (http://www.jfda.jo/).

Jordan Ministry of Industry & Trade. *Industrial property: Statistics*. Amman, Jordan Ministry of Industry & Trade, 2011 (http://www.mit.gov.jo/tabid/465/Statistics.aspx).

Jordan Social Security Corporation. *Highlights on SSC's progress during His Majesty King Abdullah II's leadership*. Amman, Jordan Social Security Corporation, 7 June 2009

JPM. *Partnerships*. Amman, Jordanian Pharmaceutical Manufacturing Co. PLC, 2011a (http://www.jpm.com.jo/alli_Part.aspx).

JPM. *Technologies transfer*. Amman, Jordanian Pharmaceutical Manufacturing Co. PLC, 2011b (http://www.jpm.com.jo/alli_Tech.aspx).

LESI. *LES International conference: Power networking, organization profiles*. Alexandria, VA, Licensing Executives Society International, 2008.

Oxfam. *All costs, no benefits: How TRIPS-plus intellectual property rules in the US–Jordan FTA affect access to medicines*. Briefing paper 102. Oxfam, 2007 (http://www.oxfam.org.uk/resources/issues/health/downloads/bp102_trips.pdf).

Saad S. *Case study: MeTA Jordan*. London, Medicines Transparency Alliance, 2010 (http://www.medicinestransparency.org/fileadmin/uploads/Documents/Global_Forum/Global_Forum__-_case_studies/MeTA_Jordan_-_Standard_Treatment_Guidelines.pdf).

SESRIC. *Research and scientific development in OIC countries*. Ankara, Statistical, Economic and Social Research and Training Centre for Islamic Countries, 2010.

UN comtrade. *International merchandise trade statistics (IMTS)*. Geneva, United Nations comtrade, 2010.

UNCTAD. *The least developed countries report 2007: Knowledge, technological learning and innovation for development*. Geneva, United Nations Conference on Trade and Development, 2007.

UNDP. *Jordan*. Geneva, United Nations Development Programme, 2010 (http://www.undp-jordan.org/).

UNESCO. *UNESCO supports development of science, technology and innovation policy in Jordan*. Paris, United Nations Education, Science and Culture Organization, 2010 (http://www.unesco.org/en/amman/).

USAID. *Assessment of the current pricing policy on the pharmaceutical sector*. Washington, DC, United States Agency for International Development, 2009 (http://pdf.usaid.gov/pdf_docs/PNADT035.pdf).

US Department of State. *2009 investment climate statement – Jordan*. Washington, DC, United States Department of State, 2009 (http://www.state.gov/e/eeb/rls/othr/ics/2009/117412.htm).

USTR. *2010 special 301 report*. Washington, DC, Office of the United States Trade Representative, 2010 (http://www.ustr.gov/webfm_send/1906).

USTR. *Free trade agreements*. Washington, DC, Office of the United States Trade Representative, 2011 (www.ustr.gov/trade-agreements/free-trade-agreements).

WHO. *Jordan: Medicine prices, availability, affordability and price components*. WHO-EM/EDB/087/E. Geneva, World Health Organization, 2007 (http://www.emro.who.int/dsaf/dsa786.pdf).

WHO. *Country profile: Jordan*. Geneva, World Health Organization, 2011 (http://www.who.int/countries/jor/en/).

World Bank. *Project appraisal document on a proposed loan in the amount of US$25 million to the Hashemite Kingdom of Jordan for a higher education reform for the knowledge economy*. Report no. 46823. Washington, DC, World Bank, 2009.

World Bank. *Data: Countries and economies – Jordan*. Washington, DC, World Bank, 2011 (http://data.worldbank.org/country/jordan).

WTO. *Report of the working party on the accession of the Hashemite Kingdom of Jordan to the World Trade Organization*. WT/ACC/JOR/33. Geneva, World Trade Organization, 1999a (http://docsonline.wto.org/DDFDocuments/t/WT/ACC/JOR33.DOC).

WTO. *Protocol of accession of the Hashemite Kingdom of Jordan to the Marrakesh Agreement establishing the World Trade Organization*. WT/ACC/JOR/35. Geneva, World Trade Organization, 1999b (http://docsonline.wto.org/DDFDocuments/t/WT/ACC/JOR35.DOC).

WTO. *Report of the working party on the accession of the Kingdom of Saudi Arabia to the World Trade Organization*. WT/ACC/SAU/61. Geneva, World Trade Organization, 2005 (http://docsonline.wto.org/DDFDocuments/t/WT/ACC/SAU61.doc).

WTO. *Trade policy review report by Jordan*. WT/TPR/G/206. Geneva, World Trade Organization, 2008 (http://www.mit.gov.jo/portals/0/g206.pdf).

Zawya. *Jordan pharmaceutical manufacturing: company profile*. Dubai, Zawya, 2010.

Annex: Interviewed individuals and institutions

Pharmaceutical experts

Sakher Adli, Vice President, Sales and Marketing, Hikma Pharmaceuticals

Mohammed Al-Jafari, Business Development Department, Jordanian Pharmaceutical Manufacturing Co. PLC

Adnan Badwan, General Director, Jordanian Pharmaceutical Manufacturing Co. PLC

Neyla Gargouri Darwaza, Medical Officer, Hikma Pharmaceuticals

Maher Kurdi, Managing Director, Hayat Pharmaceuticals

Lina Nabulsi, Technical Director and R&D Manager, Jordanian Pharmaceutical Manufacturing Co. PLC

Hanan Sboul, Secretary General, Jordanian Association of Pharmaceutical Manufacturers and Medical Appliances

Leaders of contract research organizations

Ahmed Al-Ghazawi, Chief Executive Officer and President, Triumpharma

Maher Matalka, Chief Executive Officer, International Pharmaceutical Research Centre

Representatives of the Jordanian Government

Khouloud Alkhamis, Dean, Faculty of Pharmacy, Jordan University of Science and Technology

Maisa K Alsaket, Director General, Jordan Joint Procurement Department

Basher Al-Taani, Industrial and Physical Pharmacy, Jordan University of Science and Technology

Issah Gammoh, Acting Chief Executive Officer, Jordan Investment Board

M Rawashdeh, Director General, Jordan Food and Drug Administration

Representatives of the World Health Organization

Hashim Elzein Elmousaad, Head of Mission, WHO Mission Jordan

Sana Naffa, National Programme Officer, WHO Mission Jordan

Member of the Jordan Specialty Hospital

Sahar Moh Elmasri, CQI and Pharmacy Deputy Director, Jordan Specialty Hospital

*Representatives of pharmacies**

Mayas Abu Saleh, Group Pharmacy Coordinator, Pharmacy1

*Additionally, the case study team visited Nairoukh Pharma and the Ministry of Health Distribution Unit.

Case study 7

Thailand

This case study on Thailand was prepared for UNCTAD by Cecilia Oh, an independent consultant based in Bangkok, under the supervision of Kiyoshi Adachi, Chief of UNCTAD's Intellectual Property Unit. Inputs for the study were collected during September and October of 2010. The case study report was finalized under the overall responsibility of Mr James Zhan, Director of the Division on Investment and Enterprise, and Mrs Nazha Benabbes Taarji, Officer-in-Charge, Investment Capacity-Building Branch.

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Abbreviations

ACIP	Advisory Committee on Immunization Practice
BCG	bacille Calmette–Guérin
BIOTEC	National Center for Genetic Engineering and Biotechnology
EPI	expanded programme of immunization
GAP	WHO Global Pandemic Influenza Action Plan to Increase Vaccine Supply
GAVI	Global Alliance for Vaccines and Immunisation
GPO	Government Pharmaceutical Organization
ITPIV	International Technology Platform for Influenza Vaccine
LAIV	live attenuated influenza vaccine
NSTDA	National Science and Technology Development Agency
NVCO	National Vaccine Committee Office
OPV	oral poliomyelitis vaccine
TRC/QSMI	Thai Red Cross/Queen Saovabha Memorial Institute

1. Background and methodology

This study is one in a series of case studies commissioned by UNCTAD to examine local production and the transfer of technology within the pharmaceuticals and vaccines sector in developing countries. The case studies comprise one component of a collaborative project between the World Health Organization (WHO), UNCTAD and the International Centre for Trade and Sustainable Development (ICTSD) funded by the European Union (EU). The project is an input to the implementation of the WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI). It is hoped that analysis of the dynamics of firm-level activities with the wider policy environment can provide important insights to help meet the challenges of, and address the obstacles, to sustainable pharmaceutical innovation and production in developing countries.

UNCTAD thanks the Government Pharmaceutical Organization (GPO) of Thailand for agreeing to be the subject of this case study. This case study highlights the initiative for domestic production of the influenza vaccine at GPO of Thailand, with the aim of identifying the opportunities and challenges applicable and relevant to vaccine development and production in Thailand. The GPO project is analysed within the context of the following factors: (i) the vaccine needs and priorities in Thailand; (ii) the technological capacity for vaccine development in Thailand; and (iii) the legal and policy environment for research and development (R&D) and innovation in Thailand. It is hoped that this study will contribute to a better understanding of the role of the state-sponsored pharmaceutical sector in the context of vaccine development in Thailand. Another objective is to distil relevant lessons for the promotion of sustainable pharmaceutical innovation and production in Thailand, through analysis of the dynamics of vaccine development and technology transfer.

A case study research methodology was used for this study, with data collected from both primary (face-to-face interviews with identified people) and secondary (literature review) sources. The interviewees were identified in consultation with UNCTAD and WHO. Given the focus on the GPO and its influenza vaccine project, a number of interviewees were drawn from GPO staff involved in this project. Other people include representatives from government and public sector agencies with mandates related to the pharmaceutical innovation, R&D and regulatory processes; research institutes and universities; and private-sector pharmaceutical companies. Interviews were guided by a list of sample questions that could be asked. During the period September–October 2010, a series of interviews were conducted with a number of individuals. The list of sample questions and the names of the people who were interviewed are given in Annexes I and II, respectively.

This case study construes innovation as any new products, processes and organizational changes that are new to the enterprise, context and country in question, although not necessarily to the world at large (UNCTAD, 2007). In keeping with the scope of the project, technology transfer was defined as all components of technology, both codified (in terms of blueprints, hardware,

machine parts and plant technologies) and tacit (know-how and skills), that are essential to enhance the capacity of the organizations in the recipient country to produce pharmaceutical products.[1]

2. Description of the firm, structure and product

The GPO is the amalgamation of the Government Pharmaceutical Laboratory – set up in 1942 to serve as the domestic pharmaceutical factory to reduce reliance on imported medicines and to produce medicines for national emergencies – and the Department of Medical Depot (founded in 1901), which was tasked with the procurement of medical products for the Thai Government. The Government Pharmaceutical Organization Act of 1966 (B.E. 2509) formally established the GPO as a state enterprise under the Ministry of Public Health, with the following mission:

- to engage in the pharmaceutical industry and business through manufacturing, selling, and exchanging of quality medicines, as well as other health products;
- to reinforce pharmaceutical research and development on both new and existing drug formulas, by integrating modern technology;
- to promote quality analysis of both finished pharmaceutical products and raw materials (GPO, 2007).

GPO currently has over 2400 staff. More than 1000 people are employed within its "production cluster", comprising the 3 departments of pharmaceutical production, biological products, engineering and technology, and GPO's antibiotics plant. Another 320 people are employed within its "technical advisory cluster", which consists of the Research and Development Institute and the Quality Assurance Department (GPO, 2008, 2009).

GPO manufactures over 300 pharmaceutical items, which are primarily medicines (including biological products) on the National List of Essential Drugs. For the fiscal year 2009, GPO's total income from sales of pharmaceuticals and medical supplies was 8.127 billion baht (approximately US$ 263 385 000) in 2009, although the sales from products manufactured by GPO was 6.029 billion baht (US$ 195 448 000), with the balance comprising largely imports of medicines and medical supplies from other suppliers (GPO, 2008, 2009).

As a state enterprise, GPO enjoys the privilege of being the main supplier to the public health system. Preference is given to GPO in terms of Thai Government procurement of pharmaceutical products; hence, public health facilities are obliged to use 80% of their budget allocations to procure their essential medicines requirements from GPO, provided that GPO prices do not exceed 3% of the reference price established by the Ministry of Public Health

1 A uniform definition of technology transfer was used for all components of the project, including the trends survey, the regional dialogues and the stakeholder analysis.

for the products.[2] It is understood that changes to hospital budget allocation and procurement procedures – with the establishment of the National Health Security Office in 2002 to manage the national health insurance scheme and centralization of aspects of pharmaceutical procurement – now mean that public health facilities effectively procure only about 30% of their medicine needs from GPO. Nevertheless, the public sector remains GPO's biggest customer, representing 92.8% of the total sales income, while the private sector accounts for 6.8% of sales, and exports only make up a scant 0.4% (GPO, 2009).

It is estimated that GPO spends about 1.6% of its sales income on R&D. Although this is not a significant amount, GPO's R&D efforts have played a significant role in Thailand's success in responding to the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) epidemic. Since 1992, the Research and Development Institute at GPO has been working on formulation development and bioequivalence studies of HIV/AIDS treatments, and it was successful in producing zidovudine, its first generic antiretroviral (ARV) medicine in 1995. GPO's continued R&D and success in generic ARV production, and particularly the subsequent development and manufacture in 2002 of GPO-VIR S, a triple ARV therapy fixed-dose combination of stavudine, lamivudine and nevirapine, would later be an important factor in convincing the Thai Government of the viability of instituting a policy on universal access to ARVs.

Generic production of ARVs and other medicines remains a focus at GPO, more recently with the grant of a series of Thai Government use licences by the Ministry of Public Health for the import or local production of seven medicines for use under the national health insurance scheme. The first licence, granted in November 2006, was for the ARV efavirenz. The second and third licences, granted in January 2007, were for the ARV combination of lopinavir/ritonavir and clopidogrel (an antiplatelet agent used in the treatment of coronary artery disease). Four licences were granted in January 2008 for the cancer medicines letrozole, docetaxel, erlotinib and imatinib, used in the treatment of breast cancer, lung cancer, gastrointestinal stromal tumour and leukaemia, respectively.

The grant of the Thai Government use licences[3] attracted much controversy within and beyond Thailand. Despite the controversy and vociferous opposition from multinational pharmaceutical companies, the validity of the licences has not been challenged before the courts or at the World Trade Organization (WTO) dispute settlement system to date, and GPO has since proceeded with the implementation of the licences by importing the generic

2 See OPM (1992, Articles 60–64).

3 The licences were granted under Section 51 of the Patent Act 1979 of Thailand, which authorizes Thai Government use of patents in the general public interest, so that "any ministry, bureau or department of the Government" may exercise the rights in any patent "to carry out any service for public consumption".

equivalents for six of the seven medicines under licence.[4] According to GPO's estimates, importation of the generic versions of the medicines has so far accounted for savings of over 10 billion baht (US$ 324 621 000) in medicine expenditure (GPO, 2009). GPO is concurrently developing generic versions of the medicines, with the expectation that eventually GPO will be able to manufacture the medicines to supply the national health insurance scheme.

With regard to vaccine production and supply, GPO is one of the three domestic producers for the national health system. GPO, the Thai Red Cross/Queen Saovabha Memorial Institute (TRC/QSMI) and GPO-Mèrieux Biological Products (GPO-Mèrieux) provide most of the vaccines used in Thailand's expanded programme of immunization (EPI). GPO-Mèrieux is a joint venture company established between GPO and Sanofi Pasteur, with each party holding 49% of the shares, and the remaining 2% being held by the Crown Property Bureau. Under the terms of the joint venture agreement, EPI vaccines supplied by GPO-Merieux will be purchased by the Ministry of Public Health of Thailand, through GPO, for use in the public health system.

GPO currently produces the Japanese encephalitis vaccine, while TRC/QSMI produces the bacille Calmette–Guérin (BCG) vaccine. GPO-Mèrieux currently supplies five of the EPI vaccines. Domestic production, in this context, means both upstream and downstream production processes in the case of GPO and TRC/QSMI for the Japanese encephalitis and BCG vaccines, respectively. GPO-Mèrieux supplies the oral poliomyelitis vaccine (OPV), the measles (M) vaccine, the measles, mumps and rubella combination (MMR) vaccine, the hepatitis B vaccine, and the diphtheria, tetanus and pertussis–hepatitis B vaccine by importing the bulk vaccines for production in downstream process – i.e. formulation, blending, filling and packaging.

3. Technological capacity of GPO and Thailand

This section gives an overview of initiatives at the various stages of vaccine development as an illustration of the existing capacities for vaccine development and production in Thailand.

3.1 Manufacturing

The three main vaccine suppliers/manufacturers mentioned in Section 2 undertake varying degrees of vaccine development and production. As noted above, GPO and TRC/QSMI carry out both upstream and downstream production processes for the "traditional" vaccines that they produce, i.e. Japanese encephalitis and BCG vaccines, respectively. Although the present production operations at GPO-Mèrieux are limited to the import of vaccines in bulk form or in naked vials for formulation and filling in Thailand, it is

4 Implementation of the Thai Government use licence on the cancer medicine imatinib was suspended on condition that the medicine would be provided free of charge by the patent-holding pharmaceutical company to patients under the Universal Health Coverage Scheme.

understood that the expectation is for the joint venture company to eventually progress towards upstream production activities.

The three manufacturers currently produce vaccines for the domestic market. It was recently announced, however, that GPO-Mèrieux would soon be able to export its Japanese encephalitis vaccine to Australia and New Zealand. This will make it the first vaccine to be exported by the joint venture company, as well as Thailand's first export of the Japanese encephalitis vaccine (Bangkok Post, 2010). GPO-Mèrieux is currently the only Thai-based vaccine manufacturer with WHO prequalification for its measles vaccine.

As well as the three manufacturers above, a small handful of private-sector pharmaceutical companies are involved in vaccine development. Of note are BioNet-Asia Co., Ltd. and Greater Pharma Co., Ltd. BioNet-Asia was initially established as an international vaccine consultancy in 2001, offering business and technical services, including facilitating strategic collaborations between vaccine manufacturers through joint development and licensing. More recently, BioNet-Asia has invested in the establishment of a vaccine facility in Ayutthaya for R&D and pilot-scale vaccine production, in a move to establish itself as a centre of excellence in vaccine R&D and as a potential partner in joint development collaborations. BioNet-Asia's current product pipeline includes the acellular pertussis and Haemophilus influenzae type b vaccines.

Greater Pharma, a private family-owned pharmaceutical company, has a core business in pharmaceutical, food supplement and cosmetic production but has in recent years begun to venture into the biotechnology industry and biopharmaceutical production. With support from the National Center for Genetic Engineering and Biotechnology (BIOTEC) and the Thailand Board of Investment, Greater Pharma is currently collaborating with the Siriraj Medical School at Mahidol University on the commercial scale-up and manufacture of a biological allergy vaccine for treating allergies caused by house dust mites, developed by the Siriraj Medical School (Thailand Biotech Guide, 2008).

3.2 Preclinical development

There is significant capacity for academic research in the biotechnology field. In the health sector, there is particular interest in diseases prevalent in Thailand, including dengue, malaria, thalassaemia and HIV.

A number of universities and public research institutes in Thailand are undertaking vaccine-related R&D. Mahidol University is one of the premier institutions, housing a number of the key centres of medical biotechnology and health research, including the Medical Biotechnology Unit and the Centre for Vaccine Development. The Centre for Vaccine Development has been conducting research on dengue vaccine candidates, with recent success in developing live attenuated candidates. The Faculty of Medicine at Chiang Mai University is also undertaking dengue vaccine research, where promising vaccine candidates have been developed and are currently in animal testing (Hongthong, 2010). Meanwhile, the King Mongkut University of Technology

in Thonburi is planning to establish a facility for microbial and cell culture fermentation, with a view to servicing the biopharmaceutical industry in the region, including a proposed collaboration with GPO.

The Ministry of Public Health's Department of Medical Sciences undertakes vaccine-related research, in addition to its function as the National Control Laboratory, which conducts analysis of pharmaceutical products, including vaccines that are submitted to the Thai Food and Drug Administration for marketing approval. BIOTEC, one of four national research centres under the National Science and Technology Development Agency (NSTDA), also houses several vaccine R&D projects at the preclinical stage, notably for Japanese encephalitis, avian influenza and dengue.

Table 1 lists the key vaccine R&D projects at the preclinical stage at these institutions, for which the National Vaccine Committee Office (NVCO) evaluation study (see Section 3.4) had identified the potential next stages of development.

***Table 1** Vaccine research and development*

Organization	Vaccine	Development stage	Potential development
CVD	Dengue, Japanese encephalitis	Preclinical	WHO reference laboratory for dengue and Japanese encephalitis research
MBC, DMSC	H5N1, H3N2, HIV (reverse genetics)	Preclinical	Industrial process development (HIV/ influenza/hepatitis B)
Department of Parasitology, Siriraj Hospital	Avian influenza allergy vaccine	Preclinical/ bioequivalence study	Phage display human antibody library/ monoclonal antibody
BIOTEC	Avian influenza, dengue, Japanese encephalitis	Preclinical	Plasmodium falciparum genetic structure mapping

BIOTEC, National Center for Genetic Engineering and Biotechnology; CVD, Centre for Vaccine Development; DMSC, Ministry of Public Health's Department of Medical Sciences; MBC, Medical Biotechnology Centre.
Source: NVCO (2009).

3.3 Vaccine clinical trials

There is demonstrated capability for hosting vaccine clinical trials in Thailand. This capacity is regarded as an important building block of the country's vaccine development programme.

Clinical trials of note include the phase III vaccine clinical trial for RV144, conducted by the United States of America Armed Forces Research Institute of Medical Sciences in collaboration with the Ministry of Public Health and Mahidol University, the world's largest HIV/AIDS vaccine trial to date, with 16 000 participants. Another large clinical trial in Thailand is that to test efficacy of the live attenuated dengue vaccine candidate developed by Sanofi

Pasteur. The paediatric clinical trial, which began in 2009, is conducted in collaboration with Mahidol University, the Ministry of Public Health and the Paediatric Dengue Vaccine Initiative with the enrolment of 4000 4- to 11-year-old children (Hongthong, 2010; Senior, 2009).

It is, however, noted that these clinical trials have been undertaken in collaboration with international partners, and no locally developed vaccine candidate has been used in any of the clinical trials in Thailand.

3.4 Analysis

Although the National Vaccine Policy of 2005 prioritized self-reliance and vaccine supply security as policy goals and proposed a strategic plan for vaccine development, effective implementation has been hampered by a lack of advocacy, coordination and budget within the Thai Government. In light of this, an evaluation of the state of vaccine development was conducted by NVCO (2009). This study sought to assess, among other things, existing domestic capacity in the vaccine development cycle and the potential opportunities and challenges for domestic vaccine development.

The NVCO study concluded that although there were significant capabilities for vaccine R&D at both the preclinical and clinical phases, the capacity for quality control and assurance and downstream production was limited. Although researchers in Thailand have had successes in the development of potential vaccine candidates – including for dengue, Japanese encephalitis, HIV and avian influenza (see Section 3.2) – much of the progress has thus far been confined to the preclinical phase. The limited capacity in terms of downstream vaccine development and production can be attributed to the lack of effective linkages between vaccine researchers and manufacturers. The NVCO study also pointed to the lack of essential infrastructure needed for vaccine development, such as facilities for pilot-scale production and industrial plants, and the lack of appropriate and qualified personnel, as factors that have contributed to the limited downstream vaccine development.

This view was corroborated by a number of interview subjects. The so-called "Valley of Death" problem is well illustrated in the vaccine field in Thailand, according to one interviewee, by which he meant the gap between capabilities in basic research and that of product development and industrial production. To narrow the gap, Thailand needs to address the needs for capacity-building and technological advancement in mid- and downstream vaccine development, namely toxicology, quality control and assurance, and production scale-up.

4. The vaccines market in Thailand

Thailand is a middle-income country, with a population of over 67 million and a gross domestic product (GDP) per capita (in purchasing power parity US$) of US$ 8328. Thailand's public spending on health, currently at 2.7% of GDP, has been consistently higher than that of its closest neighbours in the

Association of South-East Asian Nations (ASEAN) region, Malaysia, Indonesia and the Philippines (1.9%, 1.2% and 1.3% of GDP, respectively) (UNDP, 2010).

Thailand has an extensive public health system infrastructure and a good track record for health services provision. In 2002, the National Health Security Act was passed by the Thai Parliament to extend health coverage under the universal health care scheme to 78% of the population, which had previously not been covered by health insurance plans (e.g. the social security scheme for private-sector employees and the Thai Government employee health care scheme). Previously known as the "30 baht scheme" (the 30 baht premium was abolished in 2007), the universal health care scheme has expanded health insurance coverage to an estimated 97–98% of the population (UNDP, 2009).

The accessibility of health services has made significant contributions to poverty reduction and overall human security in Thailand, and these achievements have helped to ensure Thailand's steady rise in the human development index (HDI). Ranked 92nd out of 169 countries in the 2010 HDI, Thailand has seen a growth of 1% per annum in its HDI over the past 3 decades, above the HDI regional average in Asia and the Pacific (UNDP, 2009).

Thailand officially launched its nationwide immunization programme in 1977 and has, since then, continued the expansion and strengthening of its immunization service infrastructure. In this respect, the Ministry of Public Health is guided by a set of principles and policies, namely: the right of all people to be protected from vaccine-preventable diseases; the inclusion of immunization in the basic health services package; and the provision of safe, high-quality immunizations to all people free of charge (Muangchana et al., 2010). Immunizations and related costs are financed under the universal health care scheme. Accordingly, vaccines included in the EPI schedule are provided free of charge by public-sector hospitals and health-care centres.

The public health infrastructure in Thailand is designed to cover the entire population, with at least 1 community hospital in each of the country's 926 districts, and 1 health-care centre in each subdistrict. The EPI is fully integrated into these basic health services. Currently, Thailand's EPI includes vaccines that cover the following 10 antigens: tuberculosis, hepatitis B, diphtheria, tetanus, pertussis, poliomyelitis, measles, mumps, rubella and Japanese encephalitis (Muangchana et al., 2010).

In accordance with Thailand's pandemic preparedness plan, seasonal influenza vaccinations are now provided to priority-risk groups. The vaccine was first provided to health-care workers in 2004, and then in 2008 vaccination was extended to elderly people and people with chronic diseases. Changes to the immunization programme, including the introduction of new vaccines to the EPI schedule, are based on the recommendations of the Advisory Committee on Immunization Practice (ACIP) of Thailand. Established nearly 40 years ago, ACIP, which comprises 28 experts in immunization and related fields, develops written recommendations for the Ministry of Public Health on the introduction of new vaccines, after review of relevant and available

data. Vaccine procurement and related technical support and evaluations are carried out at the national level, while responsibility for implementing the programme is decentralized to the country's 76 provincial health offices.

Vaccine coverage in the country is high: it is estimated at more than 95% for the EPI vaccines, although there are exceptions within specific population groups, including the hill tribes, and the urban and rural poor (Bureau of Policy and Strategy, Ministry of Public Health, 2009). According to the Ministry of Public Health, the immunization policy has been successful in considerably reducing the burden of vaccine-preventable diseases. Cases of polio due to the wild poliovirus have been absent since 1997. Over the 5-year period of 1999–2004, the incidence of diphtheria has reduced from 51 cases in 1999 to 8 cases in 2003; the incidence of pertussis decreased from 47 cases in 1999 to 26 cases in 2003; and the incidence of tetanus in infants decreased from 26 cases in 1999 to 6 cases in 2003.

Thailand's current vaccine expenditure is reported to be around 3.6 billion baht (US$ 116 732 000), with approximately 80% of the vaccines being imported (Government Public Relations Department, 2010; Vonghangool & Pham, 2010). Procuring for the national immunization programme, the Ministry of Public Health is the biggest purchaser. Data from WHO indicate that Thai Government spending on vaccines in 2009 amounted to 1.19 billion baht (US$ 38 586 000); of this amount, over 48% (582 million baht) was spent on procurement of vaccines under the EPI schedule (WHO, 2011).

Calculations of data from other sources indicate that the annual expenditure in 2008 for the EPI vaccines was well over 800 million baht (US$ 25 954 000). Table 2 lists the EPI vaccines supplied for 2008, their suppliers/manufacturers, the doses of vaccines needed and supplied, and the prices. Other vaccines not included in the EPI schedule are largely imported; Table 3 provides a similar listing of the non-EPI vaccines used in Thailand (although some pricing data were unavailable).

Table 2 EPI vaccines: manufacturers/suppliers, production process, demand/supply and prices

Vaccine	Manufacturer	Production process			Demand (doses)[a]	Supply (doses/year)[b]	Price (baht/dose[c] (total vaccine expenditure[d]))
		Upstream	Downstream	Finished product			
Tuberculosis vaccine (BGC)	QSMI	Yes			2 million	2 million (production capacity up to 5 million)	7.00 (14 million)
Japanese encephalitis (inactivated mouse brain-derived Japanese encephalitis)	GPO	Yes			3.7 million	2.4 million (production capacity up to 3 million)	51.50 (278.1 million)
				Yes		1.3 million (imported by Cosma Medical Co. Ltd, and Biogenetech Co. Ltd)	72.62 (94.406 million)
Measles vaccine	GPO-Mèrieux		Blending, filling freeze-drying, packaging, testing		0.89 million	0.89 million (batch size 33 000 vials (10 doses/vial))	16.20 (14.418 million)
Polio vaccine (OPV)	GPO-Mèrieux		Packaging, testing		8.23 million for children <5 years; 5 million for campaign	13.23 million (production capacity up to 20 million)	7.94 (105.04 million)
Measles, mumps, rubella mixed vaccine protection (MMR)	GPO-Mèrieux		Blending, filling freeze-drying, packaging, testing		0.89 million	0.89 million (batch size 33 000 vials (10 doses/vial)) (production capacity up to 2 million)	57.44 (51.12 million)
Hepatitis B vaccine protection (HB)	GPO-Mèrieux		Filling, packaging, testing		0.95 million	0.95 million (batch size 34 000 vials (2 doses/vial)) (production capacity up to 3.2 million)	43.23 (41.06 million)
Diphtheria, pertussis, tetanus, hepatitis B (DPT-HB)	GPO-Mèrieux			Yes	3.7 million	3.7 million in 2009 (imported by GlaxoSmithKline (Thailand) Co. Ltd, Biogenetech Co. Ltd, and 3.Masu Co. Ltd)	50.00 (185 million)
			Filling, packaging, testing			Batch size 62 000 vials (2 doses/vial) (production capacity up to 4 million)	65.14 (4.038 million)
Diphtheria, pertussis, tetanus combined vaccine (DPT)				Yes	2.5 million	2.5 million (imported by Biogenetech Co. Ltd, and Masu Co. Ltd)	9.49 (23.72 million)
Diphtheria and tetanus vaccine (dT)				Yes	4.18 million	4.18 million (imported by Biogenetech Co. Ltd, and Masu Co. Ltd)	5.50 (22.99 million)

GPO, Government Pharmaceutical Organization; QSMI, Queen Saovabha Memorial Institute.
a The data on demand are derived from vaccine allocations to provinces/districts for the fiscal year 2008.
b The data on supply are obtained from the relevant organizations.
c Price refers to the price per dose in 2008.
d Total vaccine expenditure, based on supply and price data: 833.892 million baht.
Source: NVCO (2009).

Table 3 Non-EPI vaccines: manufacturers/suppliers, production process, demand/supply and price data

Vaccine	Manufacturer	Production process		Finished product	Demand (doses)[a]	Supply (doses/year)[a]	Price (baht/dose (total vaccine expenditure))
		Upstream	Downstream				
Equine rabies immune globulin (ERIG)	QSMI	Yes				0.1 million bottles, 1000 IU/5 ml (production capacity up to 0.2 million)	520.00 (52 million)
Purified chick embryo cell rabies vaccine				Yes	0.11 million	110 000 (imported by Biogenetech Co. Ltd)	280.80 (30.088 million)
Vero cell rabies vaccine	GPO-Mèrieux		Blending, filling freeze-drying, packaging, testing		0.55 million	550 000 (batch size 70 000 vials (1 dose/vial)) (production capacity up to 0.8 million)	281.41 (154.775 million)
Influenza	GPO-Mèrieux		Filling, packaging, testing		0.8 million	800 000 (batch size 62 000 vials (0.5 ml/vial)) (production capacity up to 2 million)	228.58 (182.864 million)
Influenza				Yes	1 171 126	Imported by: Sanofi Pasteur Ltd	280.00 and 308.60
						GlaxoSmithKline (Thailand) Co., Ltd	308.60
						Norvartis Vaccines/Biogenetech	340.00
						Berna Biotech Co. Ltd	480.00
						Solway Co. Ltd	No information
Haemophilus influenzae type b				Yes	48 910	Imported by: Sanofi Pasteur Co. Ltd	588.50
						GlaxoSmithKline (Thailand) Co., Ltd	481.50
						MSD Co. Ltd	642.00
						Novartis Vaccines/Biogenetech	450.00

Continues...

Continued

Vaccine	Manufacturer	Production process		Finished product	Demand (doses)[a]	Supply (doses/year)[a]	Price (baht/dose (total vaccine expenditure))
		Upstream	Downstream				
Varicella VAR				Yes	133 332	Imported by: GlaxoSmithKline (Thailand) Co., Ltd	973.70
						Sanofi Pasteur Co. Ltd	856.00
Streptococcus pneumonia vaccine protection				Yes	56 805	Imported by Sanofi Pasteur Co. Ltd	802.50
Rotavirus vaccine				Yes	43 530	Imported by: GlaxoSmithKline (Thailand) Co., Ltd	1444.50
						MSD Co. Ltd	No information
Typhoid vaccine				Yes	18 156	Imported by: Sanofi Pasteur Co. Ltd	268.57
						Berna Biotech Co. Ltd	247.17
Human papilloma virus				Yes	58 105	Imported by: MSD Co. Ltd	No information
						GlaxoSmithKline (Thailand) Co., Ltd	No information

QSMI, Queen Saovabha Memorial Institute.
a Data from the Thai Food and Drug Administration, based on vaccines imported in 2008.
Source: NVCO (2009).

In recent years, the Thai Government has placed increasing focus on domestic vaccine development and production. Driven by concerns about timely vaccine access in the wake of the avian influenza outbreaks and the H1N1 pandemic influenza situation, as well as the higher prices of newer vaccines such as human papilloma virus, the stated policy objective is to strengthen Thailand's preparedness against vaccine-preventable diseases and reduce spending on imported vaccines. As stated by the then Public Health Minister, Witthaya Kaewparadai: "[V]accine development is a national agenda ... [its] direction ... in the long term must be addressed by the government … If we could develop vaccines by ourselves, that would mean standing on our own feet and no longer depending on other countries for imported vaccine" (Sarnsamak, 2009).

In this context, the National Vaccine Committee was established in 2001, with the mandate of promoting vaccine supply security and self-reliance in Thailand. The objectives of vaccine supply security and self-reliance were later formalized as national policy goals in the National Vaccine Policy in 2005, along with the objectives of promoting science and technology development for vaccine R&D and investment in domestic vaccine production. The National Vaccine Policy also enshrined the right of basic immunization for the Thai people.

NVCO was established in 2007 as the secretariat office of the National Vaccine Committee to oversee and facilitate the implementation of the National Vaccine Policy. In its capacity as the focal point for vaccine research and development, NVCO conducted an evaluation of vaccine research and development in 2008, with a view to developing recommendations to reinvigorate the vaccine industry and promote greater domestic production. NVCO has identified as a priority the development and production of ten vaccines for domestic use – dengue, diphtheria, tetanus, pertussis, mumps, measles, encephalitis, polio, hepatitis B and tuberculosis (Government Public Relations Department, 2010). The findings of the NVCO evaluation study are discussed in greater detail in Section 5.

5. The framework for local production and technology transfer

This section examines key aspects of the policy and legal environment in Thailand, with a view to discussing the operating environment for the pharmaceutical industry and analysing the existing policy approaches towards promotion of domestic vaccine development and production.

5.1 GPO influenza vaccine project

The 2009 declaration of the H1N1 influenza pandemic and the preceding avian influenza outbreaks in 2005 raised the spectre of insufficient supplies of antiviral treatments and vaccines to meet the world's needs. In the event of an influenza pandemic, it was estimated that there would be a need for

up to 13.4 billion doses of pandemic vaccine within a period of 6–9 months: WHO warned that the existing global production capacity and timely scale-up potential would result in a shortfall of several billion doses of vaccines needed to immunize the world. Furthermore, given that 90% of influenza vaccine production is located in 9 countries in Europe and North America, WHO anticipated that many developing countries, where the need for vaccines was likely to occur first, would have little or no access to them.[5]

In this context, WHO sought to increase and diversify influenza vaccine production in developing countries, with the expectation that large-scale seasonal influenza vaccine production in selected developing countries could be rapidly operational, cost-effective and sustainable, and could be switched to pandemic influenza production at short notice. Establishing or increasing domestic production of influenza vaccine in developing countries would decrease dependence on the availability and accessibility of vaccines produced by multinational manufacturers, and would also support outbreak responses by ensuring greater equity in deployment of vaccines in the early stages of a pandemic. Accordingly, the WHO Global Pandemic Influenza Action Plan to Increase Vaccine Supply (GAP) sought to effect a strategy for increasing the production capacity for seasonal influenza production in developing countries, as a means to ensure access to pandemic influenza vaccines.

Hence, a call for proposals was issued in October 2006 to fund developing country vaccine manufacturers willing to initiate domestic production of the influenza vaccine. Grant recipients were also expected to make up to 10% of their production output available to United Nations purchasers in the event of a pandemic. Six developing country manufacturers – from Brazil, India, Indonesia, Mexico, Viet Nam and Thailand – eventually received grants of US$ 2–2.7 million each to establish pilot facilities for the production of seasonal and pandemic influenza vaccine. All projects were initiated between June and September 2007.

The GPO influenza vaccine project commenced in 2007, with a grant of US$ 1.9 million from WHO for the purpose of establishing pilot facilities for the production of seasonal and pandemic influenza vaccine.

Before the GPO project, there was no domestic production of influenza vaccine. Thailand imported up to nearly 2 million doses of influenza vaccine in 2008. Of this, GPO-Mèrieux supplied 800 000 doses, by formulating and filling imported seasonal influenza vaccine; the remainder was imported as finished products. Although GPO currently produces only the Japanese encephalitis vaccine, it had previously produced diphtheria, tetanus and pertussis vaccine, tetanus vaccine, and diphtheria and tetanus vaccine. Production of these vaccines was discontinued 5 years ago due to the fact that the GPO production facility was not compliant with good manufacturing processes (GMP).

In this respect, WHO support can be seen as a significant step towards the revitalization of GPO's vaccine production operations. The GPO influenza

5 For more details, see WHO (2009a).

vaccine project also puts into effect the long-term component of Thailand's strategic framework for pandemic influenza vaccine preparedness – namely, to establish a human vaccine plant. The strategic framework, outlined in a policy recommendation paper entitled "National strategies on pandemic influenza vaccine preparation for Thailand" (hereinafter, the National Strategies paper), represents Thailand's national strategy for ensuring continuity and sustainability of pandemic vaccine supply, comprising four strategies for the immediate, medium and long term (HSRI & BIOTEC, 2007).

As a pharmaceutical manufacturer, GPO meets the prerequisites for vaccine development and production, namely established processes and facility with access to trained staff familiar with GMP requirements and necessary quality control/assurance and other regulatory standards. However, technical and advisory support from WHO, particularly in facilitating the acquisition of technology for influenza vaccine production, helped to resolve many of the issues and challenges that GPO would have otherwise had to address or overcome in the effort to initiate development and production of a new vaccine. Similarly, the National Strategies paper, while proposing the establishment of an influenza vaccine plant, noted the lack of experience and human resources in vaccine production on an industrial scale in Thailand and stressed the need for technology transfer, particularly in terms of the production plant and process design (HSRI & BIOTEC, 2007).

Both WHO and the National Strategies working group had determined that the transfer of technology for the development and production of influenza vaccine was the most effective and time-efficient route for developing countries to secure sustainable access to good-quality influenza vaccine technology. The major considerations in terms of technology transfer relate the assessment and selection of the appropriate production technologies and address the related intellectual property rights issues. These two issues are considered below.

5.1.1 Technology transfer

Under the GAP framework, WHO commissioned a review of production technologies for influenza virus vaccines in the context of their suitability for deployment in developing countries (WHO, 2009a). The use of egg-based production technology was determined as the best currently available, given the different considerations of capital investment, production time, regulatory requirements and technology transfer opportunities. The egg-based technology could also be used to produce both inactivated vaccine and live attenuated influenza vaccine, within the same production plant. This ability to switch production from inactivated to live attenuated vaccine was a vital element in the strategy to scale up production in a pandemic situation, since the live attenuated vaccine provided a much higher yield (approximately 50 times greater than for inactivated vaccine). In its review of vaccine production technologies, the National Strategies working group arrived at the same conclusions.

In light of the above, the first stage of the GPO influenza vaccine project began with R&D into the development of the virus strain to be used for the production of the seasonal influenza vaccine. Over a period of 2 years, and working with the assistance of an external consultant (a former staff member of a multinational pharmaceutical company), GPO was able to successfully produce inactivated seasonal influenza vaccine using the egg-based production technology.

In addition to technical assistance from the external consultant, transfer of technical know-how related to the production processes was effected through the International Technology Platform for Influenza Vaccine (ITPIV). ITPIV was established by the Netherlands Vaccine Institute with WHO/GAP support as a "technology hub" to offer a technology platform for the transfer of a single robust production process at pilot scale. Under the GAP framework, ITPIV provided a comprehensive technology package using the selected production technology – inactivated whole virion influenza vaccine produced in embryonated eggs – that could be transferred to vaccine manufacturers in developing countries. It is understood that staff members of GPO received technical assistance from ITPIV for the establishment of the production process of the inactivated seasonal influenza vaccine.

In the second stage of the project, GPO began developing the live attenuated influenza vaccine (LAIV) in order to increase vaccine yields sufficient to meet demand in a pandemic situation. LAIV was recommended, as noted above, for a number of reasons: the higher yield (roughly 50 times greater than for inactivated vaccine), the smaller infrastructure investment (including the use of the same building and equipment for seasonal influenza vaccine), simpler manufacturing process, and ease in vaccine administration (no injection). Using the Leningrad attenuated virus strain (supplied through the WHO negotiated licensing agreement; see Section 5.1.2) and with technical assistance from an external consultant, GPO developed and produced the working seed, from which the clinical lot (and later the industrial production lot) would be derived.

Reporting on the progress of GAP, WHO noted that a major barrier in initiating the influenza vaccine project was finding manufacturing partners to transfer technology; the transfer of bulk manufacturing technology was unsuccessful, causing delays in the initiation of projects (WHO, 2009a). Although WHO and the developing country manufacturers had access to assistance from consultants with expertise in the field during the development phase, the production phase involving the establishment of all processes and documentation from the start is a challenging task. In the case of influenza vaccine production, technical know-how and access to regulatory dossiers may present more significant challenges than patent issues. According to WHO, production and manufacturing know-how – even where the older production technology is used – may not be readily accessed outside of pharmaceutical companies.

In this context, the technology hub concept was seen as an effective and promising means to ensure the transfer of technology. This approach involved the bundling of the various components of available research, production knowledge, technical expertise, documentation, clinical dossiers and standard

operating procedures within one technology package – as was done by the Netherlands Vaccine Institute in ITPIV. This technology package can then enable technology transfer in a cost-effective and timely manner.

5.1.2 Intellectual property rights

In terms of intellectual property protection, WHO had conducted an evaluation and patent landscaping exercise under the GAP framework in an effort to identify the most feasible approach for vaccine development, both from the technical perspective, of increased global capacity for influenza vaccine production, and from the legal perspective, of intellectual property considerations (WHO, 2007). The evaluation concluded that the production technology to produce egg-based inactivated vaccines is already long established and it was unlikely that patents would create an absolute barrier to the production of vaccines via this process. There are, however, a number of patents relating to recent improvements to the process and final composition, but it is not clear that GPO has already assessed or evaluated the implications of these patents on the eventual use of its vaccine.

Access to LAIV technology and the Leningrad attenuated virus strain was made possible through a licensing agreement negotiated by WHO with Nobilon International BV in 2008. The LAIV technology was developed by the Russian Institute of Experimental Medicine, which licensed the exclusive rights to commercialize LAIV outside Russia to BioDiem Ltd, an Australian pharmaceutical company. BioDiem Ltd later licensed world manufacturing rights to Nobilon International BV[6] and marketing rights throughout the world except North America (WHO, 2009b; BioDiem, 2009).

Although WHO's patent evaluation exercise had considered that there were no intellectual property obstacles to the basic concept of making live attenuated influenza vaccines, and patents on the attenuated virus strain were geographically limited to Russia (WHO, 2009a), the vaccine development process would still be too lengthy and costly without access to the original development and regulatory dossiers documenting vaccine characterization and safety.

The licensing agreement with Nobilon International BV enabled access to the original development and regulatory dossiers and the associated knowledge for seasonal and pandemic influenza production. Nobilon International BV granted WHO a nonexclusive licence to develop, register, manufacture, use and sell seasonal and pandemic LAIV produced on embryonated chicken eggs. It also allowed the Institute of Experimental Medicine in Russia to supply WHO with LAIV reassortants. Under the licensing agreement, WHO is permitted to grant a sub-licence to vaccine manufacturers in developing countries working within the framework of WHO/GAP. Vaccine manufacturers to whom a sub-licence is granted would be able to manufacture and distribute seasonal and

6 Nobilon International BV is a subsidiary company of Schering-Plough, which was acquired by Merck in 2009.

pandemic influenza vaccines royalty-free to the public sector in developing countries (PharmaNews.eu, 2010).

Given the patent evaluation study and the licensing agreement negotiated by WHO, the issue of intellectual property rights did not arise as a major consideration for GPO in proceeding with the influenza vaccine project. It is clear, however, that intellectual property and licensing issues have been a major consideration for WHO in its effort to establish influenza vaccine projects in developing countries. It also remains to be seen whether other aspects of intellectual property rights and licensing will arise at a later stage. Given that the licensing agreement with Nobilon International BV restricts the distribution of influenza vaccines to the public sector, it may be likely that issues relating to sale or distribution to the private sector or export outside of the GAP framework will arise, as may the question of royalty payments to the various technology licensors. This eventuality is explicitly noted by BioDiem Ltd on its website.

5.2 Assessment of GPO influenza vaccine project

In collaboration with Silapakorn University (for use of its semi-industrial influenza vaccine plant), GPO has completed the bulk production and filling of the H1N1 influenza vaccine. Phase II clinical trials are now under way. The Vaccine Trial Centre of the Faculty of Tropical Medicine at Mahidol University is conducting the clinical trial with participants in 3 age groups: adults (18–49 years), young adults (12–18 years) and older people (>49 years). At the time of writing (i.e. mid-2010), the initial trials were expected to be complete by the end of 2010, and a second clinical trial was planned for the seasonal influenza vaccine developed by GPO, following completion of the trial for the H1N1 vaccine.

The goal is for GPO to eventually build capacity for the manufacture of 2–3 million doses of seasonal inactivated influenza vaccine a year, with the ability to convert production process to produce the LAIV, with a production capacity of at least 60 million doses of pandemic influenza vaccine sufficient to immunize the entire Thai population in the event of a pandemic. The GPO influenza project enjoys the active support of the Thai Government, since it is regarded to be a crucial component of the national pandemic preparedness plan. The Thai Government has taken several measures, including the increased use of seasonal influenza vaccine, to establish the domestic market for the vaccine, and has also approved financial support of 1.411 billion baht (US$ 45 730 000) to GPO to enable the building of an industrial-level manufacturing plant.

Although the scenario for the future looks promising, a number of factors will be critical in ensuring the success and sustainability of the project. Apart from the issues of technology transfer and intellectual property rights discussed above, the National Strategies paper also highlighted the following (HSRI & BIOTEC, 2007): First, there is a need for a guaranteed supply of critical components; in particular, the egg-based production technology demands the continuous supply of specific pathogen-free eggs or embryonated eggs.

These eggs are currently imported, and the concern is that supplies may well be jeopardized in an emergency situation. Second, it should be expected that further technology and know-how transfer will be required to strengthen the R&D and production capacities in GPO to ensure efficacy of the vaccine, including research on adjuvants, production efficiency and standards. Third, human resource development will be an important factor, given that vaccine production at an industrial level will require personnel with expertise. It is estimated that the personnel numbers will have to be increased from the current 30 to 180 when the new production facility is in operation.

5.3 The legal and policy environment for domestic vaccine production

The outbreaks of H5N1 and the pandemic H1N1 influenza helped to focus renewed attention on domestic vaccine development in Thailand. The threat of the H5N1 outbreak was taken seriously, and a multisectoral working group was appointed to formulate the National Strategic Plan for Avian Influenza Control 2005–2007, which was adopted by the Cabinet in 2005. Another working group was appointed by the Deputy Prime Minister in 2007 to develop the second national plan, which was to be aimed at ensuring availability and sustainability of vaccine supply during an avian influenza pandemic.

The second working group's deliberations resulted in the 2007 policy paper, the National Strategies paper, which represented a strategic framework for pandemic influenza vaccine preparedness comprising four strategies (HSRI & BIOTEC, 2007). When WHO made its announcement on pandemic H1N1 influenza in June 2009, the Thai authorities considered themselves ahead in their planning for pandemic influenza preparedness, since the strategies proposed were also relevant and applicable. For the immediate and medium term, the National Strategies paper recommended stockpiling of finished vaccine and stockpiling of bulk vaccine; while for the longer term, the recommendation was to consider the option of modifying an already existing veterinary vaccine plant for production of human vaccine in an emergency situation or to establish a new human vaccine plant. The National Strategies paper noted that the strategy to stockpile vaccines should be deemed only a short-term measure – and an unreliable one. If a pandemic were to occur, vaccine access from external sources would probably be compromised, and the stockpiled vaccines would be sufficient only for deployment to high-priority groups. A more permanent strategy would be the development of domestic capacity to manufacture influenza vaccine.

The GPO influenza vaccine project is seen as the implementation of the long-term strategy – the establishment of a new human vaccine plant recommended by the National Strategies paper. Hence, it has the Thai Government's political and financial support: the Thai Government allocated a budget of 1.411 billion baht for the construction of the GPO industrial influenza vaccine plant (see also Section 5.1), which is planned as a WHO GMP-certified plant with the capacity to produce 2 million doses of inactivated injecting vaccines per year. In the event of a pandemic influenza outbreak, production can be switched

to live attenuated vaccine to enable production of approximately 60 million does per year, 30 times that of the inactivated type, to cover the population of Thailand. Construction began in mid-2009 and the plant is expected to be able to commence production operations in 2013.

5.3.1 National Vaccine Policy

Apart from the strategic considerations for pandemic preparedness planning, there exists specific policy guidance for the broader context of vaccine R&D and development in Thailand. Premised on the goals of self-reliance and vaccine supply security, the National Vaccine Policy 2005[7] seeks to promote the development of science and technology for vaccine R&D, quality control and assurance, human resource development and increased investment in domestic vaccine production.

The policy identified the need for a clear strategy to promote opportunities and build capacity for vaccine R&D, and for greater coordination of all parties working on vaccine R&D at the national level. As noted above, NVCO undertook an evaluation exercise to identify the reasons for the ineffective implementation of the National Vaccine Policy, and the key challenges to sustainable domestic vaccine development and production. Among other things, the NVCO study[8] found that the lack of effective linkages between vaccine research and manufacturing, the lack of essential infrastructure needed for development (e.g. pilot plant and GMP-compliant industrial plant) and lack of appropriate and qualified personnel would need to be addressed.

To address these issues, NVCO is developing a "road map" intended to support and advance domestic vaccine development. This effort is seen as a potential driver for effective implementation of the National Vaccine Policy, providing the needed coherence and planning for each stage of vaccine development. A National Vaccine Institute is proposed (the draft regulation for its establishment was submitted for approval by the Cabinet in September 2010 , i.e. at the time of writing this study), which will have the mandate of coordinating and developing the capacity of the vaccine network in Thailand (comprising universities, government agencies and producers), including the implementation of projects to fill identified gaps in infrastructure strengthening, human resource development, and facilitation of the development and eventual production of identified priority vaccines.

Although the influenza vaccine project has been an important step towards revitalizing GPO's vaccine development and production, the broader context of vaccine development can be expected to receive greater policy focus with the NVCO road map and the expected establishment of the National Vaccine Institute.

7 Information based on unofficial translations of the relevant sections of the National Vaccine Policy, available only in Thai at http://www.nvco.go.th/attach/ebook2.pdf.

8 Based on unofficial translations of the relevant sections of the study. See NVCO, 2009.

5.3.2 R&D investment and infrastructure

The National Biotechnology Policy Framework 2004–2011 sets out the policy directions for "propelling Thailand into a knowledge-based economy", including inter alia, through the establishment of infrastructure and human resources for development of new biotechnology, such as genomics and bioinformatics and encouraging investment in life sciences. In line with this policy approach, the Thailand Board of Investment provides incentives to encourage greater foreign investment in the industry's R&D. The Board of Investment's incentive package comprises an 8-year corporate income tax exemption, an additional 50% corporate income tax break for 5 years where facilities are located in science and technology parks, and an exemption of import duty on machinery (BIOTEC, 2007).

It is understood that this scheme, which began in 2007, has attracted only nine projects so far (Viboonchart, 2010). One factor for this low subscription, as pointed out by an interviewee in the industry, may be that the tax exemption period is too short, given that the timeframe for new drug and vaccine development stretches beyond 8 years. Financial incentives are clearly not the only considerations for the biotechnology and vaccine industry; other essential factors, such as the availability of skilled personnel and access to markets, may be the decisive factors. The industry interviewee pointed out that although GPO dominated the public-sector market in Thailand, there was still potential to access the private-sector market and to use Thailand as the base for export markets.

NSTDA was established to be the driving force for a broad-based, systematic approach to rapid development of science and technology in Thailand. Set up as an independent government organization, NSTDA provides technical assistance and R&D services to Thai industry. NSTDA also implements in-house research at four national centres: the National Metal and Materials Technology Center, National Electronics and Computer Technology Center, National Nanotechnology Center and BIOTEC.

Housed at the Thailand Science Park, these national centres also provide the infrastructural facilities for research within their respective fields, such as ready-made wet laboratories for rent, and long-term land leases. BIOTEC, for example, operates research units with specialized laboratories, incubator units, pilot plants and greenhouses, with over 500 members of staff conducting research in agricultural science, biomedical science and environmental science, among others. In public health, BIOTEC focuses on R&D in diseases such as malaria, tuberculosis and dengue.

Although much attention has been drawn to the vaccine industry in recent years as a result of concerns over the influenza pandemic, the discussion above indicates that the policy focus on science and technology in Thailand, particularly with regard to the biotechnology and pharmaceutical industries, predated the influenza outbreaks. The existing policy approach, however, appears to be directed mainly at promoting private-sector investment in the biotechnology industry, through the offering of financial and tax incentives,

coupled with infrastructural development for the industry, as described above. Although this indicates a degree of commitment and initiative from the Thai Government, concern remains over the still relatively low level of public investment in R&D (Poopat, 2010). Thailand's overall R&D expenditure is reported at 0.24% of GDP, lower than that of its neighbours in the region, with Malaysia and Singapore investing, respectively, 3 and 10 times more (field interviews). A question that arises is whether the focus on private-sector investment can ensure a national R&D agenda that is able to adequately meet the public interest and, in particular, public health needs.

The NVCO initiative in formulating a road map to intensify focus on R&D and production of specific vaccines is a welcome development. The road map can help to further illuminate the public health priorities for vaccine development, and identify the challenges for meeting these priorities. NVCO has urged for higher levels of public funding to implement the road map but, as pointed out by an interviewee from the Ministry of Public Health, NVCO needs to boost its capacity to be able to effectively implement its road map. The proposed National Vaccine Institute, when established, will have a clear mandate for decision-making and will be able to provide greater institutional coherence and coordination, but it will also have similar needs in terms of funding and capacity, given that it will be staffed from the current NVCO.

5.3.3 Intellectual property rights and the regulatory process

Beyond the policy and strategic directions for vaccine development in Thailand, the overall legal framework in terms of intellectual property protection and regulatory approval must also be taken into account.

Although patents have not been considered a significant barrier to the manufacture and production of traditional vaccines using older production technologies, intellectual property rights are increasingly a vital consideration in the development and production of vaccines. As noted above, intellectual property and licensing issues were an important consideration when WHO sought to identify production processes that could rapidly render high yields of influenza vaccines. Although the WHO patent evaluation exercise noted that patents did not present significant barriers for the majority of existing vaccines, it did find patents on recent improvements to the existing egg-derived production processes, on cell lines that are used to produce cell-culture-derived vaccines, and on adjuvants used to reduce the vaccine dosage (WHO, 2007). These findings indicate that there is still a degree of uncertainty with regard to potential intellectual property barriers, and it will be important for GPO to consider the specific patent landscape applicable in Thailand for the production of its seasonal and pandemic influenza vaccines.

Intellectual property rights can also be expected to have a significant impact within the broader context of vaccine R&D and development in Thailand. Vaccine manufacturers in developing countries have raised concerns that their entry into the vaccine market will be impeded by complex patent landscapes for the new generation of vaccines, and they have stressed the need for greater focus on building capacity for the handling of intellectual

property issues (Jadhav et al., 2009). A study has found that at least 81 United States patents related to human papilloma virus vaccines have been granted (Morgan, 2010). An earlier patent landscaping exercise by the Malaria Vaccine Initiative also found a complicated patent landscape for the top 10 antigens for malaria, comprising 167 patent families filed by 75 different organizations (Shotwell, 2007). In Thailand, a study on the status of biotechnology-related patents found over 440 such patents granted over the period 1981–2007 (Changthavorn & Chanvarasuth, 2010). Although this is still a relatively small number, there is an obvious preponderance of patents within the medical/pharmaceutical category, with 51% of those patents being related to drugs, vaccines and biomaterial products. The analysis also indicated that 85% of the biotechnology patents granted during the period 1980–2005 were foreign-owned, with individuals or companies from the United States and Japan holding the highest number of patents.

The commercial successes of the human papilloma virus and pneumococcal vaccines, coupled with the global demand for influenza vaccines, have led to the pharmaceutical industry's renewed interest in vaccine products, now no longer considered low-profit products. It can be expected that the vaccine-related patent landscapes in vaccine-producing developing countries such as Thailand will become increasingly populated, as the pharmaceutical industry seeks patent protection over new vaccine products and their related production processes and components. There will be a need to examine the impact of such protection on the access to technology and availability of vaccines.

Another factor that can have significant implications for sustainable domestic development and production of vaccines relates to the regulatory requirements for the marketing approval of vaccine products. Unlike small-molecule drugs, follow-on vaccines cannot be approved for marketing on the basis of bioequivalence as generic drugs. Hence, even where a new vaccine is closely modelled on an existing one, its safety and efficacy must be demonstrated independently in clinical trials – although regulators may accept evidence that the new vaccine consistently produces a similar protective response shown in previous trials. This makes much smaller trials possible.

To supply the domestic market, manufacturers must obtain the national regulatory authority's marketing approval for the use, distribution and sale of their vaccines in the domestic market. In terms of exports to developing countries, obtaining WHO prequalification is a practical way for manufacturers to enter markets in developing countries through sale of their vaccines to procurement agencies such as the United Nations Children's Fund (UNICEF)/Global Alliance for Vaccines and Immunisation (GAVI). WHO prequalification is preconditioned on obtaining marketing approval from the national regulatory authority in the country of manufacture, which has been defined as "functional" by the WHO. The Thai Food and Drug Administration, along with the National Control Laboratory, was certified as functional in 2008 – that is, it fulfilled the six regulatory functions defined by WHO to assess, monitor and improve national regulatory authorities.

There is, however, a need for greater capacity within the Thai Food and Drug Administration and the National Control Laboratory. The current number of staff with a mandate on vaccine regulatory approval is six. As a means of capacity-building and strengthening of national regulatory authorities, WHO has introduced the concept of parallel review of dossiers, wherein national regulatory authorities of two countries collaborate on a review of a vaccine dossier; for example, the regulatory authorities of Thailand and Australia have undertaken a parallel review of the Japanese encephalitis vaccine, and the regulatory authorities of India and Canada have undertaken a parallel review of the meningitis vaccine. This mechanism, apart from strengthening capacity of regulatory authorities in developing countries, also allows for a distribution of work between regulatory authorities, which is helpful where capacity is limited.

The Thai Food and Drug Administration's certification thus paves the way for vaccines produced in Thailand to receive WHO prequalification. Thailand is the eighth vaccine-producing developing country with eligibility for WHO-prequalified products (the other seven are Brazil, Bulgaria, Cuba, India, Indonesia, the Russian Federation and Senegal). The Thai Food and Drug Administration's functional status may provide an impetus for greater private-sector investment to locate vaccine production in Thailand, as a base from which to enter export markets in the region.

6. Analysis of the GPO project

GPO has had some notable successes in its R&D and manufacture of generic medicines, particularly in the case of ARVs. Its capacity to develop and produce GPO-Vir S was a decisive factor prompting the Thai Government to adopt its policy on universal access to ARV treatment. GPO was also able to produce its version of oseltamivir, GPO-A-FLU, to meet the demand for antiviral treatments in the wake of the H1N1 influenza outbreak in Thailand. It can be said that GPO has built sufficient research and production capacities in terms of small-molecule drugs.

In the case of the influenza vaccine project, a number of challenges remain. As noted in Section 5.2, a number of critical issues will need to be addressed to ensure the success and sustainability of the project, namely the need for a guaranteed supply of critical components for production, including a continuous supply of embryonated eggs; and the need to further strengthen the R&D and technological capabilities and human resource capacities of GPO.

The GPO influenza vaccine project illustrates the importance of government support in building domestic capacity for vaccine production. Pandemic preparedness, including the purchase and domestic production of vaccine, has been treated as a matter of national security. Hence, the Thai Government has extended both policy and financial support to facilitate the execution of the project. Policy measures, such as implementation of seasonal influenza vaccination as part of its pandemic preparedness plan, will build up the demand for the GPO-produced seasonal influenza vaccine. It is also clear that

GPO's status as a public-sector pharmaceutical manufacturer has helped this process. In this instance, it was possible to ensure a coherence and balance between the national priority for pandemic preparedness, the public health imperative of ensuring equitable access, and the industrial policy objective of promoting domestic production.

Although the GPO influenza vaccine project is regarded as a means to revitalize vaccine development in GPO, it must be noted that the main challenges to new vaccine development – technology acquisition and intellectual property issues – were largely addressed with significant technical support from WHO. This experience provides an illustration of how international technical cooperation and technology transfer programmes can play an essential role in strengthening domestic capacity for vaccine development in developing countries. It does, however, raise the question of whether GPO would be able to deal with these challenges in the absence of such support. A number of options for addressing these challenges within the broader context of promoting vaccine development in Thailand are discussed below.

7. Implications of local production and related technology transfer on access to vaccines

Ensuring the timely access to needed vaccines is the explicit policy objective of Thai Government support for the GPO influenza vaccine project. As stated in the National Strategies paper, the primary concern for Thailand in the event of a pandemic is access to sufficient supplies of vaccine. In evaluating the options for a sustainable pandemic vaccine supply, the National Strategy paper cautioned that reliance on imported vaccines would be an unreliable approach and, at best, only a short-term strategy. Similar concerns have been expressed by WHO, which had cautioned that many developing countries would have little or no access to needed vaccines in the event of a pandemic. Given that most influenza vaccine production is located in Europe and North America, the expectation is that vaccine manufacturers would be required to first meet the needs within their domestic markets in the event of a pandemic. Where there may be surplus supply, the concern is also that for-profit companies may price the needed vaccines at levels unaffordable to developing countries.

In light of the above, strengthening the domestic capacity to produce vaccines (including ensuring the transfer of needed technology and know-how) has been seen as an important national security issue for Thailand. As noted in Section 5, the GPO influenza vaccine project is regarded as the implementation of Thailand's strategic framework for pandemic influenza vaccine preparedness – as a means to ensure continuity and sustainability of pandemic vaccine supply for the Thai population. In line with the strategy adopted by GAP – increasing production capacity for seasonal influenza production in developing countries as a means to ensure access to pandemic influenza – the production output for the GPO project is expected to be 203 million doses of seasonal inactivated

influenza vaccine per year, with the ability to convert the production process to produce a minimum of the 60 million doses required to immunize the entire Thai population in the event of a pandemic.

Although it is too early to determine the actual impact of the GPO influenza vaccine project on access to vaccines – the GPO influenza vaccines are still under clinical trials – it can be envisaged that after approval, the vaccines will be available for use within the public health system. Section 4 describes Thailand's well-established immunization programme and delivery system; it would be reasonable to assume that the Thai population's access to both seasonable and pandemic influenza vaccines will be an achievable objective.

As a state-owned enterprise with an explicit public health mandate, GPO's efforts to develop and manufacture influenza vaccines represent a clear example of local production with access as the primary goal. Vaccine manufacturing in the recent past was largely seen as a low-profit, high-volume business, and in developing countries it tended to have a greater component of public investment compared with pharmaceutical production. In fact, five of the six developing country manufacturers implementing the GAP influenza vaccine projects are state-owned enterprises or at least have significant public-sector investment. This heavy public-sector involvement can arguably be an important means of facilitating and ensuring access to vaccines.

Public-sector investment can also be an important driver for strengthening domestic capacity in vaccine development, both upstream and downstream, and in both the public and private sectors. Given the increasing complexity of the new vaccines, a major barrier to the market entry of manufacturers in developing countries will be the lack of technological capacity. Building the capacity of vaccine manufacturers in developing countries will require intensive technological and know-how transfer, and the attendant financial costs. Public-sector involvement can also be important in addressing the challenges of creating the conditions that can reduce the risks and costs of R&D and upgrading – in short, an enabling environment to sustain innovation in, and development of, vaccines in developing countries.

The GPO influenza vaccine project further illustrates the importance of building local vaccine production capacity beyond the requirements of a pandemic situation. The existence of a multiplicity of vaccine manufacturers can be presumed to have positive access implications. In the long term, increasing the number of vaccine manufacturers in developing countries, with the twin objectives of ensuring vaccine supply security and introducing greater competition, will be an important strategy for price reduction and access increase.

8. Policy-relevant findings

In terms of broader lessons for the objective of promoting sustainable vaccine development and production in Thailand, a number of observations might be made.

First, there is a need to promote an enabling environment for vaccine development, from the upstream R&D activities to the downstream capabilities in product development and industrial production. As noted in Section 3.4, the gap between capabilities in basic R&D and capabilities in product development and industrial production can be narrowed through a greater focus on identifying the needs for capacity-building and technological advancement in mid- and downstream vaccine development, namely toxicology, quality control and assurance, and production scale-up. The establishment of a coherent national vaccine network comprising the various actors from upstream to downstream of the vaccine development process, as proposed by NVCO for its vaccine development road map, can help to identify these needs and build the necessary linkages to address the gaps. Equally important, a road map for vaccine development can and should be used to highlight and address the gaps between promotion of R&D and technological advancement, and the public health priority for affordable access, within the vaccine development process.

The second observation relates to the issue of technology and technical know-how. As discussed above, a major barrier in initiating the influenza vaccine project was finding willing manufacturing partners to transfer technology. Production and manufacturing know-how – even where older production technology is used – may not be readily accessed outside of pharmaceutical companies. It can be envisaged that the effective transfer of technology will present a challenge in the development of other vaccines. Effective technology transfer, however, requires not only the right partner but also the capacity to identify the technology needs. Although the joint venture initiative between GPO and Sanofi Pasteur was ostensibly driven by the desire to promote domestic vaccine development through the transfer of technology and know-how in a partnership with an established vaccine producer, the concern is that this aspect of the joint venture has not been fully realized, due in part to the lack of clarity in terms of the technology needs and priorities of the GPO.

Beyond such partnerships, there may be a need to explore other innovative ways of technology acquisition. As demonstrated in the influenza vaccine project, the technology hub concept – wherein public-sector knowledge and expertise are accumulated to generate a robust technology package for transfer to multiple recipients – can be a potentially promising means to ensure the transfer of technology and continued R&D. There should be further analysis as to how this model of public-sector technology transfer can provide an alternative to, or be a complement of, private-sector bilateral technology licensing arrangements. Multinational pharmaceutical companies do transfer technology to manufacturers in developing countries, but such arrangements may be largely dependent on appealing to the commercial interests of the multinationals and may often include restrictions on the use of the technology.

The third observation relates to the need to address the intellectual property issues. As discussed in Section 5.1.2, it is clear that intellectual property and licensing issues have been a major consideration for WHO in its effort to establish influenza vaccine projects in developing countries. Although these aspects were addressed before the start of the influenza vaccine project, it

is possible that when the vaccines are eventually manufactured, some issues relating to sale or distribution to the private sector or export outside of the GAP framework will arise, as may the question of royalty payments to the various technology licensors.

Clearly, there is a need to address the impact of intellectual property on vaccine development in Thailand. NVCO's efforts in formulating the road map for vaccine development in Thailand should incorporate an assessment of intellectual property rights issues. There is a need for greater focus on building capacity on intellectual property management issues and the negotiation of technology licensing agreements. As noted in Section 3, there is significant capability and activity in the basic research and preclinical stages of vaccine development in Thailand, but as efforts move downstream towards the industrial production and manufacturing it is likely that intellectual property issues will become more prominent. The Developing Country Vaccine Manufacturers Network has expressed concern that developing country manufacturers' entry into the vaccine market will be increasingly impeded by complex patent landscapes for the new generation of vaccines (Jadhav et al., 2009).

Beyond addressing these immediate concerns, there should also be a more critical assessment of the role of intellectual property protection in the context of innovation and access issues, with a view towards alternative innovation systems. Exclusive reliance on a patent-driven system of innovation may also have adverse implications on access to the end-product, as has been well-illustrated in the case of Thailand's decision to grant compulsory licences to enable local production or import of more affordable generic medicines (see UNCTAD, "Using Intellectual Property Rights to Stimulate Pharmaceutical Production in Developing Countries: A Reference Guide", New York and Geneva, 2011, pp. 125-127).

References

Bangkok Post. First vaccine exports bound for Australia. *Bangkok Post*, 21 September 2010 (http://www.bangkokpost.com/news/health/197303/first-vaccine-exports-bound-for-australia).

BioDiem. Melbourne, BioDiem Ltd., 2009 (http://www.biodiem.com/index.php/technology/laiv).

BIOTEC. *BOI debuts incentives for biotech industry*. Pathumthani, National Center for Genetic Engineering and Biotechnology, 2007 (http://www.biotec.or.th/biotechnology-en/en/newsdetail.asp?id=2186).

Bureau of Policy and Strategy, Ministry of Public Health. *Health policy in Thailand 2009*. Bangkok, Bureau of Policy and Strategy, Ministry of Public Health, 2009 (http://whothailand.healthrepository.org/handle/123456789/589).

Changthavorn T, Chanvarasuth N. Thailand biotech patent: Status and opportunities. *Thailand Biotech Guide 2008–2009*, 2010 (http://home.biotec.or.th/NewsCenter/my_documents/my_files/1EA97_4931.pdf).

GPO. *History*. Bangkok, Government Pharmaceutical Organization, 2007 (http://www.intergpomed.com/default.aspx?tabid=2128).

GPO. *Annual report 2008*. Bangkok, Government Pharmaceutical Organization, 2008.

GPO. *Annual report 2009*. Bangkok, Government Pharmaceutical Organization, 2009.

Government Public Relations Department. *Thailand moves to set up national vaccine institute*. Bangkok, Government Public Relations Department, 2010 (http://thailand.prd.go.th/view_around_thailand.php?id=5170#).

HSRI, BIOTEC. *National strategies on pandemic influenza vaccine preparation for Thailand: Policy recommendation paper*. Nonthaburi, Health Systems Research Institute, National Center for Genetic Engineering and Biotechnology, 2007 (English version published 2008; http://dspace.hsri.or.th/dspace/handle/123456789/601).

Hongthong P. Spreading influence. *The Scientist: Transformational Science – Life Sciences in Thailand*, 2010, May (http://www.the-scientist.com/templates/trackable/display/supplementarticle.jsp?name=thailand&id=57323).

Jadhav SS, et al. Emerging markets and emerging needs: Developing countries vaccine manufacturers' perspective and its current status. *Biologicals*, 2009, 37:165–168.

Morgan K. An HPV vaccine cheap enough for the developing world? Could be. *Duke University Office of News and Communications*, 13 July 2010 (http://www.dukenews.duke.edu/2010/07/HPV.html).

Muangchana C, et al. Immunization policy development in Thailand: The role of the Advisory Committee on Immunization Practice. *Vaccine*, 2010, 28S:A104–A109.

NVCO. *Evaluation of the current situation of vaccine development in Thailand*. Nonthaburi Department of Disease Control, National Vaccine Committee Office, 2009 (http://www.nvco.go.th/attach/ebook1.pdf).

OPM. *Regulations on government procurement*. B.E. 2535. Bangkok, Office of Prime Minister, 1992.

PharmaNews.eu. Schering-Plough announces collaboration with World Health Organization. *PharmaNews.eu*, 24 February 2010 (http://www.pharmanews.eu/schering-plough/136-schering-plough-announces-collaboration-with-world-health-organization).

Poopat T. Investment strategies. *The Scientist: Transformational Science – Life Sciences in Thailand*, 2010, May (http://f1000scientist.com/article/display/57308/).

Sarnsamak P. Push to revive Thailand's vaccine industry. *The Nation*, 14 August 2009 (http://www.nationmultimedia.com/2009/08/14/national/national_30109761.php).

Senior K. Dengue vaccine efficacy trials in progress. *The Lancet Infectious Diseases*, 2009, 9: 662–663.

Shotwell SL. Patent consolidation and equitable access: PATH's malaria vaccines. In: Krattiger A, et al., eds. *Intellectual property management in health and agricultural innovation: A handbook of best practices*. Oxford, MIHR, 2007.

UNCTAD. *The least developed countries report 2007: Knowledge, technological learning and innovation for development*. Geneva, United Nations Conference on Trade and Development, 2007.

UNDP. *Human security, today and tomorrow: Thailand human development report*. Geneva, United Nations Development Programme, 2009 (http://hdr.undp.org/en/reports/nationalreports/asiathepacific/thailand/name,19749,en.html).

UNDP. *International human development indicators: Thailand*. Geneva, United Nations Development Programme, 2010 (http://hdrstats.undp.org/en/countries/profiles/THA.html).

Viboonchart N. BOI seeks more investment in biotechnology. *The Nation*, 7 August 2010 (http://www.nationmultimedia.com/home/2010/08/07/business/BoI-seeks-more-investment-in-biotechnology-30135401.html).

Vonghangool V, Pham HT. A shot in the arm. *The Scientist: Transformational Science – Life Sciences in Thailand*, 2010, May (http://www.the-scientist.com/templates/trackable/display/supplementarticle.jsp?name=thailand&id=57323).

WHO. *Mapping of intellectual property related to the production of pandemic influenza vaccines*. Geneva, World Health Organization, 2007 (http://www.who.int/entity/vaccine_research/diseases/influenza/Mapping_Intellectual_Property_Pandemic_Influenza_Vaccines.pdf).

WHO. *Global pandemic influenza action plan to increase vaccine supply: progress report 2008*. WHO/IVB/06.13. Geneva, World Health Organization, 2009a. (http://www.who.int/vaccines-documents/DocsPDF06/863.pdf).

WHO. *Questions & answers on the WHO–Nobilon agreement for access to the LAIV TECHNOLOGY*. Geneva, World Health Organization, 2009b (http://www.who.int/vaccine_research/Questions_and_Answers_Nobilon.pdf).

WHO. *Immunization surveillance, assessment and monitoring*. Geneva, World Health Organization, 2011 (http://apps.who.int/immunization_monitoring/en/).

Annex I: Sample interview questions

Section A

These are open-ended questions that will be asked of interview subjects, with the aim of establishing the appropriate context for the study. The interview session will typically commence with a series of questions to compile data and establish factual details such as these:

1. Determining vaccine needs and priorities for vaccine supply in Thailand:

- Which agencies are responsible for the development and implementation of the national immunization policy?
- How is the need for vaccines supplied – by domestic firms or through imports?
- What are the size and the key characteristic of the domestic vaccine market?

2. Establishing the current level of technological capability for vaccine R&D and production in Thailand, including details of the H1N1 influenza vaccine development project at GPO:

- How many domestic vaccine producers are there in Thailand? Are they involved in both the upstream and downstream stages of vaccine R&D, i.e. from basic research to production?
- Do firms in Thailand export vaccine products? What is the size of the vaccine export market?
- What was the key component(s) of technology transfer in the H1N1 influenza vaccine development project? And how was it addressed?

3. Assessing the legal and policy environment for pharmaceutical R&D and innovation in Thailand:

- What are the key policies related to the promotion of pharmaceutical R&D and innovation?
- Is there specific policy guidance related to vaccine R&D and production? If so, what are the main policy priorities?
- Supplementary questions may be asked to elicit further details, depending on the interviewee's area of work and familiarity with/expertise on the issues.

Section B

In addition to the questions in Section A, the interviewees were asked questions related to the dynamics of vaccine R&D, technology transfer and production in Thailand. The list below is intended only as a guide to the conduct of the interview sessions; the questions will be directed to the interviewees as appropriate, depending on their area of work and expertise.

1. At which stage of vaccine R&D process chain do you find the most need for new technology or know-how?

- p Upstream (basic scientific research and laboratory-based R&D)
- p Mid-stream (scale-up and preclinical stages)

- Downstream (clinical stage and industrial manufacturing)

2. In your experience, what has been the main channel for transfer of technology and know-how? Is licensing of technology involved? Potential answers may include:

- Research collaboration or co-development with partners
- Joint ventures and mergers/acquisitions
- Public sector technical assistance (universities, international organizations)

3. From whom do you most often license technology? Potential answers may include:

- Public sector (e.g. technical assistance agencies (international nongovernmental organizations), public-sector research institutes)
- Private sector (multinational corporations or smaller companies)
- Product development partnerships or public–private partnerships (e.g. Drugs for Neglected Diseases Initiative, Medicines for Malaria Venture)

4. In your experience, have you found, or have knowledge of, a successful model of technology transfer in vaccine R&D? Please describe and indicate the relevant aspects of that model.

5. Have you faced difficulties negotiating licensing agreements? If so, what has been the main obstacle? Potential answers may include:

- Finding suitable partner(s)
- Insufficient capacity or experience
- Unfavourable terms and conditions (e.g. excessive royalties, restrictions including geographical/market and export limitations)
- Exclusion of technical know-how

6. Have intellectual property rights been an obstacle in getting access to technology? If so, what has been the main problem? Potential answers may include:

- Lack of information or knowledge about intellectual property ownership
- Refusal to license technology
- High transaction costs (e.g. numerous intellectual property holders)

7. Is the policy and legal environment in Thailand conducive to promoting vaccine R&D? Which initiative has been most helpful?

8. Which of the following have you found to be major obstacles to new product development?

- Inadequate infrastructure (including utilities, skilled personnel, equipment and facilities)
- Insufficient financing/capital
- Onerous regulatory requirements/lack of generic pathway
- Access to technology
- Availability of technical know-how and skills
- Intellectual property (including blocking access to new technologies, and risk of infringement)

Annex II: Interviewed individuals and institutions

Representatives of producers/manufacturers

Achara Eksaengsri, Director, Research and Development Institute, Government Pharmaceutical Office of Thailand

Sumana Khomvilai, Thai Red Cross/Queen Saovabha Memorial Institute

Hong Thai Pham, Joint Managing Director, BioNet-Asia Co., Ltd.

Sit Thirapakpoomanunt, Director, Department of Biological Products, Government Pharmaceutical Office of Thailand

Vitoon Vonghangool, Managing Director, Bio-Net Asia Ltd

Ponthip Wirachwong, Research and Development Institute, Government Pharmaceutical Office of Thailand

Representatives of Thai Government agencies

Suphamit Chunsuttiwat, National Vaccine Committee Office, Department of Disease Control, Ministry of Public Health

Darin Kongkasuriyachai, BIOTEC, National Science and Technology Development Agency

Charung Muangchana, National Vaccine Committee Office, Department of Disease Control, Ministry of Public Health

Duanthanorm Promkhatkeaw, Medical Biotechnology Center, Department of Medical Sciences, Ministry of Public Health

Sirirat Techathawat (with Nakorn Premsri, Attaya Limwattayingyong, Unchalee Siripitayakunkit, Kesinee Meesap, Worrawan Klinsupa, Somrudee Muangnoy, Nisa Prathummas and Nantaporn Kaewaroon), National Vaccine Committee Office, Department of Disease Control, Ministry of Public Health

Prapassorn Thanapholler, Food and Drug Administration, Ministry of Public Health

Suwit Wibulpolprasert, Senior Advisor in Disease Control and Prevention, Ministry of Public Health

Yongyuth Yuthavong, BIOTEC, National Science and Technology Development Agency

Representatives of universities and research institutes

Chutima Akaleephan, International Health Policy Programme

Niyada Kiatying-Angsulee, Faculty of Pharmaceutical Sciences, Chulalongkorn University

Jongkol Lerttiendamrong, International Health Policy Programme

Representatives of intergovernmental organizations

Stephane Guichard, Immunization and Vaccine Development, Office of the WHO Representative to Thailand

Chawalit Tantinimitkul, Immunization and Vaccine Development, Office of the WHO Representative to Thailand

Case study 8

Uganda

This case study on Uganda was carried out by Padmashree Gehl Sampath, formerly with the Intellectual Property Unit and now Economic Affairs Officer, Science, Technology and Innovation Branch, Division on Technology and Logistics, UNCTAD, and Christoph Spennemann, Legal Expert, Intellectual Property Unit, UNCTAD. Inputs for the study were collected during a field mission to Kampala, Uganda, from 9 to 12 November 2009. The case study report was finalized under the overall responsibility of Mr James Zhan, Director of the Division on Investment and Enterprise, and Mrs Nazha Benabbes Taarji, Officer-in-Charge, Investment Capacity-Building Branch.

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Abbreviations

NDA	National Drug Authority
UIA	Ugandan Investment Authority
UIRI	Ugandan Industrial Research Institute
UNCST	Uganda National Council for Science and Technology

1. Background and methodology

This case study seeks to analyse how pharmaceutical technology is transferred from a major Indian generic pharmaceutical producer to a Ugandan local manufacturer under a joint venture agreement. The study also deals with the investment incentives that were needed in the particular case to attract the foreign investor, and explains the legislative and institutional framework for technology transfer in Uganda, seeking to highlight the strengths and weaknesses of the country's present innovation context.

Uganda was chosen for the investigation since it presents an archetypical example of a least-developed country (LDC) where the government actively supported a specific deal with a major manufacturer from a developing country to establish a joint venture in the country with the aim of producing high-quality, low-cost antiretrovirals (ARVs) and antimalarials for the east Africa region. Uganda represents a country where a firm from a developing country has opted to transfer technology to manufacture finished pharmaceutical products in an LDC. Many LDCs take advantage of the fact that they are not obliged to offer patent protection on pharmaceutical products as required by the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) until 2016, and therefore would be able to offer a base for manufacturing generic versions of drugs that are patent-protected in certain non-LDCs. As LDCs, however, they nonetheless face numerous constraints in establishing viable local production facilities that meet quality standards; this case study was structured to analyse such constraints at length.

UNCTAD thanks Quality Chemicals Industries Limited (hereafter, Quality Chemicals) for agreeing to be the subject firm for this case study, and Ms Elizabeth Tamale, Principal Commercial Officer, Ministry for Tourism, Trade and Industry, Uganda, for invaluable assistance in the arrangement of interviews with Ugandan stakeholders.

A case study research methodology was used in the study. Data were collected through open-ended face-to-face interviews in Uganda. Interviewees were identified based on earlier UNCTAD missions to Kampala in the context of advisory work related to development implications of intellectual property rights. During the fact-finding mission to Kampala from 9 to 12 November 2009, 23 individuals from the following institutions were interviewed: 9 pharmaceutical experts (from Quality Chemicals, Cipla, Medipharm Industries Limited and the Indian Pharmaceutical Alliance); 5 representatives of the Ugandan Government (from the Uganda Industrial Research Institute, the Uganda National Council for Science and Technology (UNCST), the Uganda National Drug Authority, the Ugandan Ministry of Health, and the Ugandan Ministry of Tourism, Trade and Industry); 6 members of the pharmaceutical distribution network (from Mulago Hospital and private pharmacies); 1 representative of a nongovernmental organization (NGO) (HEPS Uganda); 1 academic researcher (from Makerere Medical School); and 1 private lawyer (from Mwesiga Rukutana & Co. Advocates).[1]

1 See Annex: Interviewed individuals and institutions.

In addition, a semi-structured questionnaire designed to capture the dynamics of firm-level activities related to production and technology transfer was administered to the firms, the results of which are included in the case study.[2]

This case study construes innovation as any new products, processes and organizational changes that are new to the enterprise, context and country in question, although not necessarily to the world at large (UNCTAD, 2007). In keeping with the scope of the project, technology transfer was defined as all components of technology, both codified (in terms of blueprints, hardware, machine parts and plant technologies) and tacit (know-how and skills), that are essential to enhance the capacity of the organizations in the recipient country to produce pharmaceutical products.[3]

2. Description of the firm, structure and range of products

Quality Chemicals, a local Ugandan pharmaceutical company, has been producing drugs for the treatment of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) and malaria since the beginning of 2009. As a result of its joint venture with the Indian company Cipla Pharmaceuticals, Quality Chemicals has transformed from a local distributor of imported drugs to the largest local producer of drugs of importance to public health.[4] This venture and ongoing production activity is of particular local, regional and global significance for a variety of reasons. The production of good-quality ARVs that could cater to the local demand is of immense significance for Uganda because the number of people requiring ARVs has risen steadily while the percentage of people receiving treatment has not expanded drastically since 2005 (UNAIDS, 2008).[5] Regionally, Quality Chemicals has the potential to become an important supplier of first-line ARVs and antimalarial medicines, despite the presence of other firms in Kenya and the United Republic of Tanzania with similar product lines.[6] Globally, the Quality Chemicals–Cipla venture presents a very interesting case of south–south technology transfer for local production capacity.

The joint venture was initiated in 2007, as part of which the new plant based in Luzira (near Kampala) has launched production of two ARV combinations (containing zidovudine, lamivudine, stavudine and nevirapine) and one antimalarial drug (an artemisinin lumefantrine preparation) since February 2009.[7] At the time of the field interviews in November 2009, there were plans

2 See Annex: Field questionnaire.

3 A uniform definition of technology transfer was used for all components of the project, including the trends survey, the regional dialogues and the stakeholder analysis.

4 Uganda's pharmaceutical sector is relatively small (ten local firms), and Quality Chemicals is presently the only producer of ARVs and antimalarial drugs.

5 As the report notes, although Uganda was the African country with the greatest success in curbing AIDS transmission, recent years have seen a surge in risky sexual behaviour (UNAIDS, 2008, p. 125).

6 This includes Cosmos Pharmaceuticals and Universal Corporation (Kenya) and Tanzania Pharmaceutical Industries (Tanzania).

7 Source: information gathered through the questionnaire survey, 2009.

to expand into other ARV segments in the future, once full capacity utilization of the present plant is achieved. The plant has been constructed according to Cipla's design specifications and resembles its own production facility for generics in India (Haryana).[8] According to the terms of the joint venture, Cipla has a foreign equity share of 38.55% and Quality Chemicals has a local equity of 61.45%.[9] The two companies have an equal share (50%) in the profits, although their respective investments vary.[10] The Government of Uganda played a key role in facilitating the joint venture, not only by adopting a variety of incentives to attract the initial investment but also through an agreement to invest a 23% stake (as part of Quality Chemical's local equity) to allow the plant to be completed as intended in 2008.[11]

Quality Chemicals presently exports to Burundi, eastern Democratic Republic of the Congo, Kenya, Rwanda and the United Republic of Tanzania, and also supplies to the Ugandan Ministry of Health.[12] The drugs are cheaper than comparable products being sold by multinational companies in the local market (for example, the Quality Chemicals antimalarial drug is cheaper than Novartis's Coartem) but more expensive than the artemisinin-based combination therapies offered by some Chinese and Indian generic producers.[13] In January 2010, the Quality Chemicals production site at Luzira received the World Health Organization (WHO) good manufacturing practice (GMP) certification. Prequalification by WHO of the medicines produced at the plant was still pending at the time of writing (WHO, 2010).[14] Production was ongoing for 8 hours per day as of November 2009, thereby using only a third of the capacity of the production plant. Despite the fact that only three drugs (two ARV combinations and one antimalarial drug) were being produced, the plant is equipped with production lines to expand into other oral solid dosage forms in these and other therapeutic segments.

3. Quality Chemicals' technological capacity/technology transfer activities

The most outstanding feature of the joint venture is the focus on the tacit know-how and skills training that Cipla is expected to provide. This is central to ensure the sustainability of the venture and also to promote the entrepreneurial base of Uganda. The joint venture envisages not only training for scientists, chemists and other management personnel, but also training in organizational issues.

8 Source: field interview with Dr Ravi Reddy, Cipla, November 2009.

9 Source: information gathered through the questionnaire survey, 2009.

10 Ibid.

11 Source: field interview with Mr George Baguma, Chief Marketing Officer, Quality Chemicals, November 2009.

12 Ibid.

13 Source: field interviews with private pharmacies, Kampala, November 2009.

14 In this announcement, WHO specifies that GMP certification, which concerns the production site, is one element of the WHO prequalification process. The other element, which in the case of Quality Chemicals was still pending at the time of writing, concerns the quality, safety and efficacy of the pharmaceutical products made at the Luzira site.

In particular, skills and know-how that have been transferred over the past 2 years relate to (i) plant design and installation, (ii) product and process know-how, (iii) good laboratory practices, (iv) engineering for plant maintenance and (v) sourcing of raw materials.[15] Skills are transferred on the job in a day-to-day interactive environment, as well as in regular weekly teaching sessions in a dedicated on-site classroom. The Government of Uganda provides the salaries for Cipla experts from India to conduct this skills transfer for a total period of 3–5 years.[16]

4. The pharmaceutical market in Uganda

The Ugandan economy has experienced relatively rapid growth, although the growth rate of the gross domestic product (GDP) has slowed somewhat since the early 1990s compared with the previous decade (GDP grew 5.2% in 2003 and 5.9% in 2004 and beyond). The most impressive sectors in terms of performance over the past 5 years have been agriculture, construction and communications.

The Ugandan pharmaceutical sector, despite being small and nascent, has been working towards expanding its local production capacity in recent years. It comprises about ten local firms, all of which are predominantly involved in formulation of pharmaceutical medicines. The firms interviewed stated that all raw materials required for the formulations – active pharmaceutical ingredients (APIs) and packaging material – are usually imported.[17] The Ugandan market for pharmaceutical products was worth about US$ 120 million in 2009.[18] A tenth of this is catered to by local firms;[19] the remaining 90% of the market is supplied by drugs imported into the country by local distributors. Kampala Pharmaceutical Industries (KPI), which is perhaps the largest firm in Uganda, has about 200 employees.[20] Abacus Pharmaceuticals (producing liquids and injectables) and Quality Chemicals (the subject of this case study) are two of the other large companies in the sector.

5. Productive capacity for pharmaceutical innovation in Uganda

One objective of Uganda's National Drug Policy is "to maximize appropriate procurement of locally produced essential drugs". The Policy seeks to "encourage local pharmaceutical manufacturers to produce essential drugs at competitive prices and encourage procurement agencies to source available

15 Source: results from field questionnaires.

16 Source: field interviews with Indian experts on site.

17 Source: Medipharm interviews.

18 Source: field interview with Dr Apollo Muhairwe, Executive Secretary, Ugandan Drug Regulatory Authority, November 2009.

19 Ibid.

20 In contrast, established large firms in India, China and Brazil have a full-time equivalent staff strength of over 1000 employees.

essential drugs locally in order to support the local industry" (Ministry of Health, 2002).

This objective, which had a bearing on the creation of the Quality Chemicals–Cipla joint venture, clearly states the need to build local productive capacity. This has to be seen against a background of other developing countries, such as India, that are major suppliers of global generic drugs, being fully compliant with the TRIPS Agreement since 2005. The Ugandan Government aimed primarily to create productive capacity and ensure a sustainable supply of reasonably priced drugs of importance to public health. Such a health perspective was motivated by the increasing need within Uganda to claim more ownership over the HIV/AIDS issue,[21] in order to increase public trust in the ability of the country to respond to the growing need for medicines.[22]

Despite being the key actors in the pharmaceutical sector, firms are deeply embedded in the local knowledge system that impacts upon their ability to build productive capacity. Capacity to produce generic medicines broadly involves two different types of capability: manufacturing formulations (using imported APIs, binders and secondary raw materials) and reverse engineering of APIs. Although formulating drugs is a fairly mechanical process, requiring only the ability to put together the APIs and the binders (excipients), producing APIs requires considerable technological sophistication, since it calls for the ability to reverse engineer. The knowledge-intensive nature of this process, even at relatively low levels of technological sophistication, explains the dependence of the production capacity on upstream open science that is found in public-sector laboratories and research institutes, university centres of excellence and teaching hospitals. The quality and nature of science and research in the public-sector institutions, however, also depends on the technology-absorption capacity of local actors, which can broadly be understood to mean their ability to identify, absorb, use, diffuse and create applications that cater to local demand (Cohen & Levinthal, 1990). Thus defined, technology-absorption capacity is a prerequisite for effective technology transfer to occur in the local pharmaceutical sector. Absorption capacity of the actors, in turn, depends on two major factors: (i) the level and quality of education available in the country, which determines the nature of local human resources available to engage in local production activity; and (ii) the institutional and policy framework for pharmaceutical production. Creating and fostering linkages between the different actors is very important for sustainably building pharmaceutical capacity within a country, and the institutional framework plays a critical role in this. Usually, a conducive framework that enables pharmaceutical production is one that clearly identifies the sector's priorities and establishes linkages between the organizations and actors to promote technological learning (Gehl Sampath, 2010).

21 Earlier studies have found that the Ugandan Government claimed little ownership over ongoing public–private partnerships in the area of HIV/AIDS within Uganda (Caines & Lush, 2004).

22 Additionally, Uganda suffered a major setback when it was denied participation in the donor-funded programmes for HIV/AIDS drugs in 2005–2006, which added to public mistrust of the capacity of the Ugandan Government to deal with the growing demand for ARVs.

This section begins with exploring whether there is a coherent framework for pharmaceutical production that integrates technology transfer as a part of the science, technology and innovation strategy of Uganda. It analyses whether pharmaceutical production is recognized as a priority in the present institutional context, and whether the various institutional measures put in place to support the sector are well coordinated. The level and quality of human resources available, both to engage in production and to lead key national organizations, is gauged conventionally by a set of indicators, including education enrolment and the number of scientists engaged in research and development (R&D) per 1 million people. The capacity of the public sector/local knowledge system as a whole is measured through other indicators, such as R&D expenditure as a percentage of national GDP, rate of foreign direct investment (FDI) in productive sectors, and patents applied for and granted. These indicators for Uganda are presented with the intent of highlighting the present context of human resources and R&D capabilities available for pharmaceutical production. Finally, the extent of interorganizational learning and linkages is analysed, and sources of finance available to local enterprises are briefly discussed.

5.1 Institutional framework for technology transfer activities in Uganda

5.1.1 Science, technology and innovation

Uganda's first National Science and Technology Policy only came out in 1993 following the Statutory Act of 1990 that established UNCST. Before the formulation of this Policy framework, Uganda's national planning and budgeting process gave only very limited consideration to aspects of science and technology, let alone innovation policy. In September 1997, UNCST revised the Science and Technology Policy and produced a broad policy framework and strategies, which were to guide the science and technology development policy effort. The Policy was further upgraded in September 2001 and served as the basis for all science and technology activities in Uganda until recently. In late 2009, the first National Science, Technology and Innovation Policy, which shifted focus from science and technology to science, technology and innovation, was adopted in Uganda.

Although the new National Science, Technology and Innovation Policy provides some overall direction and mentions the importance of international linkages, it does not elaborate on specific actions required to ensure the creation and promotion of various domestic policies and institutions required to coordinate and promote interorganizational linkages between the private sector and all the other actors in the system (such as universities, public research institutes, consumer and marketing organizations, standard-setting agencies and technology-transfer bodies, among others) that would be important to promote innovation in a systematic and coherent way. There is currently no ministry responsible solely for science, technology and innovation in Uganda. UNCST, whose mission is to develop strategies for the promotion and development of science and technology for sustainable integration of

science and technology in the national development process, is located within the Ministry for Finance, Planning and Economic Development. Industrial development is the forte of the Ministry of Tourism, Trade and Industry, but there is little coordination between UNCST and the Ministry of Tourism, Trade and Industry on issues of technological learning and innovation required for overall industrial development of Uganda.

5.1.2 Sectoral priorities

UNCST's priorities include biotechnology development as a means to increase agricultural productivity and improve human health. In the absence of a coherent policy framework for science, technology and innovation until 2009, science research priorities have been articulated mainly in sector-based policies, such as the National Agricultural Research Policy (2004), which provides direction for agricultural research including biotechnology, and the National Industrialization Policy, which articulates the use of applied science research to develop Uganda's infant industries. Agriculture is a major income earner in Uganda, and the prime emphasis is on using science and technology, including biotechnology, to develop agriculture capacity; whereas very little emphasis has been placed on pharmaceuticals and health. A reason for this could be that these sector-based polices draw their priorities from national development policies, such as the Poverty Eradication Action Plan, Uganda's strategic development plan that guides the formulation of Government policy, where pharmaceutical production is not a priority. As a result, most of the biotechnology-related activities within UNCST relate to the constitution of the National Biosafety Committee and the drafting of the National Biotechnology Safety Bill of 2008.

The primary emphasis for building productive capacity in pharmaceuticals has come from the health perspective in Uganda, wherein the increasing rate of HIV/AIDS and the inability of the Ugandan Government to provide for the local demand for drugs of importance to public health have been the motivating factors for the policy decision to build local productive capacity (Box 1).

***Box 1**: HIV/AIDS in Uganda*

In 2003, 157 000 people in Uganda needed treatment with ARVs, but only 10 000 received it. Although the total number of people receiving ARVs rose from 10 000 to 75 000 by 2005, the number of people needing treatment surged to 230 000. In percentages, the coverage of ARVs went up from 9% in 2003 to 34% in 2005 and then remained constant until 2008. In other words, the Ugandan Government has struggled to maintain access to ARVs for 35% of the total number of people who need them locally over the past 5 years (UNAIDS & WHO, 2008).[23] Of these 35% who receive ARVs, the Ugandan Government funds approximately half (17.5%).[24] To promote access to medicines for its people, the Ugandan Government first formulated a new policy strategy with emphasis on locally producing drugs for HIV/AIDS and malaria as its primary objective.

A new National Development Plan has been approved (2010/2011–2015/2016), which has a separate chapter on science and technology and is expected to provide resources directly to science and technology.[25] It is expected that this funding will help to organize the science, technology and innovation infrastructure for Uganda more effectively in the coming years. The National Development Plan does not include the pharmaceutical sector, however, and it is still unclear as to what extent it will help resolve the issue of coordinating science, technology and innovation capacity of relevance to pharmaceutical productive capacity.[26]

5.1.3 Intellectual property

As an LDC, Uganda is exempted until January 2016 from meeting several obligations related to pharmaceutical production as provided by the TRIPS Agreement. It does not need to provide product patents on pharmaceuticals, nor does it need to initiate a "mailbox system", (see below, section 6.2.1) of patent filings during the transition period. To review existing laws and decide on how Uganda can achieve TRIPS compliance by 2016, a Law Reform Commission has been established by the Ugandan Government. The Commission has drafted the Industrial Property Bill (version of 2009), which makes changes to the current patent legislation and is awaiting discussion in Parliament. Uganda has also opted for other TRIPS-related exemptions such as parallel imports and providing for the possibility to grant compulsory licenses for drugs of importance to public health.

Sections 10(2) and (3) of the Industrial Property Bill provide for a strict novelty standard, stating that any written or oral prior art publicly available (including other applications for patents or utility models) in any country of the world shall destroy the novelty of an invention claimed in Uganda (UNCTAD, 2010a). By restricting the possibilities to claim existing inventions as new, these section contribute to the safeguarding of a public domain needed for domestic researchers' freedom to operate. Section 55(2)(s) of the Bill considers any restrictions in licensing arrangements that "impose measures which limit technological learning and mastery, except those which relate to industrial property rights" as invalid. However, Section 55 does not limit anticompetitive practices that could impact on the technological learning of firms. The Bill is also not clear on the issue of granting research exemptions to universities and public research institutes, or the question of university intellectual property policies, of the kind that Makerere University has (see Section 5.2.2). UNCTAD has previously made a series of recommendations to the Ugandan Government on how these shortcomings can be addressed to ensure that the

23 According to the treatment guidelines in Uganda, only people with HIV/AIDS whose CD4 count falls below 200 are qualified to receive treatment, whereas WHO recommends commencing treatment when the CD4 count reaches 200–350. If the WHO standard were to be followed, the number of people needing ARV treatment in Uganda would be much higher than the figures mentioned here.

24 Source: field interviews with Ministry of Health sources, 2009.

25 Source: field interview with Mr Julius Ecuru, Assistant Executive Secretary, UNCST, November 2009.

26 Source: field interview with Mr Joseph Rubamela, Acting Director Product Development, Ugandan Industrial Research Institute, November 2009.

Industrial Property Bill is supportive of an incremental innovation system of the kind Uganda needs (UNCTAD, 2010a).

5.1.4 Investment framework and actual practice

The Ugandan Investment Code Act (1991) is the main legal instrument that extensively incorporates technology transfer stipulations of relevance to the pharmaceutical sector.[27] The Ugandan Investment Code Act has several provisions that aim to transfer technology to Ugandan counterparts as part of investment initiatives. It mandates (Section 10(1)) that all foreign investors seeking to operate in Uganda apply for an investment licence with the Ugandan Investment Authority (UIA). Section 12(d) of the Act further specifies that UIA evaluates such applications keeping in mind the potential of the proposed business enterprise to contribute to a number of economic development objectives, such as "the introduction of advanced technology or upgrading of indigenous technology". These provisions, in sum, provide UIA with a tool to specifically encourage the integration of the technology transfer of relevance to local capacity, provided UIA makes actual use of its powers. This is not always the case, however, since UIA lacks negotiating power vis-à-vis foreign investors (field interviews, C. Ocici, Enterprise Uganda). The Investment Code Act further provides a number of stipulations that aim to secure tacit know-how of relevance to the technologies transferred and ensures that it is available for application beyond the scope of the investment licence agreement, including:[28]

> "(a) technical assistance as necessary, that includes technical personnel as well as full instructions and practical explanations expressed in clear and comprehensive English on the operation of any equipment involved;
>
> (b) the right to continued use of that technology or expertise after the termination of the agreement by the Ugandan partner;
>
> (c) the supply of spare parts and raw materials that may be required to continue production locally even after the termination of the agreement, for a period of up to five years; and
>
> (d) a prohibition to the investing partner that transfer of foreign technology or expertise shall not contain a condition that restricts the use of other competitive techniques; restricts the manner of sale of products or exports to any country; restricts the source of supply of inputs; or limits the ways in which any patent or other know-how may be used."

The Investment Code Act, however, also does not list the sectoral priorities for investment for Uganda. Instead, this has been addressed as part of the

27 For a much broader discussion of this and other legislation related to technology transfer across all sectors in Uganda, see UNCTAD (2010a, Chapter I).

28 These are contained in Section 30(1), Subclauses (d), (e) and (f) and Section 30(2), Subclauses (a), (b), (c) and (d).

Presidential Investors Round Table Meetings (2004–2006), wherein agriculture and information and communications technologies (ICT) have been identified as the sectoral priorities (Ugandan Investment Authority, 2007).

The UNCST Research Registration and Clearance Policy and Guidelines (2007) have the objective of documenting R&D activities in all sectors "so as to enable research coordination and oversight, research priority setting, the protection of intellectual property and use of research results to guide public policy formulation".[29] Although the guidelines do not expressly mention technology transfer as one of the objectives, Section 9 provides a basis for collaborative agreements that promote the transfer of know-how of relevance to local research capacity.[30]

In practice, investment incentives provided to Cipla by the Ugandan Government include free land to build the plant, free set-up of the entire infrastructure (including the factory and its production facilities, roads, electricity and water), and remuneration of Cipla's pharmaceutical experts for their training activities with local staff. In addition, the Ugandan Government agreed with Cipla to procure from the new plant in Kampala ARVs worth US$ 30 million per year for 7 years.[31] Cipla, in turn, has provided a range of hardware technologies required for production. These include manufacturing and testing technologies, information on the sourcing of raw materials, packaging technologies and production plant design.[32] Cipla also provides all the tacit know-how related to the day-to-day running of the plant, including quality assurance and quality control.[33] Cipla officials also train Quality Chemicals staff in auditing requirements and WHO GMP procedures. Quality Chemicals is responsible for providing capital to finance the operation of the production plant and future expansion, local personnel and scientists (who are being trained by Cipla officials), and for strategic direction and marketing capacity to run the company.

In addition to these explicit incentives, an additional motive for investment was Uganda's LDC status, as part of which it is not obliged to adhere to the pharmaceutical product patent and undisclosed information (in particular, test data) provisions of the TRIPS Agreement.[34] Several Indian companies, including Cipla, have been scouting LDCs in the aftermath of India's full-scale compliance with the TRIPS Agreement in 2005, in order to shift their production of generic versions of drugs patented in developed and other developing countries to these destinations (Gehl Sampath, 2008). Although India has been actively promoting the use of all existing TRIPS flexibilities in order to protect the local generics industry, firms like Cipla have been engaged

29 See Section 3.0 of the Guidelines.

30 Section 9 provides that "[l]ocal institutions of affiliation should support the researchers and work, as far as it is practicable, towards building long-term collaborative partnerships with the foreign researchers."

31 Source: interview with G. Baguma, November 2009.

32 Source: survey responses to questionnaire, Cipla.

33 At the time of the field visit, the electrical, mechanical and civil engineering maintenance required to run the plant was completely handed over to the Ugandans.

34 Source: field interview with Dr Yusuf Hamied, Chief Executive Officer, Cipla, December 2009.

in considerable litigation with multinational companies in the Indian market over the production of generic versions of drugs that were patented between 1995 and 2005, i.e., after the adoption of the TRIPS Agreement but before India's full compliance.[35]

5.1.5 Summing up the institutional framework for pharmaceutical production

On the whole, although the overall policy framework covers a range of important issues from investment, technology transfer, intellectual property, and science, technology and innovation policy, these are rather fragmented and contained in several separate policies that are not well coordinated. This policy fragmentation can be traced back to three main factors. First, Uganda's first National Science and Technology policy only came out in 1993, following the Statutory Act of 1990 that established UNCST. These science and technology developments have not been well coordinated with those under the Uganda Investment Code Act and the activities of UIA, or with more recent developments related to intellectual property rights. Second, the articulation of the sectoral priorities has not been integrated into the overall science, technology and innovation policy framework. Third, the science research priorities have placed little emphasis on innovation capacity and local production, and changing the emphasis from research alone to research and production will be one of the major challenges of the new Science, Technology and Innovation Policy. There is a current lack of close and coherent linkages between all of these recent policy prescriptions, and a corresponding lack of one overarching strategy that guides science, technology and innovation for development within Uganda. Some of the current organizational mandates do not seem to be well coordinated or specified, such as the technology transfer mandate of UIA.

On technology transfer, the policy statements contained in the current Science, Technology and Innovation Policy on building science, technology and innovation capacity with the aim of generating transfer of technology are not drafted in a degree of articulation sufficient to implement these policy goals and to realize these results. Similarly, there are other noteworthy concepts stipulated in the new Science, Technology and Innovation Policy, such as the need to create a national innovation fund to promote productive capacity within Uganda, but the success of the Policy as a guiding framework will hinge on how these elements are put into action in the years to come.

All these framework conditions that improve the capacity for national innovation will certainly matter and set the pace for pharmaceutical production and innovation in Uganda. Appropriately supporting pharmaceutical production will further require that the area of pharmaceuticals is clearly recognized as a sectoral priority in all key policy documents, including the Investment Code Act, the new Science, Technology and Innovation Policy and the

35 Cipla has been involved in several litigations with multinational firms since India's compliance with the TRIPS Agreement, including with Novartis for the grant of exclusive marketing rights on Gleevec, and with Roche for its lung cancer drug Ertolonib (Gehl Sampath, 2008).

National Development Plan, which is allocating funding to areas of economic importance. The policy framework has also to ensure the availability of good-quality education in key areas of importance, such as chemistry, pharmacy and pharmacology, the eventual development of biotechnology and molecular biology, and public-sector-based open science. Building academic disciplines in these areas now will result in significant human capacity in two decades; the time lag in initiating such policy changes has been central to the historical differences in catch-up curves of Asian and African countries (Castellacci & Archibugi, 2008; Oyeyinka & Gehl Sampath, 2009).

5.2 Technology-absorption capacity: some indicators

Indicators such as R&D expenditure, patent ownership by local firms, and researchers and scientists per 1 million population help to gauge the capacity of local actors to absorb new knowledge and innovate to a certain extent. There is emerging consensus that these measures do not accurately capture the ability to create and absorb knowledge in LDCs, since they are based on economies with more structured and advanced forms of technological activities, and other dynamic indicators that measure the levels of interorganizational learning and performance may be needed to explain the ongoing activities in such contexts. This section tries to present statistics on knowledge and R&D, as well as the main domestic actors in the pharmaceutical sector in Uganda, as captured by the field survey.

5.2.1 Knowledge and R&D: recent statistics

Tables 1 and 2 show the key proxy variables that were calculated using school enrolment at the primary, secondary and tertiary levels, which have all been steady or increased only marginally in the period 2003–2007. It is important to note the decrease in enrolment percentages from primary to secondary to tertiary (where tertiary enrolment has remained steady at 3% since 2003). Recent policy developments have sought to target this decline in the enrolment ratios by reforming the education system with an aim to create greater human capacity for innovation in science-intensive sectors. The Science Education Policy of 2005 introduces these reforms and makes science education compulsory for the 4 years of secondary schooling. The Ugandan Government has also introduced scholarships in public universities that are aimed primarily at the sciences (90% of all Ugandan Government scholarships) (Ecuru et al., 2008).

***Table 1** School enrolment in Uganda, 2003–2007*

	2003	2004	2005	2006	2007
School enrolment, primary (% gross)	134	125	118		
School enrolment, primary (% net)					
School enrolment, secondary (% gross)	19	19	16		
School enrolment, secondary (% net)	15	15	15		
School enrolment, tertiary (% gross)	3	3	3	3	3
Pupil/teacher ratio, primary	52	50	50		

Source: World Development Indicators Database.

Table 2 shows that the net flow of FDI remained constant until 2005, with greater variations at a much higher level between 2006 and 2008. R&D figures are, however, unavailable. It is difficult to ascertain the extent to which the Investment Code Act has been able to promote technology transfer and investment of importance to local production capacity in sectors that are identified as priority sectors (namely agriculture and ICT). However, there is evidence that there has been a steady increase in FDI in LDCs directed towards extractive industries over the past decade (UNCTAD, 2008). African LDCs received 87% of all FDI aimed at LDCs from 2000 to 2005, and the rise in investment was driven largely by policies of African governments seeking to increase investment and promote exports in key natural resource sectors (with Asian LDCs accounting for only 12%) (UNCTAD, 2008).

***Table 2** Knowledge infrastructure variables, Uganda, 2003–2007*

Investment and R&D	2003	2004	2005	2006	2007	2008
FDI, net inflows (% GDP)	3	3	3	5.85	5.4	4.97
Merchandise imports (US$, 100 000)	1 240 99	1478	1810			
R&D expenditure (% of GDP)	–	–	–			
Researchers in R&D (per 1 million people)	–	–	–			

Sources: World Development Indicators Database. FDI figures for 2006–2008 from UNCTAD (2010b).

5.2.2 Main actors and the potential for interorganizational learning in the pharmaceutical sector

Given the new policy developments sketched out above, a wide array of private and other actors beyond the state are emerging as important players for the pharmaceutical sector within Uganda, and there may well be a need to reconfigure their roles and relationships in the light of these developments.

Major state and public agencies

In addition to UIA, the Ugandan Industrial Research Institute (UIRI; see below), the intellectual property office and UNCST, Uganda offers an extensive network of agencies providing technical support in the form of technical assistance, training programmes, information services and joint research

opportunities. Several public science and technology policy and R&D institutions offer technical-related services to enterprises (especially small and medium-sized enterprises) for all sectors, including pharmaceuticals, such as the Management Training and Advisory Centre and Mbarara University of Science and Technology, in addition to those discussed in the previous section. The state agencies identified here are led by the Uganda National Bureau of Standards, a statutory organization established by Act 1 of Parliament in June 1983 to formulate and promote the use of national standards and to develop quality control and quality assurance systems that will enhance consumer protection, public health and safety, industrial and commercial development, and international trade, among other things. Most technical support agencies offer a combination of services, often supported by financial incentives. Gauging from the success Uganda has had in some other sectors, such as fish farming, these actors seem to be well-equipped to support production activities in order to enable local firms to capture their share in global value chains (Winters & Shahid, 2007).

The Ministry of Health in Uganda is a major actor in all activities of relevance to the pharmaceutical sector. The drug distribution system in Uganda is administered through three key nodes: the National Medical Stores, which distributes medicines that have been publicly procured on behalf of the Ugandan Government;[36] the Joint Medical Stores, which distributes medicines that have been procured through international grants (GFATM, Clinton Health Access Initiative, UNITAID and other public non-profit-making initiatives); and private medical stores that cater to people who buy medicines and pharmaceutical products as out-of-pocket expenses. The Ugandan National Drug Authority (NDA), whose members are appointed by the Ministry of Health,[37] is another very important actor. The NDA has been in place for 15 years and has two important mandates: (i) to ensure the quality, safety and efficacy of drugs being sold within the country; and (ii) to promote locally produced drugs. The NDA, however, is heavily underfunded and is unable to cope with the influx of spurious drugs within Uganda from Ethiopia and Kenya (through the Common Market for Eastern and Southern Africa trade zone).[38] It currently relies on fees from the drug companies to meet its core expenses, which is not enough to expand its activities. The NDA applies standards similar to that of the WHO GMP prequalification standards and is also mandated with conducting training programmes for local companies to ensure compliance with these standards.[39]

36 The National Medical Stores mainly distributes drugs through the major Ugandan Government hospitals, such as Mulago Hospital in Kampala; the Mulago HIV Centre, however, is funded by the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM). Source: field interview with Mr Moses Mulumba, Legal Associate, HEPS Uganda, November 2009.

37 See Section 3(3) of the National Drug Policy and Authority Act of 3 December 1993, Chapter 206, Laws of Uganda.

38 Source: field interview with Mr Apollo Muhairwe, Executive Secretary, National Drug Regulatory Authority, Uganda, November 2009.

39 Ibid.

Universities and public research institutes

The most prominent public research institute in Uganda that could potentially address pharmaceutical production is UIRI. This was established in 2005 with a mandate to assist in all areas of industrial research and business incubation, the aim being to support local capacity to create commercial innovations. Sectoral priorities are food processing and agricultural products, software development and electronics.[40] Field interviews revealed that the only pharmaceutical production that UIRI facilitated was to support a local scientist to further his work on Newcastle disease (which affects poultry), but there was no commercial innovation that resulted from this work.[41] UIRI has a staff of 150, of which over two-thirds are scientists. Most of its funding has been devoted to hiring staff and providing equipment and some basic infrastructure. Its most advanced laboratory facilities are for food processing. The first laboratory in Uganda that could help with prototyping efforts (central to industrial development and reverse-engineering capabilities across sectors) is only now being constructed on UIRI premises, with the help of a World Bank grant.[42] The delays in Ugandan Governmental funding for UIRI's activities have made it difficult for the institute to perform its key functions. As Joseph Rubamela of UIRI expressed: "This prototyping laboratory should have been operational yesterday."[43] UIRI has no internal facilities for chemical testing of local products.[44] There are eight other Ugandan Government research institutes with the mandate to perform research of relevance to various aspects of health research: the Uganda Virus Research Institute, the Uganda Cancer Institute, the Uganda Tuberculosis Investigation Centre, the Natural Chemotherapeutics Laboratory, the Central Public Health Laboratory, the Uganda Trypanosomiasis Research Organization, the Uganda Joint Clinical Research Centre and the Uganda Heart Institute; 31% of all research projects sanctioned by the Ugandan Government between 1997–1998 and 2006–2007 were related to health sciences and carried out by these institutes. However, as Table 3 shows, product development efforts have been few and far between. As an effort to reinvigorate the research apparatus and organizational coordination in these institutes, the Uganda National Health Research Organization was set up in May 2009 to bring the activities of the eight institutes under a single institutional mandate.

The Makerere University Medical School has limited capacity to perform chemical testing for generic drugs to obtain approval from the Ugandan Drug Regulatory Authority. The medical school does not have any major product development/research initiatives. The Department of Pharmacology is involved in some minor R&D on pharmaceuticals, such as purification of herbs

40 Source: field interview with Mr Joseph Rubamela, Acting Director Product Development, UIRI, November 2009.

41 Ibid.

42 Ibid.

43 Source: field interview with Mr Joseph Rubamela, Acting Director, Product Development, UIRI, November 2009.

44 Chemical testing concerns only the chemical composition of a drug, such as the percentage of APIs compared with non-active elements such as binders. This differs from bioequivalence testing, which is undertaken to examine the effects of a generic drug on the human body.

into medicines, and there is some work on resistance levels within HIV/AIDS and response to treatment. The Ugandan Government does not provide any funding for university-based research, although it provides some funding for setting up laboratories.[45] The field interviews reveal that the lack of funding on research activities in the university system only helps to re-emphasize the misplaced characterization of university research as an activity that is rather unrelated to productive capacity, which is accurate neither generally nor specifically for pharmaceutical production. Makerere University also has a University Intellectual Property Policy, which was enacted in 2006.[46] The main driver behind this policy initiative was the Swedish International Development Cooperation Agency; interviews suggest that local stakeholders are not fully aware of the potential of such a policy for technology development.[47] As a consequence, the implementation of the policy is weak and there have been no attempts to patent based on this to date.[48]

***Table 3** Products and processes being developed in Uganda's research institutes*

Product	General area	Organization	Description
Aloe vera	Topical – for skin conditions	Makerere	Traditional medicine; available for use
Aloe vera	Topical – for wounds	Natural Chemotherapeutics Laboratory	Traditional medicine – said to promote synthesis of collagen; available for use
Artemisia annua/ elephant grass	Malaria	Natural Chemotherapeutics Laboratory	Traditional medicine – beverage preparation for treatment; in clinical trials
MDR-TB diagnostic kit	TB	Makerere	Detection of MDR-TB; rapid identification of multi-drug-resistant TB; targets gene by amplifying primers; passed proof of concept
Peptide-based malaria vaccine	Malaria	Makerere	Proof of concept successful but stagnated at next stage of development.

TB, tuberculosis.
Source: Kamunyori et al. (2009).

Until 1998, Makerere University was the sole institution providing graduate training in Uganda.[49] However, the past decade has seen the emergence of a few more state-run and private universities that provide graduate and postgraduate courses in core disciplines.[50] Of these, graduate training for health sciences is now provided by Makerere University and Mbarara University, but

45 Source: field interview with Dr Charles Ibingira, Deputy Dean, Makerere Medical School, November 2009.

46 A copy of the University Intellectual Property Policy could not be retrieved to analyse its strengths and weaknesses.

47 Source: field interview with Mr Julius Ecuru, Assistant Executive Secretary, UNCST, and Dr Charles Ibingira, Deputy Dean, Makerere Medical School, November 2009.

48 Ibid.

49 Ecuru et al. (2008).

50 There are now five state-run public universities and five private universities in Uganda.

none of the private universities (five in total) provides education programmes in health sciences.

Private sector

As noted earlier, the local pharmaceutical sector is comprised of a few firms, all of which are predominantly involved in formulation of pharmaceutical medicines. The firms interviewed expressed that all raw materials required for the formulations – APIs and packaging material – are usually imported.[51]

Non-profit-making agencies

Another set of agencies are the non-profit-making institutions founded either jointly or independently by industrial associations and the Ugandan Government. Most of these assist small and medium-sized enterprises through their educational and training programmes and publications on quality standards.

5.3 Sources of finance to local enterprises

Ugandan Governmental agencies remain a significant source of R&D expenditure within the country.[52] However, as Uganda's national budget is financed by donors, the total donor contribution to R&D is higher in reality. Ugandan Government-supported grant schemes for science, technology and innovation proposals have so far resulted in little response from the private sector, which indicates a lack of coordination between the latter on the one hand and public research institutes and universities on the other hand.[53] Moreover, the private sector is composed of small and medium-sized enterprises operating in a broader enterprise level environment that underemphasizes innovation and product differentiation.

The Presidential Support to Scientists Initiative is the second Ugandan Government funding programme that supports commercialization. Pharmaceutical innovation is part of this initiative, which receives US$ 4.2 million (8 billion Ugandan shillings) per year to promote research that is close to commercialization. Currently, the only health-related projects being considered as part of this initiative are a potential of herbal tea to act as malaria prophylaxis, and plant extracts that help to prevent mosquito bites. Field informants were of the view that there is a need to provide more funding and to institutionalize this initiative.[54]

51 Source: field interviews with staff of Medipharm Industries Limited, Kampala, November 2009.

52 This observation does not necessarily mean that the Ugandan Government is playing a significant role in the sector, but rather that within the existing low levels of R&D investment of relevance to creating productive capacity in the sector, the Government still plays a large role.

53 Source: field interview with Mr Julius Ecuru, Assistant Executive Secretary, UNCST, November 2009.

54 Ibid. Several other people interviewed were also of the view that the initiative needs to be institutionalized so that there is a clear procedure that can be followed to qualify for funds, since currently the fund is administered primarily by the President of Uganda himself.

6. Strengths and future challenges for local production: analysing the Quality Chemicals–Cipla joint venture

Despite the initial successes of the joint venture in its initial 2 years (i.e. initiating production of two ARVs and one antimalarial), the field interviews indicate mixed views about the project's long-term perspective, with most actors outside the Ministry of Health and UIA expressing a degree of scepticism. A key aspect that bothered some respondents was the sustainability of the joint venture in terms of being able to address the needs of the Ugandan people in the health sector. The fact that the Quality Chemicals venture was sponsored by the Ugandan Government on an ad hoc basis,[55] without a clear competitive procedure,[56] was mentioned by a number of the people interviewed. At the time of writing, a second firm was expected to receive a major grant from the Ugandan Government for its expansion plans into producing liquid injectables,[57] but there are no official guidelines on how and when local pharmaceutical firms will qualify for Ugandan Governmental support of the kind bestowed on Quality Chemicals, or why these firms have been chosen at the expense of others. Several of the individuals interviewed pointed to the fact that at the time of the decision, Quality Chemicals was not a manufacturing firm at all but was merely distributing imported products within Uganda. Despite this, Quality Chemicals was chosen to be the firm for this joint venture while all the other local manufacturers were apparently left out. Therefore, the viability of this particular model for the sector at large, and the extent to which the Ugandan Government plans to expand and support other local pharmaceutical firms in a similar way, remain unclear.

6.1 Strengths and good practices

One of the essential elements for the successful long-term production of pharmaceuticals at Quality Chemicals is the firm's technology transfer agreement with Cipla, as described above. Such transfer of tacit know-how enhances the ability of the local company to compete internationally. Quality Chemicals also benefits from Cipla's goodwill and reputation (compared with local producers), since the products are currently being manufactured through a licensing arrangement between the two companies.

Second, the commitment of the Ugandan Government to promote the production of drugs of importance to public health is commendable, as demonstrated by the case study. Before the joint venture, Quality Chemicals served as a local distributor for Cipla's products within Uganda. Although the plan to build upon the pre-existing relationship to establish production

55 The Ministry of Health officials interviewed for the study responded that they "were the ones who came up with a good idea, and so we funded them" when asked why Quality Chemicals was chosen as the national counterpart in this venture.

56 Most respondents were of the view that the procedure should have been transparent, wherein all firms and organizations were allowed to compete for the Government funds and special treatment of the kind that is currently being conferred on Quality Chemicals.

57 Source: interview with Dr Martin Oteba, Secretary, Ministry of Health.

capacity came from Quality Chemicals, the case study serves as an interesting and rare example of how the technology transfer provisions of the Ugandan Investment Code Act can be leveraged to build local capacity.

6.2 Challenges

The most important challenge that lies ahead of Quality Chemicals and the Ugandan Government is to ensure sustainable production and to leverage the ongoing technology transfer initiative to build the capacity of the local pharmaceutical sector. The empirical findings on this issue indicate that there is a need to integrate investment more closely with the science, technology and innovation priorities of the sector.

6.2.1 Ensuring sustainable production at reasonable costs

Currently the drugs produced by Quality Chemicals are approximately about 20% more expensive than other branded generic drugs available in the local market for the treatment of HIV/AIDS and malaria.[58] Despite this price difference, the Ministry of Health is committed to continue purchasing the products manufactured by Quality Chemicals. Interviews showed that the Ministry's emphasis is on promoting greater access to medicines locally. The Ugandan Government perspective is in this instance an interesting one, especially from the point of view of health security, that can be defined as the need for countries to be self-sufficient in securing access to medicines to the extent possible on their own terms. At the onset of an initiative to launch local pharmaceutical production, any LDC such as Uganda that clearly has no first-mover advantage in the sector would incur greater costs in local manufacture of drugs. The 20% increase in cost of the products is due primarily to the fact that all raw materials – APIs, excipients and packaging materials – are currently supplied to Quality Chemicals by Cipla or the sources that supply Cipla's own plants in India.

However, this cost represents a trade-off, and as long as it is not borne directly by the poor consumer (in this case, patients), the cost is one of building a secure production base. Furthermore, from a mid- or long-term dynamic perspective, such local production could be sustainable, depending on the ability of Quality Chemicals to bring down its product price and the future product portfolio of the firm.[59] As shown in Box 2, a major component of the cost of generic drugs is the APIs, and eventual price reduction and competitiveness of Quality Chemicals' products will depend on its ability to manufacture APIs in-house or procure them from another source within Uganda at internationally competitive prices.

58 This difference in cost has been calculated by comparing prices of the drugs in various pharmacies in Kampala that were surveyed during November 2009 by the UNCTAD team.

59 At the time of field interviews, there were no plans to concretely expand into second-line ARVs that are patented in India, but company officials on both sides were clear that they did not rule this out of the purview of the partnership.

Box 2 Cost considerations of producing generic drugs in LDCs

Generic manufacturing of pharmaceutical drugs consists of three main components: (i) the production of APIs, which requires chemical synthesis skills commonly referred to as reverse-engineering capabilities; (ii) production of excipients and other non-active ingredients; and (iii) formulation manufacturing skills, which involves the mixing of APIs with other, non-active ingredients into pills, tablets or other dosage forms.

The cost of API as a percentage of the total cost of the finished dosage form varies significantly from molecule to molecule. For instance, high-value, low-volume drugs such as cardiovascular medicines, where it is common to have tablets of 1 mg or 5 mg, may have a higher component of the API compared with low-value, high-volume drugs such as aspirin, which has tablets of 250 mg and 500 mg. Low-value, high-volume drugs will have a relatively lower component of API in the cost of the finished dosage form. On average, however, one could consider API as 50% of the total cost of the finished dosage form. In the case of simple drugs, the API costs comprise around 40% of the total cost of the finished formulation. However, the API component of drugs rises significantly in the case of specialized drugs, such as those used to treat cardiovascular system disorders and ARVs, where it can be as high as 90% (Pinheiro et al.).

Producing APIs and excipients locally therefore is essential in order to lower the costs of production in the mid- or long term. This calls for a larger set of skills that goes beyond simple formulation capabilities. It calls for developing reverse-engineering skills that are primarily chemistry-based, with some expertise in biotechnology and genomics.[60]

Source: Gehl Sampath (2010).

According to the original plans of the joint venture, expansion of production to include a separate plant on the Quality Chemicals premises that will transfer technology for reverse engineering of APIs to the Ugandan company was foreseen for 2010.[61] However, interviews with Cipla officials reveal that the viability of the API plant and the proposed expansion will depend on whether or not certain amendments are made to the Ugandan patent regime. Senior Cipla staff have voiced concern regarding a pending implementation, by the Ugandan legislator, of the TRIPS Agreement mailbox provision (Article 70.8 of the TRIPS Agreement).[62] According to that provision, LDCs availing themselves of the transition period for the implementation of the TRIPS Agreement provisions on product patents and undisclosed information (i.e. 1 January 2016) must in certain circumstances provide a system for the filing of pharmaceutical product patents before 2016, after which date these applications would have to be examined and, depending on the case, granted.

60 Although several drugs currently in use require chemistry-based skills to reverse engineer, there are a range of newer drugs that employ biotechnology, such as second-line ARVs.

61 Source: interview with Mr George Baguma, Chief Marketing Officer, Quality Chemicals, November 2009.

62 Source: personal interview with Dr Yusuf Hamied, Chief Executive Officer, Cipla, December 2009.

This may affect Cipla's possibilities after 2016 to produce at the proposed Luzira API facility a number of APIs that may be patent protected in other countries.[63] The Industrial Property Bill of 2009 contains a mailbox provision. However, Uganda is not obligated to implement such a mailbox, because the TRIPS Agreement makes such obligation dependent on certain preconditions, which are missing in the case of Uganda (UNCTAD, 2010a).

Another potentially important intellectual property issue in this context is the Ugandan Anti-Counterfeit Bill of 2010 and parallel draft legislation developed by the East African Community (EAC). These drafts have raised some stakeholders' concerns over the possibility for generic producers to continue their activities throughout the EAC.[64] Such concerns are, inter alia, based on the fact that the above-mentioned draft legislation in both Uganda and the EAC extends the definition of "counterfeiting" beyond the minimum standard of the TRIPS Agreement to include, inter alia, patent infringements.[65] The Ugandan Anti-Counterfeit Bill appears to have addressed some, albeit not all, of these concerns.[66] At EAC level, the adoption of anti-counterfeiting legislation has been halted[67] after the suspension, by the Kenyan High Court, of three sections of the national Anti-Counterfeit Act (The Standard, 2011). The final outcome at EAC level could have important repercussions in Uganda, as the EAC Treaty provides for primacy of EAC law over national law in matters pertaining to the implementation of the EAC Treaty.[68]

Two other factors that will eventually determine the kind of support that local firms receive to branch out into more knowledge-intensive activities of API production are policy coherence and policy implementation (see Section 6.2.2) and improved organizational competence for agencies that provide technical assistance of relevance to production. Although Uganda has numerous agencies that operate under the mandate of providing technical assistance to industry, their impact is limited if not questionable, due to the

63 Ibid. The concerns about the mailbox provision seem to relate to APIs that for the time being are off-patent in Uganda. Note that under Uganda's current patent law, pharmaceutical products are not exempted from patent protection. See Uganda's Patents Statute No. 10 of December 1991. The 2009 Industrial Property Bill in its Section 10(2) provides a standard of worldwide, written and oral novelty. Under this draft provision, APIs that have been on-patent abroad could no longer be considered new in Uganda and would thus have to remain in the public domain. By contrast, APIs that are newly developed abroad between now and 2016 could be considered as patentable in Uganda as of 2016, as a result of the mailbox provision.

64 See, for example, Musungu (2010).

65 Subjecting patent infringements to criminal sanctions (which are provided as remedies in the case of counterfeiting) could expose generic producers to fines and imprisonment, rather than mere civil remedies such as liability for damages and injunctions, as usually occurs in the case of patent infringement. The threat of criminal sanctions could potentially have a chilling effect on generic producers' activities. In cases where the validity of a pharmaceutical patent is doubtful, generic producers might nevertheless be hesitant to face infringement litigation, out of fear of possible imprisonment.

66 For details on the Ugandan draft legislation, see UNCTAD (2010a, pp. 51–53).

67 Source: personal communication with the authors from the representative of the German International Cooperation Agency (GIZ) at the EAC Secretariat, 20 January 2011.

68 See Article 8 of the EAC Treaty. According to the EAC Treaty, science, technology and health are areas of EAC cooperation.

very low levels of resources and organizational staffing on which they have to perform their tasks.

Earlier surveys of firm-level production capacity in Uganda confirm this finding. In 2000, although 254 firms reported receiving some form of technical assistance, the most important source of such assistance for the largest number of small and medium-sized enterprises (56.6%) was non-profit-making agencies. The next most important technical assistance providers were private agencies (36%), of which friends, buyers, suppliers and other firms were by far the most important. However, although state and public agencies were consulted by small and medium-sized enterprises almost as frequently as non-profit-making and private sources, the state and public agencies were evaluated as only moderately useful, i.e. considerably less useful than the private sources. Nonetheless, state and public agencies were ranked a distant third, providing assistance to just 7.4% of the 254 firms (Oyeyinka & Gehl Sampath, 2000). These conclusions are useful, but there is a need to seek additional insights by examining some key differences in the use of technical support across industrial sectors, and how this can be specifically addressed in the case of the pharmaceutical sector.

6.2.2 Ensuring policy coherence of relevance to local production capacity

The joint venture is predominantly being viewed by stakeholders as an investment issue (given UIA's major role) with a health dimension, with almost no coordination with the science, technology and innovation agencies within Uganda. Neither the Ugandan Ministry of Tourism, Trade and Industry nor UNCST has been involved in decisions made in this regard. This is an issue that needs to be addressed in order to ensure sustainability of the venture on the one hand and the expansion of the sector on the other hand. Pharmaceutical innovation (even at relatively lower levels of technical intensity) relies on support from public-sector institutions – both in terms of providing the requisite skills for firm-level activities, and also for research activities that could feed into commercial innovations. This is especially true if firms such as Quality Chemicals are to expand beyond simple formulations to achieve cost-effective production in the mid- or long-term. Quality Chemicals officials and the Cipla experts at the production plant were of the view that the availability of skilled human capital that could be trained to handle production was a major challenge. Further, Cipla staff interviewed at the plant were of the view that there were not enough people trained in chemistry and pharmacy who could be trained to perform responsible tasks at the firm.[69] Quality Chemicals is trying to resolve this problem by partnering with the University of Makerere's Medical and Pharmacy Schools and the Chemistry Department to generate more awareness among university professors and staff regarding the type of training that need to be imparted to graduates to enable them to work effectively in local companies.[70]

69 Source: field interview with Mr Ravi Reddy, Cipla, November 2009.

70 Source: field interview with Mr George Baguma, Chief Marketing Officer, Quality Chemicals, November 2009.

The predominant emphasis on investment and health is explained by two factors: Uganda's own internal health demands, and the fact that the overall contribution of the pharmaceutical sector to national GDP has been very low (less than 0.2%) (UNIDO, 2007). Given the nature of the technologies underlying pharmaceutical production capacity, this emphasis seems misplaced. If the goal is to provide access to medicines at the most reasonable cost, then the policy framework has to integrate strategies that allow local actors to integrate backwards to produce raw materials required to produce generic drugs, thereby reducing their dependence on foreign partners.

Fostering this form of technological learning required for reverse engineering calls for greater involvement and coordination with the science, technology and innovation agencies in Uganda and also for an express recognition that the pharmaceutical sector is a clear sectoral priority in economic development. Currently this is not the case in all the policy developments, whether on the investment front or on the science, technology and innovation policy front. Field interviews in 2009 with UIA reveal that the pharmaceuticals sector has been considered a priority in practical terms, but this needs to be laid out clearly to ensure coherent strategic action.

Further, it would be important to clearly specify procedures that lay down the conditions under which local firms can expect support of the kind received by Quality Chemicals. In the absence of clear guidelines to promote the strategic advancement of the sector beyond a single firm, ad hoc policy inputs of the kind currently observed are not likely to bear many results in the mid- or long term. This point is also related to an observation made in Section 5.1.5: The policy framework for pharmaceutical production needs to set out clear aims and strategies to accomplish these aims, failing which there will be no good way to evaluate success achieved as part of the fragmented initiatives. Finally, technology transfer needs to be promoted as a key element of enhancing local productive capacity for pharmaceuticals, and not only as part of the investment agenda of Uganda.

6.2.3 Enhancing linkages between public research institutes and local firms

Questionnaire responses gathered through the survey of the key actors indicate that the main sources of technology for the public research institutes are foreign university collaborations on projects of limited scope and collaborations with other universities and public research institutes. As Table 3 (above) shows, the few product development initiatives being carried out in the local public research institutes are on a relatively low scale (mainly developing proof of concept) or deal with low-technology issues (traditional medicine). There is almost no funding available to research activities at the university centres (field interviews).

At the same time, the low levels of collaboration are a reflection of the low levels, and relatively small numbers, of product development activities going on in local firms.

6.2.4 Ensuring easy availability of financial alternatives

Interviews with executives from Quality Chemicals reveal that the firm has struggled to obtain easy access to credit at reasonable interest rates right from its inception. Apart from the two financial initiatives that the Ugandan Government has initiated (see Section 5.3), which many firms have not qualified for, other sources of finance for local firms are very difficult to secure in Uganda. Field interviews and regional consultations held on this issue indicate this to be a key concern in promoting local production activities.

In the case of Quality Chemicals, a critical issue that delayed production of drugs was the unavailability of the company executives to secure continuous and easy credit even after the initial investments had already been made and the plant was being set up. The Ugandan Government bought out a 23% stake in the company to provide the requisite finances that could help production. Any other local company that seeks to technologically upgrade its facilities and expand into local production of drugs or other medicinal products will have to necessarily anticipate such financial hurdles.

6.2.5 Improving market access of the local firms and the capacity of the National Drug Authority

The expansion of production will depend on the possibility to supply more to the local and regional markets. Quality Chemicals faces two primary hurdles in fully accessing the local market. First, there are restrictions over the sale of ARVs in private medical stores in Uganda as a result of the Ugandan Government's initiative to control the parallel exportation of cheaply supplied branded drugs out of the country. This initiative is meant to respond to concerns in other countries where ARVs sold as generics in Uganda are on-patent. By restricting the sale of generic drugs in private medical stores in Uganda, the Uganda Government hopes to limit private parties' possibilities of seeking to sell purchased drugs in on-patent markets.[71] This restriction not only limits the ability of local firms such as Quality Chemicals to interact directly with consumers to create goodwill and reputation, but also does not make it possible for people in need of the medicines to access treatment through out-of-pocket expenses. This could be a serious limitation to access to medicines, especially since several Ugandan Government-held dispensaries are often able to cater to only a quarter of the total demand for ARVs in a month. For example, the public pharmacy at the Mulago Hospital in Kampala was able to provide ARVs to only 25% of people with HIV registered there.[72] Second, there is very little consumer confidence in the quality of the medicines produced locally, and this needs to be promoted through Ugandan Government intervention that strengthens the capacity of the drug regulatory authority.[73] Improving the capacity of the drug regulatory authority is also crucial because, in the absence of a well-established capacity to register drugs, several drugs

71 Source: field interviews with Dr Martin Oteba, Secretary, Ministry of Health, November 2009.

72 Source: field interviews with staff at the Mulago Hospital, November 2009.

73 Source: field interview with Mr George Baguma, Chief Marketing Officer, Quality Chemicals, Uganda, November 2009.

of importance to public health remain unregistered. Previous studies have shown that even when there is a clear public health objective, obtaining authorization to import non-registered drugs is extremely cumbersome and time-consuming in Uganda (MSF, 2007).

As stated earlier, in January 2010 the joint venture was granted WHO's GMP certification, as a first step to full WHO prequalification. The latter would open up possibilities to participate in international tenders, such as by WHO and other multilateral organizations engaged in drugs procurement activities. If Quality Chemicals receives full prequalification, the company could, in theory, participate in the international tendering processes for ARVs and antimalarials. However, current rules under which such tenders operate show that the tenders are usually granted to the cheapest bidder, which may not be possible for Quality Chemicals at this stage of its production capabilities.[74] Therefore, it may be necessary to review such procurement guidelines to allow for a special mark-up (approximately 20%) to producers from newly established facilities in LDCs to participate in such tenders.[75]

7. Implications of local production and related technology transfer on access to medicines

The Ugandan Government's decision to procure 100% of the joint venture's output of ARVs will no doubt contribute to greater access to medicines. Without the presence of a local producer such as Quality Chemicals, the Ugandan Government would not have been prepared to make a comparable commitment. Several Ugandan Government officials have stressed the fact that the Ugandan Government considers the support of local production from an industrial development perspective,[76] thus willing to make expenditures in favour of local champions that foreign suppliers of finished pharmaceutical products alone would not be able to claim. However, from an access-to-medicines perspective, this calls for a reduction of total production price to a level where the products from Quality Chemicals are no more than 5–7% more expensive than internationally competitive generic prices in these therapeutic segments. In the absence of a clear strategy to accomplish this, not only at the company level but also at the national level, the Ugandan Government risks compromising on health objectives by securing less for the same price.

As pointed out in previous sections, a reduction of the price of production will hinge on the ability of Quality Chemicals to attain price competitiveness

74 As noted earlier, Quality Chemicals' products are about 20% more expensive than comparable branded generics, due to the need to import into Uganda all raw materials required for the formulations.

75 This opinion was expressed very strongly by all regional producers during the WHO–UNCTAD–ICTSD Regional Dialogue on Local Production Capacity and Technology Transfer, held in Cape Town on 10–11 December 2009.

76 For example, according to a field interview with Dr Martin Oteba, Ministry of Health, Uganda, November 2009.

by building capacity for local API production and expanding sales into the regional African market. This will be the principal means to lower the price of medicaments to a level where the joint venture could compete with Chinese and Indian manufacturers. Nonetheless, the joint venture also shows that Indian firms are already seeking active partners to which they can outsource their manufacturing, provided the right incentives and absorptive capacity exists. According to the Cipla senior management, future investments in building domestic API production capacity will depend on the effective implementation of TRIPS Agreement flexibilities under Ugandan patent law, which may therefore directly contribute to improving access to medicines in Uganda.

8. Policy-relevant findings

This study has analysed a case of technology transfer to enhance local production capacity in pharmaceuticals in an LDC through a developing country firm. The analysis presents a very interesting case of successful technology transfer where both tacit and codified elements have been shared in setting up local production in Uganda. Despite this achievement, it may be too early to predict how much of this will shape the technological trajectory of the sector as such, and whether spillovers of the kind required to foster innovation and productive capacity more broadly in the entire sector will materialize. Uganda has put in place several important policies that deal with various aspects of science, technology and innovation, investment, technology transfer and intellectual property. The task that lies ahead is one of strengthening linkages, both at the policy implementation stage and in the day-to-day functioning of the key actors, in equal measure in the public sector and enterprise domains. This study has identified the key constraints in achieving local production of pharmaceuticals that also meet globally accepted quality standards that need to be addressed through policy actions in order to ensure sustainable local production.

However, more generally speaking, the fact that LDCs are not obliged to offer patent protection on pharmaceutical products as required by the TRIPS Agreement until 2016 has not resulted in investment and technology transfer in the sector on a large scale-up until now. Indian companies have been reluctant to invest in Africa using the 2016 deadline for two reasons, namely the weak framework conditions for investment and innovation in African countries and the gradual reorientation of the Indian companies towards more R&D-based production. Addressing these issues may need to go hand in hand with efforts to use the policy space provided by the 2016 deadline in this area.

Leading producers of low cost, good quality generics, like India's Cipla, have been indicating over the past years their willingness to transfer to LDCs pharmaceutical technologies of relevance to public health.[77] Most Cipla

77 Dr Yusuf Hamied, Chief Executive Officer of Cipla, interview of December 2009.

officials interviewed stated that the joint venture has been established "for philanthropic reasons.[78] The goodwill and public health interest notwithstanding, Cipla receives a good financial deal as part of the joint venture. In return for a relatively risk-free investment, it receives 50% of the profits from the sale of the products, and it is to be the sole supplier to the Government of Uganda for the next 7 years. This guarantees Cipla a share of the Ugandan market that it would perhaps have to compete hard for, as an internationally competitive supplier. In fact, the questionnaire-based information collected from Cipla officials points out that retaining domestic markets, retaining export markets, reducing rising R&D costs (in India) and manufacturing locally within Africa were four important underlying motives that led to the creation of the joint venture.[79] While the Ugandan Government considers this joint venture as an important possibility to promote both industrial development and the production of public health-relevant medicines,[80] the support provided to Cipla does imply considerable costs for the national budget.

This study has emphasized the importance of considering technology transfer as a cross-cutting issue and of strategically integrating technology transfer into the policy framework for pharmaceutical production and innovation in Uganda. This implies laying out a clear technology-transfer strategy as part of Uganda's overall innovation policy, in addition to identifying the technology needs of the pharmaceutical sector. On the institutional side, it would seem appropriate to establish a technology-transfer office that handles the coordination and promotion of technology of relevance to key sectors. To enhance domestic stakeholders' potential to benefit from technology transfer, actors need improved technology-transfer negotiation capabilities, including that of UIA and other key Ugandan Governmental agencies that negotiate on behalf of local firms and organizations.

Promotion of technology transfer will result in productive capacity only when the technology-absorption capacity of the sector is enhanced through appropriate interventions. This study has identified these interventions as skilled human resources of relevance to the pharmaceutical sector; good-quality open science research in public research institutes; availability of technical assistance services of the kind required for the sector (especially to promote the production of good-quality drugs through the NDA); adequate financial alternatives for private-sector enterprises to emerge, expand and be risk-taking (including business incubation and fledgling services); and easy market access for their products. These need to be fostered at the sector level in equal measures for all firms engaged in production.

The pharmaceutical sector is a very distinct one, and the question of making local firms competitive in an LDC context raises a number of challenges that relate to ensuring technological upgrading of relevance to globally acceptable quality standards, while at the same time ensuring that the firms involved in

78 Source: information gathered through the questionnaire survey.

79 Source: information gathered through the questionnaire survey.

80 Source: field interview with Dr. M. Oteba, Ministry of Health.

making the investments are able to market their products. In other words, there is a need for incentives that bridge the time gap between production of drugs for the local market and production of drugs of globally acceptable standards, and the Ugandan Government has a large role to play. This calls for introduction of specific industry-related measures designed to alleviate the initial hiccups of production and market access for local firms. It is perhaps not realistic to expect firms to diverge from a normal catch-up path, wherein firms and sectors gradually accumulate capabilities to emerge as globally competitive suppliers. Markets, both local and regional, tend not to function competitively as a result of oligopolistic practices of firms, anticompetitive constraints, information asymmetries and difficulties of codifying demands of consumers in a clear and predictable manner. These impose added barriers to entry and costs for nascent local firms. Therefore, measures to enable local firms to upgrade in a staggered manner and access markets more easily are important to allow firms to recoup revenues against their investment. In the Ugandan case, it will also be important to ensure that the strong link to public health and local access to medicines that seems to be a key driver for the development of production capacity is retained and strengthened further during expansion of the sector.

References

Caines K, Lush L. Impact of public–private partnerships addressing access to pharmaceuticals in selected low and middle income countries: a synthesis report from studies in Botswana, Sri Lanka, Uganda and Zambia. Geneva: Initiative on Public–Private Partnerships for Health, 2004.

Castellacci F, Archibugi D. The technology clubs: The distribution of knowledge across nations. *Research Policy*, 2008, 37:1659–1673.

Cohen W, Levinthal D. Absorptive capacity: a new perspective on learning and innovation. *Administrative Science Quarterly*, 1990, 35:128–152.

Ecuru J et al. *Research in Uganda: Status and implications for PUBLIC POLICY*. Kampala, Uganda National Council for Science and Technology, 2008.

Gehl Sampath P. India's product patent compliance: Emerging strategies for global and local access to medicines. London, Department for International Development, 2008.

Gehl Sampath P. Health innovation in late economic development: Local capacity for disease of the poor. London, Routledge, 2010.

Kamunyori S et al. *Health and biotechnology innovation in Uganda*. 2009. Draft on file with author.

Ministry of Health. *Uganda national drug policy*. Kampala, Ministry of Health, 2002.

MSF. *Untangling the web of price reductions*. Geneva, Médecins sans Frontières, 2007 (http://www.accessmed-msf.org).

Musungu S. *Public health and anti-counterfeiting initiatives: Legislative principles and model provisions*. Presented at the Second EAC Regional Multi-Sectoral Stakeholders' Meeting on EAC WTO-TRIPS and Pharmaceutical Sector Promotion, Arusha, Tanzania, 8–10 December 2010.

Oyeyinka B, Gehl Sampath P. *Innovation in African development*. Washington, DC, World Bank, 2000.

Oyeyinka B, Gehl Sampath P. *Latecomer development: Innovation and knowledge for economic catch-up*. London, Routledge, 2009.

Pinheiro ES et al. A survey of the syntheses of active pharmaceutical ingredients for antiretroviral drug combinations critical to access in emerging nations. *Antiviral Research*, 2008, 79:143–165.

The Standard. High Court enjoins UN in case against generic ARVs ban. *The Standard*, 17 January 2011 (http://www.standardmedia.co.ke/InsidePage.php?id=2000026980&cid=4&).

Ugandan Investment Authority. *Making Uganda a leading investment destination*. Report of the Presidential Investors Round Table meetings, 2004/2006. Kampala, Ugandan Investment Authority, 2007.

UNAIDS. *Report on the global AIDS epidemic*. Geneva, Joint United Nations Programme on HIV/AIDS, 2008.

UNCTAD. The least developed countries report 2007: Knowledge, technological learning and innovation for development. Geneva, United Nations Conference on Trade and Development, 2007.

UNCTAD, Least Developed Countries Report 2008: Growth, Poverty and the Terms of Development Partnership, Geneva, United Nations Conference on Trade and Development, 2008.

UNCTAD. *Development dimensions of intellectual property in Uganda: Transfer of technology, access to medicines and textbooks*. Geneva, United Nations Conference on Trade and Development, 2010a (http://www.unctad.org/en/docs/diaepcb200913_en.pdf).

UNCTAD. *GlobStat UNCTAD statistics*. Geneva, United Nations Conference on Trade and Development, 2010b.

UNIDO. *Pharmaceutical sector profile: Uganda*. Vienna, United Nations Industrial Development Organization, 2007.

WHO. *Prequalification update: 12 March 2010*. Geneva, World Health Organization, 2010 (http://apps.who.int/prequal/info_press/pq_news_12March2010_UGA_Manufacturer.pdf).

Winters LA, Shahid Y. *Dancing with the giants: China, India and the global economy*. Washington, DC, World Bank, 2007.

Annex: Interviewed individuals and institutions

Pharmaceutical experts

George Baguma, Marketing Director, Quality Chemicals, Ltd.

Yusuf Hamied, Chief Executive Officer, Cipla

M.O. Ogalo, Managing Director, Medipharm Industries Limited

Paul Okware, Technical Director, Medipharm Industries Limited Ravi S. Reddy, Chief Operating Officer, Quality Chemicals Ltd.

Dilip Shah, President, Indian Pharmaceutical Alliance

Three technical experts from Cipla

Representatives of the Ugandan Government

Julius Ecuru, Assistant Executive Secretary, Uganda National Council for Science and Technology

Apollo E Muhairwe, Executive Secretary, Uganda National Drug Authority

Martin Oteba, Ministry of Health

Joseph Rubamela, Acting Director, Product Development, Uganda Industrial Research Institute

Elizabeth Tamale, Principal Commercial Officer, Ministry of Tourism, Trade and Industry

Six Members of the Pharmaceutical Distribution Network

Two pharmacies at Mulago hospital, Kampala

Four pharmacists in private pharmacies in Kampala

Representative of a nongovernmental organization

Moses Mulumba, Legal Associate, HEPS Uganda

Academic researcher

Charles Ibingira, Deputy Dean Research, Makerere Medical School

Private lawyer

Edgar Tabaro, Legal Consultant, Mwesiga Rukutana & Co. Advocates

Annex

Field questionnaire

The information required is for the year 2008, unless otherwise stated.

Please note: For the purposes of this project, "innovation" is defined as the application of new practices and production of all products and process technologies that are new to the firms in question (Nelson and Rosenberg, 1993). Innovation is measured by the number of new products and processes developed and applied by the firms/organizations in the past five years that helped to enhance the local production capacity of pharmaceuticals.

1. Firm/organization demographics

1.1 Name of firm/organization: _____

Year established: _____

1.2 What is the nature of your firm's (or organization's) main industrial production activity? (*You may tick more than one.*)

□ *(a) Bulk drugs/active pharmaceutical ingredients*

□ *(b) Formulations manufacturer (please tick one or more of the following):*

- □ (i) Prescription medicines
- □ (ii) Over-the-counter formulations
- □ (iii) Branded formulations/under licence
- □ (iv) Generic formulations

□ *(c) Vaccines*

□ *(d) Drug delivery: capsules*

□ *(e) Others (please specify)* _____

1.3 How many products do you produce and market right now?

(*Please state number of products.*) _____

1.4 What is the ownership structure of your firm/organization?

□ *(a) State-owned (100%)*

□ *b) Foreign-owned (100%)*

□ *(c) Locally owned (100%)*

□ *(d) Joint venture*

Local equity _____ % *Foreign equity* _____ %

1.5 Is your firm part of a larger group?

□ *(a) Yes* □ *(b) No (If No, go to Question 1.8.)*

1.6 How many overseas affiliates does your firm have?

(Please give total number.) _____

1.7 What are the main activities of your firm's foreign affiliate?
(*You may choose more than one answer.*)

□ *(a) Production of the final drug*

□ *(b) Production of active pharmaceutical ingredients (APIs)*

□ *(c) Marketing*

□ *(d) Research and development (R&D)*

1.8 Was your firm a result of a merger or acquisition?

□ *(a) Yes* □ *(b) No*

1.9 What are the history and philosophy behind setting up this firm? How do you think it fits into the local market?

1.10 Are there specific local or regional export considerations that led to your activities? If yes, please elaborate.

1.11 What were the underlying motives to set up the firm/joint venture? (*Please circle your rating for each point, from 1 (weakest) to 5 (strongest).*)

(a) To retain domestic market	1	2	3	4	5
(b) To retain export markets	1	2	3	4	5
(c) To reduce rising R&D costs	1	2	3	4	5
(d) To acquire technical expertise	1	2	3	4	5
(e) Other (*please specify and rate*)					
_____	1	2	3	4	5
_____	1	2	3	4	5
_____	1	2	3	4	5

1.12 What was your firm's/organization's total employment (full time) in the following years? (If your firm was been set up recently, respond only to the years in which the firm has been in operation.)

2004	2005	2006	2007	2008

1.13 What is the breakdown of your firm's/organization's workforce (%) between 2004 and 2008? (If your firm was set up recently, respond only to the years in which the firm has been in operation.)

Year/level	2004	2005	2006	2007	2008
(a) Managers					
(b) Skilled (e.g. chemist, engineer)					
(d) R&D					
(c) Marketing					
(d) Clerical					
(e) Others					

1.14 If producer of bulk drugs and formulations:

1.14.1 In which categories do your products fall?

□ (a) Cardiac therapies
□ (b) Antibiotics
□ (c) Anti-tuberculosis
□ (d) Antiparasitics and antifungals
□ (e) Vaccines
□ (f) Respiratory ailments
□ (g) CNS and psychiatric therapy
□ (h) NSAIDs and anti-rheumatics
□ (i) Anti-AIDS
□ (j) Other therapeutic segments

1.14.2 Are you involved in the production of first- and second-line antiretroviral drugs?

□ (a) Yes □ (b) No

1.14.3 If yes, which ones? (Please select from the list below. You may select more than one.)

□ (a) Staduvine
□ (b) Zidovudine
□ (c) Lamivudine
□ (d) Nevirapine
□ (e) Efavirenz
□ (f) Tenofovir
□ (g) Indinavir
□ (h) Emtracitabine
□ (i) Didanosine
□ (j) Lopinavir
□ (k) Nelfinavir
□ (l) Abacavir

1.15 What percentage of your firm's/organization's raw materials or API/bulk drug (for formulation manufacturer) do you source domestically?

2004	2005	2006	2007	2008

1.16 What was the breakdown of your purchases for 2008? (*Please give percentages.*)

Firm type/purchases	Production inputs	Machinery and related components
(a) From foreign firms		
(b) From local firms		

Total	100%	100%

2. Technology transfer and knowledge generation

2.1 How would you rate the average quality of your firm's production machinery? (*Please tick only one.*)

□ a) World class

□ (b) Highly advanced

□ (c) Advanced

□ (d) Not very advanced

□ (e) Dated

2.2 What kind of technologies do you consider critical to producing your products, and how do you procure them? (New technology can include acquisition of new skills and technical know-how by employees and the firm, new methods and process of production, new production equipment, and new managerial and marketing methods. Please differentiate between process technologies, product technologies, skill and technical know-how and other technologies when answering this question.)

2.3 What has been your firm's/organization's main source of new technology over the past 5 years? (Please circle your rating for each point, from 1 (weakest) to 5 (strongest).)

(a) Technology licensing	1	2	3	4	5
(b) Firms you sell your output to	1	2	3	4	5
(c) Foreign partner of a joint venture	1	2	3	4	5
(d) Strategic partner	1	2	3	4	5
(e) Turnkey contract	1	2	3	4	5
(f) Transfer from parent firm (for subsidiaries)	1	2	3	4	5
(g) Hiring of managers and skilled employees	1	2	3	4	5
(h) Suppliers of equipment or components	1	2	3	4	5
(i) Universities and public research institutes	1	2	3	4	5
(j) Reverse engineering	1	2	3	4	5

(k) Informal sources	1	2	3	4	5
(l) Technical training by private sector	1	2	3	4	5
(m) Technical training provided by government agencies or technical assistance providers	1	2	3	4	5
(n) Others (please specify and rate)					
_____	1	2	3	4	5
_____	1	2	3	4	5
_____	1	2	3	4	5

2.4. Describe your firm's/organization's experience in negotiating to secure or develop that technology. What would you rate as the biggest difficulties faced by you? (*Please circle your rating for each point, from 1 (not so important) to 5 (very important obstacle).*)

Difficulty faced	Rating				
(a) We had to search for a long time and negotiate with several partners to finally make the deal	1	2	3	4	5
(b) The other party usually was looking for a strategic partnership (with greater returns) that we could not offer	1	2	3	4	5
(c) We had no good legal bargaining skills in-house	1	2	3	4	5
(d) We had trouble agreeing on royalties with the partner firm	1	2	3	4	5
(e) We had trouble providing security against copying and infringement to the partner firm	1	2	3	4	5
(f) Restriction(s) or condition(s) under local law placed on the transfer affected the negotiations	1	2	3	4	5
(g) Others (please specify and rate)					
_____	1	2	3	4	5
_____	1	2	3	4	5
_____	1	2	3	4	5

2.5 Please elaborate how you resolved these issues.

2.6 Did you receive any governmental support in dealing with these issues?

□ (a) Yes □ (b) No

If yes, please explain the nature of the assistance:

2.7 Did your firm/organization collaborate with any government agency or other external organization to secure that technology? Which ones were they, and what was the nature of the collaboration?

2.8 What is your firm's/organization's average capacity utilization rate? (Please tick where appropriate.)

Capacity utilization	2004	2005	2006	2007	2008
(a) Up to 50%					
(b) 51–70%					
(c) 71–90%					
(d) Over 90%					

2.9 What were the main impediments that prevented the technology from being applied to its fullest extent? (Please circle your rating for each point, from 1 (weakest) to 5 (strongest).)

Impediment	Rating				
(a) The staff lacked the requisite technical skills	1	2	3	4	5
(b) The partner who transferred technology did not transfer the know-how critical to its application	1	2	3	4	5
(c) The staff who were trained to apply the technologies left the firm	1	2	3	4	5
(d) There is a lack of physical infrastructure (water, electricity and other local infrastructure) to ensure its smooth application	1	2	3	4	5
(e) Others (please specify and rate)					
_____	1	2	3	4	5
_____	1	2	3	4	5
_____	1	2	3	4	5

2.10 What kind of support have you tried to provide so that your staff are able to use the technology correctly?

2.11 What are your future technology needs, and where will you seek to obtain such technology?

3. R&D and product/process technologies

3.1 What is your R&D focus?

□ *(a) Development and supply of generics*

□ *(b) Biogenerics*

□ *(c) API supply*

□ *(d) Innovative R&D*

□ *(e) Vaccines*

□ *(f) Clinical trials support*

□ *(g) Others (please specify)* _____

3.2 How do you rate the contribution of the following to new product or process development at your firm/organization? (*Please circle your rating for each point, from 1 (weakest) to 5 (strongest).*)

Statement	Rating				
(a) Government incentives for innovation	1	2	3	4	5
(b) Scientific/skilled workforce	1	2	3	4	5
(c) Local universities for R&D collaboration	1	2	3	4	5
(d) Local R&D institutes for R&D collaboration	1	2	3	4	5
(e) Intellectual property protection	1	2	3	4	5
(f) Quality of local infrastructure services	1	2	3	4	5
(g) Availability of venture capital	1	2	3	4	5
(h) Participation in local SMI development schemes	1	2	3	4	5
(i) Participation in government–firm–technology transfer coordination councils	1	2	3	4	5
(j) Transfer of personnel to local firms or R&D institutions (for training)	1	2	3	4	5
(k) Others (please specify and rate)					
_____	1	2	3	4	5
_____	1	2	3	4	5
_____	1	2	3	4	5

3.3 How would you rate the quality of human skills and public sector research of relevance to pharmaceutical production and R&D within the country? To what extent can you rely on it while planning your firm's/organization's future strategies?

3.4 What do you think is missing in the local innovation environment to promote the activities of the sector in concrete terms?

3.5 Over the past 5 years (2004–2008), which of these has your firm/organization done? *(You may choose more than one.)*

□ *(a) Bought new capital equipment?*

□ *(b) Set up a new production line?*

□ *(c) Put in a new production system?*

□ *(d) Put in new information and communication technology (ICT) components?*

3.6 Was the new process and organizational system or its upgrade:

□ *(a) Based on in-house R&D*

□ *(b) Adapted from competitors*

□ *(c) Licensed from a technology supplier*

□ *(d) In collaboration within industry association*

□ *(e) Based on support from an intermediary organization*

□ *(f) Other (please specify)* _____

3.7 How much did your firm/organization spend on R&D (excluding quality control and testing) as a percentage of total sales in:

□ *(a) 2004* _____ *%*

□ *(b) 2005* _____ *%*

□ *(c) 2006* _____ *%*

□ *(d) 2007* _____ *%*

□ *(e) 2008* _____ *%*

3.8 Have you carried out new product development in the past 5 years?

□ *(a) Yes* □ *(b) No*

□ *(c) If yes, number of times in the past 5 years? (Please give number.)*

_____ _____ _____

3.9 Have you carried out new process development in the past 5 years?

□ *(a) Yes* □ *(b) No*

□ *(c) If yes, number of times in the past 5 years? (Please give number.)*

_____ _____ _____

3.10 How was the new product obtained?

□ *(a) Licensing*

□ *(b) Foreign subsidiaries*

□ *(c) Own development*

□ *(d) Others (please specify)* _____

3.11 Were the new products new to:

□ *(a) Your firm*

□ *(b) Local market*

□ *(c) Regional market*

□ *(d) Global market*

3.12 Were the new products registered under intellectual property rights (IPR) instruments?

□ *(a) Patents*

□ *(b) Trademarks*

□ *(c) Both*

□ *(d) Others (please specify)* _____

3.13 In which categories do your new products fall?

□ *(a) Cardiac therapies*

□ *(b) Antibiotics*

□ *(c) Anti-tuberculosis*

□ *(d) Antiparasitics and antifungals*

□ *(e) Vaccines*

□ *(f) Respiratory ailments*

□ *(g) CNS and psychiatric therapy*

□ *(h) NSAIDs and anti-rheumatic*

□ *(i) Anti-AIDS*

□ *(j) Other therapeutic segments*

3.14 How much of your research is directed towards local disease conditions (anti-AIDS, anti-tuberculosis and other infectious diseases)?

□ *(a) All*

□ *(b) 50%*

□ *(c) Less than 25%*

□ *(d) None*

3.15 If any of your research is directed towards local disease conditions other than HIV/AIDS, please give specific details:

4. Policy and institutions

4.1 How do the following constrain your firm's/organization's efforts to develop local production capacity? (*Please circle your rating for each point, from 1 (not severe at all) to 5 (extremely severe).*)

(a) Customs procedures and EXIM policy	1	2	3	4	5
(b) Entry of foreign firms into the local market	1	2	3	4	5
(c) Restrictions in licensing arrangements	1	2	3	4	5
(d) Local duties and levies	1	2	3	4	5
(e) Access to land (registration cost and procedures)	1	2	3	4	5
(f) Official corruption	1	2	3	4	5
(g) Patent protection on pharmaceuticals	1	2	3	4	5
(h) Regulations (e.g. drug policy, industrial policy)	1	2	3	4	5
(i) Patent office delays and restrictions on animal testing	1	2	3	4	5
(j) Price control of pharmaceutical products	1	2	3	4	5
(k) Regime on data protection	1	2	3	4	5
(l) Others (please specify and rate)					

_____	1	2	3	4	5
_____	1	2	3	4	5
_____	1	2	3	4	5

4.2 If yes, in which areas do you think government or other institutional support is critical to devise new strategies? (*Please circle your rating for each point, from 1 (not critical) to 5 (extremely critical).*)

(a) Improve speed of processing patent applications	1	2	3	4	5
(b) Create a more enabling R&D environment	1	2	3	4	5
(c) Reduce pricing pressures by DPCO	1	2	3	4	5
(d) Access to land (registration cost and procedures)	1	2	3	4	5
(e) Clarify ambiguities on patentability and other terms in the patent regime	1	2	3	4	5
(f) Prevent or delay data protection regimes	1	2	3	4	5
(g) Enable rules and agencies to promote technology transfer	1	2	3	4	5
(h) Improve custom procedures and EXIM policy	1	2	3	4	5
(i) Others (please specify and rate)					
_____	1	2	3	4	5
_____	1	2	3	4	5
_____	1	2	3	4	5

4.3 Are you aware of any policies to actively support the production of pharmaceuticals in your country?

□ *(a) Yes* □ *(b) No*

4.3.1 If yes, have they been recent (in the past 5 years)?

□ *(a) Yes* □ *(b) No*

4.3.2 What are they, and how successful have they been?

4.3.3 In your opinion, do certain government policies discourage the production of pharmaceuticals in your country? Which ones?

4.4 How is transfer of technology regulated in your country? *(You may tick more than one option.*)

□ *(a) Through a separate law/policy that enables and actively promotes technology transfer*

□ *(b) Within the general S&T framework*

□ *(c) Through a national technology transfer office*

□ *(d) Others (please specify)*

4.5 Are you aware of any specific policies that encourage the transfer of technology to pharmaceutical firms in your country?

4.5.1 How would you rate the effectiveness of these technology transfer policies? (Please circle your rating on a scale from 1 to 5, where 1 is least effective and 5 is most effective.)

1 2 3 4 5

4.6 What is the extent to which local pharmaceutical firms and research organizations are included to provide inputs to deliberations on the following policy issues? (*Please circle your rating on a scale from 1 to 5, where 1 is not at all included and 5 is completely included.*)

(a) Health (including issues of medicines/ insurance/access)	1	2	3	4	5
(b) Science, technology and innovation	1	2	3	4	5
(c) Industry regulation	1	2	3	4	5
(d) Investment plans and options	1	2	3	4	5
(e) Intellectual property	1	2	3	4	5

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