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Part I

The Pharmaceutical Industry in Africa

Part I of this book aims to strengthen the inadequate evidence base on pharmaceutical manufacturing on the Sub-Saharan subcontinent. Throughout this book, 'local manufacturing' and 'African manufacturing' refer to manufacture physically located in Sub-Saharan Africa, whatever its ownership. The ownership structures are certainly relevant to understanding the development of pharmaceutical production, and indeed the extent to which the current industry is in African ownership is striking, while most output is produced for local and regional consumption. The African industry is, as we show, highly 'globalized' in the competitive pressures it faces, but also highly 'localized' in its markets and policy frameworks.

Part I therefore starts with an overview of the industry in Africa, tackling the recurrent myth that it barely exists. The four following chapters analyse aspects of the industrial experience of four countries in producing medicines: Kenya, Tanzania, Ethiopia and Mozambique. The chapters do not aim simply to describe the industrial evolution, though that is certainly one objective. They also explore in detail distinct aspects of the industrial histories: the evolution of technological capabilities in Kenya; the challenges in sustaining a relatively shallow industrial sector in Tanzania; the sharp turnaround of the industry in Ethiopia and its links to joint ventures and health sector change; and the immense challenge of starting from scratch in Mozambique, with Brazilian support. In each case, the authors are looking for wider lessons for policy and practice.

The final two chapters in this part are broader, and both also reflect some West African experiences. Chapter 6 asks an important question: What can help to bring more foreign direct investment to the pharmaceutical industry in Africa, with particular reference to Indian

companies and Ghanaian experience? Finally, Chapter 7 addresses directly a question raised in several other chapters: What is the scope in African contexts for moving up the technological ladder, into producing the ingredients for medicines manufacture, and into more research and development activity?


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Making Medicines in Africa: An Historical Political Economy Overview

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Introduction

This chapter sets out to show that, contrary to widespread misperception, pharmaceutical manufacturing in Sub-Saharan Africa is an established industry with a long history dating back at least to the 1930s. Data for the industry on the subcontinent are fragmented and incomplete (Berger et al., 2009; UNIDO, 2010a; 2010b; 2011a; 2011b), and this chapter and this book contribute to building a coherent historical picture and evidence base. This chapter presents some illustrative historical evidence, drawn from secondary data, reports and fieldwork by the authors and colleagues, as well as academic and non-academic literature.[1] We show that neither industrial capabilities in pharmaceuticals nor policy frameworks to support local pharmaceutical manufacture are a new phenomenon on the subcontinent.

The chapter takes an historical political economy lens to the development of the pharmaceutical industry, providing an overview and then examining three countries' industrial history in more depth. By a 'political economy lens' we mean a view of the evolution of the industry that replaces it within its historical political and economic context. Pharmaceuticals share many elements of the broader African experiences of industrialization. The industry also has, however, some very specific characteristics concerning technology and markets.

This chapter briefly traces the pharmaceutical industry's genesis and development in the context of colonial political history, independence and post-independence industrialization. We trace the development of the industry during the era of import substitution policies in the 1960s to 1970s, the economic crises of the 1980s and early 1990s, and the industrial rebuilding from the 1990s onwards. Some key political economy

themes that are developed throughout the book are introduced here: the current context of international market liberalization, initiated in the era of economic crisis and structural adjustments policies, and its implications for manufacturing investment; the varying role of multinational corporations' (MNCs) investment in local manufacturing in Africa; the co-evolution and integration of the pharmaceutical industry with other manufacturing and industrial sectors; and the insertion of this relatively high-technology sector into local and international innovation systems and policies.

The chapter begins with an initial historical overview, based on firm-level evidence from nine Sub-Saharan African countries. It then compares and contrasts the industrial history of pharmaceuticals in three case study countries, Tanzania, Kenya and Zimbabwe, for which we have field data. These three countries cannot represent the highly diverse industrial history of Sub-Saharan Africa (henceforth often referred to as just Africa). Rather, they provide support and background for some of the generalizations suggested by the overview, and identify some illustrative similarities and differences in the pharmaceutical sector's roots and evolutionary trajectories across African countries. The case studies also identify a number of themes explored in depth in the rest of the book.

Pharmaceutical manufacturing in Africa: an historical overview

There has been substantial academic and policy questioning of the feasibility and desirability of African local pharmaceutical production (Kaplan and Laing 2005 is one of the most widely cited sources). We begin by countering this perception with evidence that pharmaceutical manufacturing companies have been setting up production facilities and manufacturing medicines in Africa since the 1930s.

A sketch of a pharmaceutical investment timeline

Figure 1.1 shows a time line of the pattern of establishment of pharmaceutical firms across different political and economic geographies on the African continent. It is drawn from a data base of start-up dates for manufacturing by larger pharmaceutical firms in a number of the major manufacturing countries in Sub-Saharan Africa, including South Africa, Nigeria, Kenya and Zimbabwe, and also some countries with smaller manufacturing sectors: Tanzania, Botswana, Uganda, Ethiopia and Ghana.

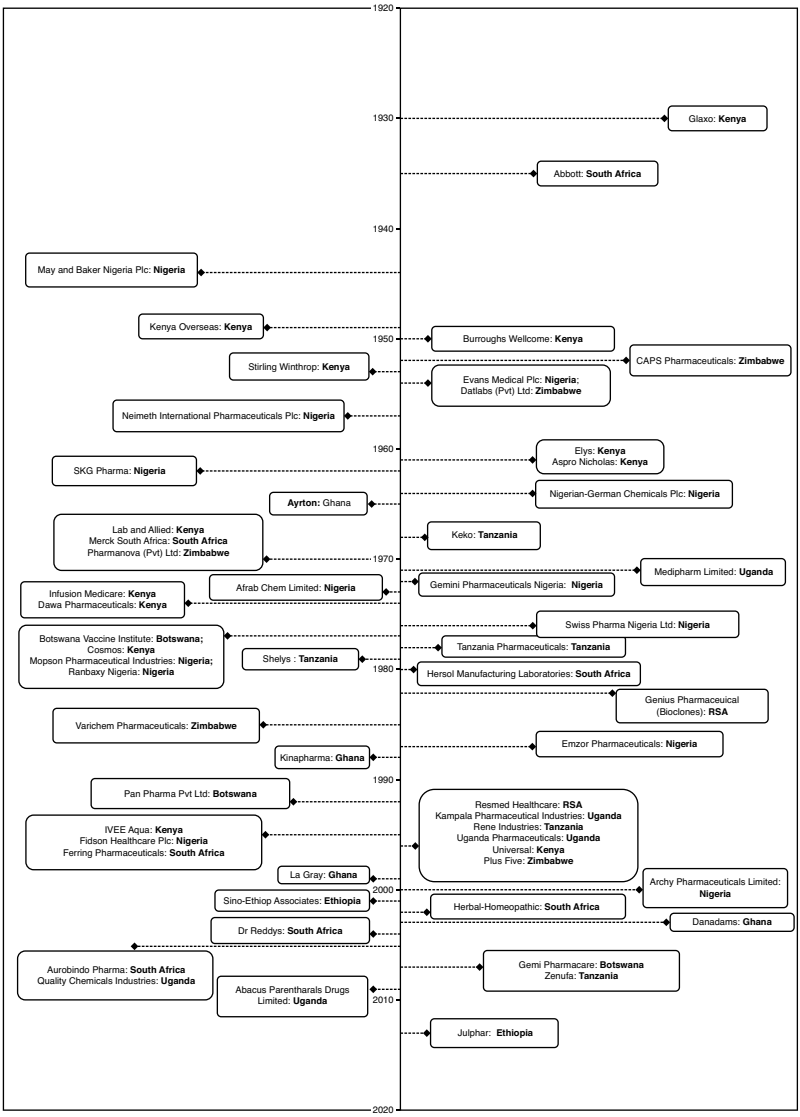

Figure 1.1 A timeline of selected pharmaceutical firm start-ups by country, 1930–2013

Source: drawn by author from created database.

The genesis of local pharmaceuticals manufacturing in South Africa, Nigeria and Kenya appears here as linked to multinational European companies setting up subsidiaries in colonies. In South Africa, Abbott was set up in 1935; in Nigeria, May and Baker was established in 1944; and in Kenya, Glaxo set up shop in 1930 (Figure 1.1). The whole period from 1930 to 1960 shows a slow take-off of local manufacturing in Kenya, Nigeria, South Africa and Zimbabwe. Historically these are the leading industrial countries in Sub-Saharan Africa. Local pharmaceutical industry set up did not occur in isolation, but was contemporary with the rise of other industrial sectors that supported mining and agricultural processing industries. Some of this industrialization was driven by pre-war supply chains with colonies and the disruptions of supplies during World War II.

Figure 1.1 suggests two major bursts of activity in setting up pharmaceutical firms. The first is the 1970s, starting in the 1960s and building up. Then there is a gap in the 1980s and early 1990s, when the rate of start-ups slows almost to zero. The second major burst of activity is from the mid-1990s and continuing into this century.

For most of the countries in Figure 1.1, the 1960s and 1970s were the early years of independence. Across the subcontinent, this post-independence era was characterized by efforts to tackle the challenge of industrialization and growth. Common approaches to industrial policy, promoted also in the development economics and planning literature, mixed public sector investment with import substitution policies, as briefly described in the case studies below. These were years of active developmental states in Africa (Mkandawire, 2001), which were also investing in public sector health and education provision to address the colonial legacies of inequality and discrimination. Domestic production of medicines, by public sector firms and locally owned private companies, found a market in expanding health sector demand.

By the late 1970s, however, this industrial development model was in trouble, and the impact of the economic crisis is reflected in Figure 1.1 by the dearth of new industrial investments in the 1980s. Key events included the oil crises of the 1970s, which severely inflated import bills, undermined balance of payments and fiscal balances and slowed down industrial activity through lack of foreign exchange. The early 1980s were years of severe economic crisis in many countries, exacerbated by severe drought.

The response across much of Africa took the form of structural adjustment programmes, linked to International Monetary Fund fiscal support and requiring extensive privatization and liberalization of trade. The

timing varied: Ghana, for example, embarked on structural adjustment as early as 1983, whereas Zimbabwe only started in 1991.

The 1980s and early 1990s were, as a result, a period of deindustrialization across much of Africa. Previous industrial gains were eroded in many countries, and economic growth turned to decline, while health and education also suffered severely (Cornia et al., 1987). This is the context for the pause in industrial investment evident in Figure 1.1: the case studies that follow add some detail on this period, including the fate of existing firms and the distinctive experience of Zimbabwe.

From the mid-1990s, Figure 1.1 shows industrial investment in new pharmaceutical plants restarting across many countries. Much of this investment was by local investors. In some countries after independence, local entrepreneurs with working experience gained in multinational companies set up their own production facilities, a phenomenon not dissimilar to the Indian pharmaceutical industry evolution.

Pharmaceutical manufacturing capabilities in Africa: an overview

In 2005, a survey found that 37 of 46 African countries possessed some pharmaceutical manufacturing capability (Berger et al., 2009). Since then, numbers and activity have continued to expand (Figure 1.1). Almost all this manufacturing capacity produces generic medicines. Generic medicines are copies of originator or innovator branded medicines; generics have the same dosage form, therapeutic effect, delivery route, known risks and side effects as the originator drug. Local manufacturers in Africa import active pharmaceutical ingredients (APIs) and excipients mainly from India and China (UNIDO, 2010a; 2010b; 2011a; 2011b). Active pharmaceutical ingredients are the therapeutic component of the drug, while excipients are pharmacologically inactive substances used as a carrier for the active ingredients of a medication or as lubricants during the manufacturing process. Local firms import plant, equipment and machinery from India and China, while analytical equipment is sourced mainly from high-income countries such as Germany. Only South Africa and Ghana had built some technological capabilities to manufacture APIs locally, according to the 2005 survey (Berger et al., 2009), though other countries are now seeking to do so as well (see Chapter 7).

The pharmaceutical technologies in use, and the range of pharmaceutical drugs manufactured in African countries, are extensive. Firms have progressed from producing basic tablets and capsules to more complex technologies such as layered and sustained-release tablets. Product portfolios include suspensions and creams, syrups for children, sprays

for inhalation and a range of sterile products such as injectables and ophthalmic preparations. The range of medicines includes anti-pain, anti-infectives including the penicillins, anti-worms and anti-virals, including anti-retrovirals for HIV/AIDS. There is a concerted effort to move into more products for chronic diseases such as hypertension and diabetes that are on the rise, implying a growing market.

Three indicative country case studies

The rest of this chapter briefly compares the industrial evolution of the pharmaceutical industry in three contrasting countries: Zimbabwe, Kenya and Tanzania. We show that their pharmaceutical sectors did not arise in isolation: in each case, the pharmaceutical industry co-evolved in important aspects with the broader industrial development. National patterns of industrial growth and periods of deindustrialization, along with shifts in industrial ownership and financing, are reflected in pharmaceutical firms' evolution. Broad industrial, macroeconomic and political economy influences are shared across industries in national industrial histories.

However, pharmaceuticals also display distinctive industrial characteristics that are observable across countries. The most striking are the technological challenges embodied in pharmaceutical production; the increasing regulatory impact on the African-based industry; and the implications of the health sector structure and funding, including the rise of donor funding, on the evolution of the local industrial structure. These issues are all explored in depth in the rest of the book. Here we present a comparative sketch of three pharmaceutical industrial histories, as an introduction to the analyses to come.

These historical sketches also employ some key concepts that will be used throughout the book, notably the concept of industrial capabilities. Given the high-skill, technologically demanding requirements of pharmaceutical production, as compared to widely produced consumer goods in these countries, the technological capabilities of the firms are key to their efforts to sustain competitiveness. By 'technological capabilities' we mean a set of skills and information the firm requires to operate a given technology and its associated organizational system efficiently (Wangwe, 1995). Firms' competitiveness in pharmaceuticals depends on their ability to obtain, absorb and use technological knowledge, capabilities which build on past skills and knowledge to cumulative effect. Successful firms' capabilities evolve from simpler to more complex activities in investment and process and product engineering (Lall, 1992).

Zimbabwe: the loss of early industrial advantage

There are elements of triumph and tragedy in the industrial history of Zimbabwe. As early as 1990, it was, after South Africa, touted as the next newly industrializing country (Pangeti et al., 2000; Phimister, 2000). The well-established and vibrant manufacturing sector was one of the most advanced and diversified in Africa (AfDB, 1994), contributing 30% to GDP and accounting for 35% of the country's gross export earnings. There were extensive linkages between manufacturing and key economic sectors such as mining, finance and agriculture. The manufacturing sector evolved to supply mining and agriculture, leveraging an extensive infrastructure (Mlambo, 2000; Phimister, 1988; 2000). Zimbabwe therefore provides a narrative of a pharmaceutical sector that arose in integration with other manufacturing and service sectors, illustrating the importance of linkages and support structures in an economy.

Early import substitution

The distinctive history of Zimbabwean manufacturing results from its political history and the related push towards industrial development through import substitution. The legacy begins from the Second World War era. Before then, the country was a destination for British and South African manufactures. During the war, the blockade of traditional trade routes from Britain and the resultant shortages prompted local industrial diversification and accelerated growth of local manufacturing. The average annual industrial growth from 1944 to 1948 was 24.4% (Pangeti et al., 2000). Later, the unilateral declaration of independence (UDI) from Britain in 1965, the trade with South Africa and the resulting UN sanctions (Pangeti et al., 2000; Phimister, 2000) reinforced the push towards industrial self-supply.

Zimbabwe's industrial history illustrates the potential benefits of import-substituting industrialization for countries that later liberalize trade. After 1945, imports from overseas recommenced, increasing competition. Local industry responded by turning to regional markets as an outlet for industrial overcapacity. The expanded markets included the 1953 Central African Federation (CAF) of Zambia, Zimbabwe and Malawi (then Northern and Southern Rhodesia and Nyasaland) (Pangeti et al., 2000). During this era, foreign direct investment by South African and British companies flowed into local manufacturing industry (Phimister, 2000). Industrial protection and import substitution were then vigorously pursued after UDI.

During the early expansionary phase, two of the five major pharmaceutical companies were established: CAPS Pharmaceuticals and Datlabs. The pioneer company, CAPS Pharmaceuticals (then Central African Pharmaceuticals [Private] Limited), was founded in 1953, manufacturing formulations and wholesaling (UNIDO, 2011b). In 1958, CAPS stopped general wholesaling and focussed on manufacturing (CAPS website, 2012). Datlabs (Pvt) Ltd was set up in 1954 as a subsidiary of Ingrams, a South African company (UNIDO, 2007; 2011b). These companies focussed on serving the regional market in the Central African Federation countries. A third major pharmaceutical company, Pharmanova (Pvt) Ltd, was established later, in 1970 in the UDI era (UNIDO, 2007). This period created an industrial base second only to South Africa in the region, including established pharmaceutical producers, inherited in 1980 by the independent government.

Industry–health care integration

A country's domestic market for pharmaceuticals is dependent on its health care spending and health care structure. At independence the new Zimbabwean government targeted the narrowing of the inherited racial gap in living standards by introducing free health care and education for all as key elements of social transformation (Davies and Ratso, 2000). Zimbabwe became renowned for high growth in education, health and public administration to promote social equity in development (Helmsing, 1990). The country also continued its inherited historically high level of reliance on domestically produced medicines (Turshen, 2001).

Zimbabwe also made a pragmatic and early shift to cheaper generic prescription policies to reduce cost of medicines: in 1981, the Ministry of Health produced an essential drugs list (EDLIZ) (WHO, 1995), and this formed the basis for local medicines production strategies. Zimbabwean entrepreneurs established Varichem Pharmaceuticals (Pvt) Ltd in 1985 to serve this expanding market (UNIDO, 2007).

The government also took industrial policy steps to address some of the consequences of 15 years of political unrest, liberation war and sanctions. Industrial machinery had become obsolete due to scarcity of foreign exchange, which continued into the early years of independence (Bond, 1998; Phimister, 1988; Chifamba, 2003). Companies struggled to import capital equipment and upgrade their technologies. The government partially eased foreign-exchange restrictions for verified export orders through an Export Revolving Fund (ERF) in 1983, followed by an Export Retention Scheme (ERS) in 1989 and later

an Open General Import Licence (OGIL) in mid-1990s (Chifamba, 2003).

However, Zimbabwe was not spared the economic crises that swept across African countries from the mid-1980s. Expansion of social services without rising revenues led to budget deficits, forcing the government to abandon their initial resistance to economic structural adjustment programmes (AfDB, 1998). On the advice of the IMF and technocrats in the Ministry of Finance, the country embarked on a structural adjustment programme in 1991. Disastrous economic outcomes included deindustrialization, unemployment and deterioration of the health care system (AfDB, 1997; Brett, 2005; Richardson, 2005).

Despite the deteriorating industrial and economic conditions, however, Plus 5 Pharmaceuticals was established in 1996. The start-up used venture capital funding (UNIDO, 2007; 2011b), a testament to Zimbabwe's financial system's capability at the time, despite deindustrialization, and also to the continuing vibrancy of the pharmaceutical sector. The country continued to rely on locally manufactured medicines (Turshen, 2001), and Zimbabwe appears to have sustained some alignment of industrial and health policy goals through this tumultuous period.

Pharmaceuticals in an era of economic collapse

After 1997, however, economic collapse set in. The decade from 1997 to 2008 saw deindustrialization on a grand scale, as manufacturing decline was driven by hyperinflation (MTDP, 2010). Manufacturing real growth rates were negative every year from 1997 to 2008 except 2005, signifying declining manufacturing capacity as well as loss of skills and technological capabilities. Manufacturing share of GDP fell from 20% in 1997 to 11% in 2008 while GDP shrank annually. The manufacturing share of exports fell from 20% to slightly over 10%. The private sector declined to the point of operating at 10% capacity, faced with shortage of capital, foreign currency, and interrupted electricity supplies. Physical infrastructure crumbled, skilled people emigrated and incentives and institutions were severely debilitated (AfDB, 2009).

Yet even in this era, aligned industry, health and social development policies did create some positive feedback mechanisms, enhancing local manufacturers' innovative capabilities. This environment was instrumental in the country being one of the first in Africa to locally manufacture anti-retroviral medicines (ARVs) to address the HIV/AIDS pandemic (Banda, 2013). As Chapter 15 describes, in 2002 Zimbabwe issued a compulsory licence allowing its local manufacturers to produce ARVs.

This demonstrated purposive application of political will and policy infrastructure, associated with sustained local manufacturing capabilities, to meet a pressing health and social need.

However, the economic crisis created a cumulative collapse in the public health system's capacity to procure drugs over the period from 2003 to 2009. The country shifted to high donor dependence for public health care funding and drug procurement (Banda, 2013). In addition there was international political isolation, acute shortage of foreign currency and dwindling foreign direct investment (FDI) coupled with skilled resources flight (AfDB, 1997; Brett, 2005). The greatest challenge for local pharmaceutical industry was the loss of public health procurement as an industry policy tool (NECF, 2010). The increased reliance on donor funding posed a demand-side constraint for local firms: drugs for HIV/AIDS, TB and malaria were procured externally because the national procurement agency NATPHARM was incapacitated through lack of funds.

Current pharmaceutical manufacture in Zimbabwe

When the government of national unity was formed in 2009, there were various initiatives to resuscitate and rehabilitate the economy. Key strategies in the Short Term Economic Recovery Programme (STERP, 2009) were social protection, including food and humanitarian assistance and education. For health care, the focus was on building capacity in human resources, drugs and medical equipment availability, and reduction of preventable diseases. The health delivery strategy included addressing drug shortages: drug stocks in 2008 were just 36% of requirements, and stock-outs of essential drugs, vaccines and medical supplies had become common. The strategy also included capacitating NATPHARM, the national drug procurement agency, to supply government health institutions. There was a gradual improvement in the sector in the 2011–14 period.

The pharmaceutical industry in Zimbabwe now consists of nine pharmaceutical manufacturing companies registered with the Medicines Control Authority of Zimbabwe (MCAZ). Of these, five are the major generic manufacturers accounting for 90% of the formulation businesses (UNIDO, 2011b). The companies operate in a competition-intensive, low-margin commodity-type business, where profitability and long-term viability depend on economies of scale, assured demand and large markets (Berger et al., 2009). Currently the country is capable of producing 50% of all drugs on the essential drugs list, and if all research and development (R&D) activities in formulations are taken

into account, the capability rises to supplying 75% (NECF, 2011). Firms used to export quite extensively in the East African region, and also to Namibia, Angola and South Africa (UNIDO, 2007; 2011b). In 2014, the local industry supplied medicines to the health sector valued at US$24 million compared to US$184.7 million of imported medicines and US$100.4 million of donated medicines (Zimstats, nd).

While Zimbabwe's experience shows that African countries can manufacture drugs for their local health system, and illustrates some ways in which health and industrial policies can be aligned, it is also a grim history of how economic crisis drives loss of industrial development opportunities in pharmaceuticals.

Kenya: creating the dominant East African producer

Kenya, like Zimbabwe, has a long history of pharmaceutical production. Local pharmaceutical manufacture can be traced back to the 1940s. The pioneer firm was the Kenya Overseas Company, established in 1947 and beginning local manufacturing activities in 1948. The next batch of firms included Sterling Winthrop (US), established in 1953; Burroughs Wellcome (East Africa) Ltd (UK) in 1955; and Aspro-Nicholas (EA) Ltd (Australia) in 1961 (Wamae and Kariuki Kungu, 2014). The early firms built up initial skills and experience in pharmaceutical manufacture in Kenya before independence in 1963.

After independence, Kenya also pursued policies of import-substituting industrialization (described and explained in Chapter 2). These policies supported manufacturing for the domestic market in the face of the 1970s balance-of-payments crises and rising oil prices. In this period pharmaceutical manufacturing expanded, benefitting from the industrial protection, and also from an active government policy to promote investment and technological upgrading. The government established the Industrial and Commercial Development Corporation (ICDC) to provide development finance, and supported a number of parastatal joint ventures, including Dawa and Infusion Medicare. The firms of Lab & Allied and Cosmos were also set up in this period.

The mid-1980s and 1990s saw in Kenya, as across Sub-Saharan Africa, a process of market liberalization, associated with structural adjustment programmes, and a shift to export promotion. In Kenya, export promotion included a number of schemes to allow bonded production for exports using duty-free inputs, but this had little impact on pharmaceuticals (Chapter 2). The early 1990s in Kenya also saw a push to 'buy local', using local health section procurement to benefit industrial

development. There was industrial investment in pharmaceuticals production in this period, including Universal (Figure 1.1).

By the turn of the century, the Kenyan domestic medicines market was opening up in familiar ways to more global competition, notably from South Asia. Donors moved in to supply medicines for malaria, TB and especially HIV/AIDS, but this was later and more patchy in Kenya than in some neighbouring countries (Chapter 2). The relative strength of the production capabilities of the Kenyan industry by 2001 allowed the government to decide to permit compulsory licensing of generic production of HIV/AIDS medicines, and the subsequent issuing of voluntary licences (UNIDO, 2010a; see also Chapter 2). However import liberalization was by this date generating increasing competition from imports of finished formulations, and this seems to have been a factor in the departure of a number of multinational producers. In 2014, almost all pharmaceutical firms in Kenya were locally owned (Chapter 2).

A local industry with regional potential

In February 2014, Kenya had 39 pharmaceutical manufacturers registered with the Pharmacy and Poisons Board (PPB). Thirty-four were producing pharmaceuticals for human health, while the rest concentrated on veterinary products (Wamae and Kariuki Kungu, 2014). There were also 20 multinational firms with local representation for marketing purposes and /or involved in clinical trials.

Like the firms in Zimbabwe, Kenyan pharmaceutical activities are mainly production of finished formulations, with some reformulation and development activities. The industry mainly produces generic products, importing APIs, excipients and other raw materials from India, China and Germany. India dominates both raw materials and finished product imports, accounting for 40% of all pharmaceutical-related imports in 2008 (UNIDO, 2010a: 49). Few key inputs can be sourced locally; exceptions are maize starch, sugar and glucose syrup, rectified spirit and ethanol, as well as sodium chloride and quite a wide range of packaging materials.[2]

The Kenyan industry continues to suffer from relative low capacity utilization, and Chapter 2 explores the reasons for this in detail. They include limitations in the functioning state of machinery, delays in sourcing spare parts from abroad and human resource issues, in particular shortages of highly specialized skills in some critical areas such as product development.

Despite these constraints, Kenya's pharmaceutical sector is the strongest producer of pharmaceuticals in the East African region, and is

upgrading to more demanding technological capabilities. In addition to the standard generic products in the dosage forms of tablets, capsules, creams and syrups, the industry in Kenya includes three firms producing injectable infusions (small and large volume parenteral preparations) and ophthalmic formulations. One firm (Universal) has achieved WHO prequalification for one of its products, allowing the firm to tender for donor contracts and also providing an indicator of the firm's technical capabilities and standards.

A further measure of the strength of Kenya-based pharmaceutical production is its export success, which accelerated from about 2002. Kenyan pharmaceutical producers' main export destinations are in the COMESA region: the Common Market for Eastern and Southern Africa, which does not include South Africa or Tanzania.[3] However, the Kenyan industry still supplies a tiny fraction of COMESA's medicines market, while provisioning only around a quarter of its own domestic market. There is substantial room for expansion. With supportive government policies, Kenya should be able to exploit effectively the integration of East African and Southern African markets to expand its role as one of the medicines production 'hubs' in Sub-Saharan Africa. Chapter 2 discusses the industrial challenges in depth.

Tanzania: a latecomer under stress

Tanzania has a shorter history of pharmaceutical manufacturing than the two countries just discussed. In the colonial period during World War II, facilities for manufacturing simple medicines were established to counter the risk of blockade. However, after the war, these closed, and the country reverted to imports. The mainland, then called Tanganyika, did not, unlike Zimbabwe and Kenya, have a large colonial settler population in the pre-independence period, and the level of industrialization at independence was correspondingly small.

Pioneering firms and public sector investment

The earliest pharmaceutical manufacturing firm in Tanzania seems to have been Mansoor Daya Chemicals Ltd., a privately owned firm. Mr. Daya, a pharmacist, began with a retail pharmacy in Dar es Salaam in 1959. He set up his own firm in 1962, originally in a small godown, later moving to his current production site.[4]

In the 1960s and early 1970s, the Nyerere government in Tanzania turned to the promotion of industrial development through public investment. In contrast to Kenya, the industrial policies were driven by

a more explicitly socialist agenda, although, as the case studies in this chapter illustrate, the use of public investment to promote industrial development was a broadly implemented approach in these post-independence years (Lall and Wangwe, 1998). Manufacturing output rose from 4% of GDP at independence to about 8% or 9% in the 1970s. The production was mainly oriented to the domestic market, although there was a slow growth of manufacturing exports to East Africa, until these markets were lost with the break-up of the East African Community in 1977 (Bagachwa and Mbelle, 1995).

This was a period of import-substituting policies, paralleling those in Zimbabwe and Kenya, with an overvalued exchange rate, import controls, protective tariffs and administrative allocation of foreign exchange. It was also a period of state-led industrialization, including public sector investments in manufacturing plants. Two public sector pharmaceutical firms were established to provide essential medicines to a rapidly expanding public health sector. Keko Pharmaceuticals was opened as a production unit within the Ministry of Health in 1968 to supply tablets, capsules and large-volume parenterals for distribution to public sector health care facilities. Tanzania Pharmaceutical Industries Ltd (TPI) began as a public enterprise in 1978 with assistance from the Finnish government.

This was thus a period when the government was placing priority on expanding health care to serve a basic need, and the pharmaceutical industry responded to an alignment of industrial and health policies. The industrial strategy prioritized production to meet basic needs, including health care, creating a conducive environment for investment in pharmaceuticals. Private clinical practice was banned in 1977, except for some religious providers, and the main market for medicines was the public sector, plus retail pharmacies. However, the domestic market expansion was sufficiently attractive for a second private start-up, Shelys Pharmaceuticals, which began production in 1979. In 1984, Shelys was bought by the Tanzanian Sumaria Group of companies and built up into the largest pharmaceutical firm in the country.

Economic crisis and liberalization

Like our other other case-study countries in this chapter, Tanzania was hit by a major economic crisis in the 1980s. However, the impact in Tanzania was particularly severe, a result of a confluence of circumstances including a small and particularly internationally uncompetitive manufacturing sector focussing on consumer goods for the domestic market, and a liberalization process that was rapid and relatively

unconstrained by transitional policy safeguards. The late 1970s and early 1980s were marked by severe shortages of goods, as foreign exchange constraints reduced inputs to local production and export manufacturing declined. Capacity utilization dropped dramatically, and manufacturing output fell back to 7% of GDP by 1985 (Bagachwa and Mbelle, 1995). Pharmaceutical manufacturers were badly affected by foreign exchange shortages that constrained their ability to import APIs and other key inputs.

The major policy framework reversal was signalled by the adoption of the Economic Recovery Programme (ERP) in 1986. This shifted policy sharply away from import substitution, liberalizing imports of final goods and providing export incentives for manufacturers. While there was some export recovery, production of consumer goods for the domestic market suffered badly as cheaper imports flowed in. Given the prior levels of industrial protection in Tanzania, the liberalization constituted a much more severe shock than in Kenya or Zimbabwe, where protection had been lower and transition was better managed. Firms in Tanzania had little time for adjustment (Lall and Wangwe, 1998: 93). The result in Tanzania was a swathe of deindustrialization, and firms serving the domestic market failed.

Pharmaceuticals faced a second challenge also: the 'battering' taken by public sector health care funding and other government provided social services as the government budget went into severe crisis (Kaijage and Tibaijuka, 1996). As a result, the two government firms, Keko and TPI, ceased to be able to compete with imported medicines, lost their markets, and closed in the early 1990s. However, the two private pharmaceutical producers, Mansoor Daya Chemicals and Shelys, survived the economic crisis years. Shelys in particular was built up into a successful business as the largest pharmaceutical firm in Tanzania and expanded exports to the region. Another privately owned local firm, Interchem Pharmaceuticals was set up in 1989 in Moshi, part-owned by the IPP group of companies.

The challenges of competitiveness and upgrading

Industrial research in the 1990s emphasized the importance of firms' technological capabilities for survival and competitiveness in a more open economy (Wangwe, 1995). In the late 1990s and early 2000s, some of these technological capabilities were rebuilt in Tanzania, in pharmaceuticals as in other industries. The challenge was particularly great in pharmaceuticals given its reliance on skills and ability to manage technological upgrading effectively.

However, from the late 1990s, the pharmaceutical industry in Tanzania was renewed and grew substantially, entirely through the efforts of local investors and managers. The government sold 60% of the equity in each of the inactive government firms, Keko and TPI, to private Tanzanian investors in 1995. Both reopened in the late 1990s. In 2003, Shelys bought Beta Healthcare International, a Kenyan pharmaceutical company (previously Boots), with private equity funding from Aureos Capital. This was the first cross-border merger whereby a Tanzanian firm purchased a Kenyan company, and it made Shelys Africa Group the largest East African pharmaceutical company at that time.[5]

By 2009, the high point of Tanzanian pharmaceutical production, there were eight firms producing for the local market and also exporting regionally. The new firms were started by a mix of local and international investment. Tanzansino started production in 2000 as a joint venture between the Tanzanian military and a Chinese provincial government body. In 2007, the ownership changed when the Chinese provincial government shares were bought by Holley Industrial Group Ltd., a Chinese industrial group including a firm producing and exporting one of the new artemisinin-based combination therapies for malaria.[6] AA Pharmaceuticals, a smaller firm established by a Tanzanian private investor who is a pharmacist, began production in 2002. And in 2007, a new plant, Zenufa Laboratories, was built and opened. Owned by a DRC (Congo)-based diversified family firm, Zenufa aimed for Good Manufacturing Practice status from the start. These new start-ups reflected the changed economic circumstances in Tanzania: faced with sharp external competition, they aimed for efficient manufacturing and regional export capability from the beginning.

Data are not easy to assemble, but Table 1.1 provides a summary overview of the pharmaceutical industry in Tanzania just before the start-up of Zenufa. Seven firms were then active. Shelys at that time was responsible for about half of local production by value (Table 1.1). Much of the rest of the output was supplied by TPI, Interchem and Keko. The main suppliers to the public wholesaler (MSD) were Shelys, TPI and Keko, while Shelys was also the main exporter. Chapter 3 analyses the Tanzanian industry after this date.

Conclusion: shifting the debate

This chapter aimed to dispel the persistent myth that pharmaceutical production is not an African industry, tracing the long industrial history of the production of medicines on the Sub-Saharan subcontinent. This

Table 1.1. Pharmaceutical production and exports, Tanzania, 2004–05

Producer	Value of production (US$ million)	Share of total production (%)	Sales to the public sector (US$ million)	Sales to private market (US$ million)	Exports (US$ million)
Shelys Pharmaceuticals	16.0	49.2	5.7	7.4	2.9
Tanzania Pharmaceutical Industries	6.7	20.4	4.0	2.5	0.2
Other firms	9.9	15.0	1.3	8.5	0.0
Total	32.6	100.0	11.0	18.4	3.1

Source: Compiled by the authors from data in MoHSW (2006). Data in Tanzanian shillings in that source converted to US$ using the average exchange rate of 0.00095 for the year July 2004–June 2005 obtained from www.oanda.com.

book aims to contribute to shifting the whole debate on *making medicines in Africa* definitively away from 'Should it be done?' to 'How can it be done well to the benefit of public health?' Despite the successes to date, local manufacturers serve only a small proportion of African domestic demand, let alone population need (Berger et al., 2009; UNCTAD, 2011; WHO, 2005; 2011). The bulk of medicines consumed are imported from India and China, and there is heavy reliance on disease-specific donor-funded imports. That situation is not sustainable. African countries need to grow their capabilities to address the health needs of their populations, and pharmaceutical manufacturing and its associated technical and scientific bases are needed for that effort.

Nationally and across the African subcontinent, efforts to expand local manufacturing and innovation are extensive. The business case for local drug manufacture – and its potential to enhance security of medicines supply – has gained ground within African Union (AU) and New Partnership for Africa's Economic Development (NEPAD) circles. Not all countries have the capacity and capability to embark on the full spectrum of pharmaceutical production, innovation and R&D. The *Strengthening Pharmaceutical Innovation in Africa* strategy report (Berger et al., 2009) and the UNIDO-AU-sponsored African Pharmaceutical Manufacturing Plan of Action (AU-UNIDO, 2013) propose a phased approach of working up the technological ladder (see Chapter 15). Given the current rates of investment and industrial development in pharmaceuticals, the debate

now concerns the policy and business determinants of cost-effective manufacture of safe and efficacious medicines, and the conditions for aligning industry, finance and public health needs. The mechanics of achieving this become a matter of strategic intent at national, regional and continental levels. This is the terrain this book explores.

Notes

1. Part of this chapter draws on research undertaken for the project *Industrial productivity and health sector performance*. The findings, interpretations, conclusions and opinions expressed here are those of the authors and do not necessarily reflect the views or policies of DFID or the UK ESRC, whose financial support is gratefully acknowledged (project ES/J008737/1). Some of the evidence is drawn from fieldwork by Watu Wamae and Joan Kariuki Kungu for this project.
2. Source: UNIDO (2010a) and interviews.
3. Source: http://about.comesa.int/, accessed 12 April 2015.
4. Source: interviews.
5. Source: Sumaria Group website: http://www.sumaria.biz/our-businesses/, accessed 6 March 2014.
6. Source: interview with Tanzansino manager, 2010.


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2

Pharmaceuticals in Kenya: The Evolution of Technological Capabilities

Roberto Simonetti, Norman Clark and Watu Wamae

Introduction

As Chapter 1 briefly outlined, Kenya has a strong and long-standing pharmaceutical industry. A 2015 Business Monitor report on pharmaceutical manufacturing in Kenya states that the country hosts the largest pharmaceutical industrial base in East Africa. The report also sees a bright future as a 'potential base for export across East Africa' (BMI Research, 2015). This chapter locates the Kenyan pharmaceutical industry within the country's historical context of industrial development and growth.

The features of the local production of medicines are shaped by the characteristics of the Kenyan economic and industrial systems, which in turn are the product of its economic history. To analyse this shaping, this chapter briefly presents and then applies an evolutionary economic understanding of industrial capabilities, focusing particularly on technological capabilities at the firm and industrial system level, their sources and evolution. This framework of industrial analysis is also used in a number of subsequent chapters in this book. It is particularly illuminating for the analysis of the development of an industry, pharmaceuticals, that is technologically demanding relative to the industrial and economic context in a low-income country such as Kenya.

Pharmaceutical manufacturers face constant competitive and regulatory pressure to upgrade their technological capabilities, and the evolutionary framework of analysis emphasizes the extent to which this upgrading relies on both firm-level investment building on existing capabilities, and also on the benefits that accrue from its surrounding industrial base. Chapter 1 briefly noted that African countries' broader

industrial base frequently stems in turn from an era of policy-led import-substituting industrialization. This chapter explores in more detail how the pharmaceutical industry has built on this basis in Kenya, and the scope that gives the industry for exploiting the opportunities opened up by the subsequent more liberalized and competitive markets. It also outlines some of policy decisions that have shaped the industry's development, and some of the challenges for firms and policy makers.

This chapter draws on a range of sources, including trade and manufacturing data, secondary published and grey literature sources and also interviews with manufacturers and distributors and other field data collected in 2012–14.[1]

The evolution of Kenya's pharmaceutical industry in the context of post-colonial industrialization

The profile of the pharmaceutical industry in Kenya is influenced by the country's broader economic and industrial history. The post-independence industrial history of Kenya can be split into three periods according to the policy regimes adopted: the early years of import substitution industrialization (ISI), until the 1970s; the liberalization and gradual opening up of the economy in the 1980s and 1990s; and the new millennium (Chege, Ngui and Kimiyu, 2014).

Pharmaceutical production was already taking place before the advent of independence in 1963, as Chapter 1 described. The early firms were mainly foreign direct investments (FDI). The newly independent country then continued to implement policies of ISI that had started during the colonial period.

Import-substituting industrialization is a set of economic and trade policies that aim to promote domestic industrialization in order to reduce the country's dependence on manufacturing from abroad. The policies seek to promote the accumulation of skills, capital and knowledge for the production of manufacturing goods by limiting imports of selected manufacturing goods through a variety of trade restrictions and subsidizing domestic manufacturing enterprises. In the Kenyan case, local producers were shielded from foreign competition in manufactures in a variety of ways. High tariffs, even reaching 100% of the goods' value, and quotas were imposed on imported manufactures, which were also charged higher rail fares, with the result that their prices were high for Kenyan consumers. Domestic manufacturing firms were also helped with financial subsidies, allocated land for production facilities, and

allowed to have import duties refunded on the inputs (raw materials and equipment) they had to import for production.

The Kenyan government also explicitly welcomed foreign-owned firms who set up production facilities in the country, as they contributed to the domestic industrial development. The large weight of FDI in Kenyan industry of the colonial period is also typical of the early years of independence, when it even reached half of industrial output (Maxon, 1992). Fearing a flight of FDI, a year after independence, in 1964, the government passed the Foreign Investment Act, which gave reassurances to foreign firms in areas such as repatriation of profits and protection from nationalization.

This policy orientation towards manufacturing for the domestic market was reinforced in the 1970s by balance-of-payments crises and rising oil prices which led to scarcity of foreign exchange. Manufacturing of consumer goods for the local market expanded rapidly in the early 1970s, and there was diversification into upstream supplier industries such as plastics. In this period, pharmaceutical manufacturing expanded, benefitting from the industrial protection, and also from an active government policy to promote investment and technological upgrading. Laboratories & Allied was incorporated in 1970. The government established the Industrial and Commercial Development Corporation (ICDC) to promote the inclusion of local people in industry by providing development finance and technical assistance. ICDC helped to develop pharmaceutical production in this period through parastatal joint ventures. Dawa was established as a 1970s joint venture between the ICDC and the Yugoslav government. A firm producing infusions, Infusion Medicare, began in the mid-1970s as a joint venture between the ICDC and Hoechst E.A. (the latter the East African arm of a German pharmaceutical producer now part of Sanofi).

ISI policy in this period successfully created an industrial base in Kenya, especially in light consumer industries such as textile and foodstuffs, but also in others such as metal products. Between independence and 1980, industrial output quadrupled, the share of GDP in manufacturing grew from 10.1% to 13.3% and the number of industrial establishments more than doubled (Ogonda, 1992: 297–98). The increase in local manufacturing reduced the multinational companies' (MNCs) share of industrial output, which however still accounted for 20% of industrial output in the early 1970s (Maxon, 1992: 385).

However, the protection from international competition encouraged local firms to focus on the protected local market and neglect exports. This created an anti-export bias that, together with external shocks such

as the oil crises and a deterioration of terms of trade, led to a shortage of foreign exchange. In 1980 Kenya had to take a loan with the World Bank, which imposed structural adjustment conditions. This marked the beginning of the phase of liberalization and structural adjustment policies in the mid-1980s and 1990s, as it happened across Sub-Saharan Africa, and the beginning of a shift to export promotion. In Kenya, export promotion included a number of measures to allow production for exports using duty-free inputs, but the implementation was slow and tentative, with little impact on export.

The gradual opening up of local markets created competition that had an adverse impact on local industrial activity. Shortage in foreign currency contributed to the decline of domestic industry as firms found it difficult to buy foreign inputs and equipment, with adverse effects on capacity utilization and therefore productivity. After an economic crisis at the beginning of the 1990s, liberalization and export promotion accelerated with the creation of Export Promotion Zones (EPZs), participation in the Common Market for Eastern and Southern Africa (COMESA) and the East Africa Community (EAC), and the removal of price controls in 1994. Export promotion and international competition, however, had little impact on pharmaceuticals in that period. More important was a push in the 1990s to 'buy local', aiming, for example to ensure that basic medicines kits should be 50% local products (Wamae and Kariuki Kungu, 2014). Local pharmaceutical companies benefitted from this policy – an example of active use of health sector procurement as an industrial policy. Among the larger Kenyan manufacturers, Regal was established in the 1980s and Universal in the 1990s. Parastatal firms were privatized.

The third phase of industrial development, in the new millennium, saw an increase in exports especially in textiles through the United States' African Growth and Opportunity Act (AGOA), which facilitated exports to the US and increased activity in EPZs. In spite of this new push to promote exports, the pressure of global competition from other low-income countries has meant that the share of manufacturing in total GDP has not changed significantly, and much of industrial activity is still carried out in the informal sector by micro enterprises, whose small size makes it difficult to find funds for investment, expansion and upgrading. During these years, most of the foreign MNCs also ceased to produce in Kenya as they reorganized their supply chains globally in the light of competition from China and India to find cheaper locations for production. It is possible that local producers may have benefitted from the flight of production from MNCs, being able to take their place

in some market segments and absorbing employees already trained by foreign MNCs.

The development of Kenya's pharmaceutical industry suggests that ISI policies were important to build an initial industrial base. Previous analyses of industrialization have argued the ISI policies followed by careful liberalization and export promotion might be useful to promote industrialization (see, e.g., Athreye, 2004, for the Indian software industry). So it is possible that ISI policies enabled Kenya to start the accumulation of basic technological know-how, perhaps through parastatal joint ventures, such as those formed by ICDC, in spite of their problems. The opening up of export markets, especially with the creation of COMESA and EAC and the policies that promoted exports such as the formation of EPZs, also enabled the strongest firms to adapt to international competition and offered opportunities for the expansion that is observed today, as the next section shows.

The Kenyan pharmaceutical industry and its market position

In historical studies of industrialization in Kenya, the pharmaceutical sector is rarely mentioned as it traditionally accounted for a very small share of industrial output. However, recently its status has been increasingly recognized. For example, pharmaceuticals are mentioned as one of the eighteen strategic sectors in the National Industrialization Policy 2011–15 (Ministry of Industrialization, 2010). Kenyan local manufacturers of medicines have shown great resilience during the years of economic difficulties and are now embarked on a process of growth and technological upgrading that, if successful, can establish them as a major player in the East African market for medicines.

Kenya's pharmaceutical production grew continuously from 2007 to 2013. As Figure 2.1 shows, in that period total production of tablets, capsules, liquid preparations for oral use and creams/ointments alone increased from US$34.1 million to US$154 million. The figure also shows that the composition of products has changed over these years, with creams and ointments becoming more popular, although virtually all product types have steadily increased with the possible exception of capsules.

Kenya has also seen strong growth in its pharmaceutical exports in the new millennium, especially since 2002. Exports started growing around 1992–93 thanks to the 'buy local' push, which promoted the expansion of local manufacturing. However, during the 1990s and early 2000s,

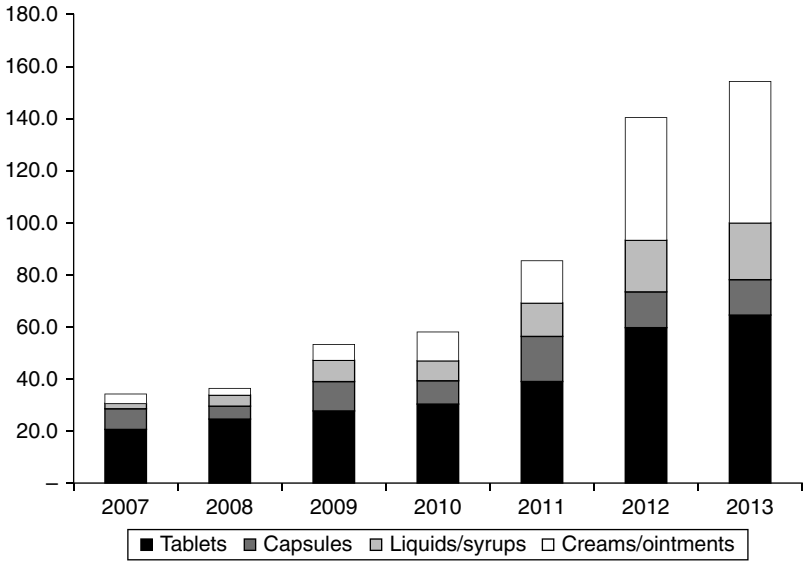

Figure 2.1 Local production of non-parenteral medicines in Kenya by type of product, 2007–13 (US$ million)

Source: Kenya National Bureau of Statistics, Production data for the period 2007 to 2013, Government of Kenya, Nairobi, obtained 4 September 2014.[2]

local production was affected by the adverse effects of liberalization policies described in the previous section, and exports remained stable. These years also saw a wave of divestments of production activities from foreign-owned companies that carried on in the new millennium as Kenya's industrial environment deteriorated and MNC producers moved out of Kenya to lower cost platforms. By 2014, only one MNC was still manufacturing in Kenya – GSK. Otherwise, pharmaceutical firms in Kenya are currently mainly locally owned.

The great majority of Kenyan's pharmaceutical exports are destined to Sub-Saharan Africa (SSA). COMESA is the main export destination for Kenya's pharmaceutical exports, with Kenya supplying about 50 per cent of the region's production. In relative terms, however, this translates into a minute share of the COMESA market.

With respect to the main importers of Kenya's pharmaceutical products, Uganda has remained a significant market over a number of decades. Somalia and Sudan have also seen significant growth of Kenyan products, particularly over the last two decades.

In spite of the growth in production and exports, the Kenyan pharmaceutical industry has to overcome important challenges in order to consolidate and expand its influence in the East African region. Kenya's pharmaceutical industry is still mainly oriented towards the home market, with an export share of domestic production only ranging between 15 and 20 per cent, at least up to 2010. Furthermore, the Kenyan producers' share of their own home market is estimated at around 25% of domestic demand (see also Chapter 8), leaving room for expansion (Wamae and Kariuki Kungu, 2014).

Kenyan manufacturers sell to the Kenyan public procurement agency KEMSA, and to the large non-profit wholesaler the Mission for Essential Drugs Supply (MEDS) that supplies predominantly the faith-based health care sector. They also sell into the large private sector (Chapter 8). Public procurement is regulated by the Public Procurement and Disposal Act of 2005, and tendering decisions are based mainly on pricing, though a 15% price preference for local manufacturers is available. Producers and distributors are free to set their own prices and mark-ups, and private mark-ups are, on average, high. The pricing of medicines in Kenya was completely liberalized in 1993.

In the new millennium the Kenyan domestic medicines market has been hit by more global competition, notably from South Asia. A key development for the pharmaceutical industry has been the large-scale movement of donors into supplying medicines for malaria, TB and especially HIV/AIDS. This has been a strong influence on the domestic market and pharmaceutical policies in a number of the countries discussed in this book. The arrival of the large donors was, however, somewhat later and more patchy in Kenya than in some neighbouring countries. PEPFAR, for example, the main US programme for funding HIV/AIDS medication, began to operate in Kenya only in 2008, and Kenya received no funding under Rounds 8 and 9 of the Global Fund financing (UNIDO, 2010: 41).

The production capabilities of the Kenyan industry were confirmed during this period by the companies' role in the campaigning that led to the 2001 government decision to allow compulsory licensing of generic production of HIV/AIDS medicines, and the subsequent issuing of voluntary licences (UNIDO, 2010). However, private importers from South and East Asia were increasingly generating price-based competition in the Kenyan medicines market as liberalization took hold. With export figures that in absolute terms remain very modest, it is essential that Kenyan manufacturers keep upgrading and also control costs in order not only to expand its foreign markets but also to keep up with

increasingly demanding technological standards and cheap foreign competition that creates a serious challenge to local producers.

Technological capabilities and sectoral systems of innovation

The previous sections have shown that Kenyan pharmaceutical manufacturers are enjoying a period of growth. However they also face challenges that arise from cheap imports and the need to constantly upgrade their technology in order to keep up with global competition and increasingly demanding technical standards and to successfully exploit new market opportunities. A key factor in the future prospects of the Kenyan pharmaceutical industry is therefore the extent to which the local producers will be able to improve their technological capabilities.

The notion of technological capabilities, which has now entered the mainstream analysis of industrial development, can be traced back to the work of evolutionary economists such as Richard Nelson, Sydney Winter, Christopher Freeman and Giovanni Dosi (Dosi et al., 1988; Nelson and Winter, 1982). Evolutionary economics started as a critique of the dominant theoretical framework in economics, the neoclassical approach. The critique arose from the observation that the tools of neoclassical analysis were not well suited to the study of technological and industrial change. Neoclassical economics focuses on the working of the price mechanism in the coordination of economic activity but makes strong and unrealistic assumptions about the nature of technological knowledge and the way firms (and, in general, other economic agents) operate. Technology is seen as information, which has public good features and is therefore easily transferred between firms. Technology transfer is simplistically seen as the transfer of free information.

Evolutionary economists, however, argue that much of technological knowledge is tacit and hence difficult to articulate, let alone transfer easily. The effective use of technology requires that any publicly available technical information be processed using know-how and skills that not only are costly to acquire but also differ across firms, industries and countries. Firms and other organizations, like people, acquire skills, or capabilities, that become embedded in their procedures (also called routines) and people through a process of learning that is shaped by the history of the firm. Technological capabilities, therefore, are the organizational skills that enable firms to make effective use of technologies, including the ability to adapt them, improve them and even develop radically new products and processes. Because of their tacit nature, capabilities

are costly to acquire, are learned over time and change slowly over time. An important consequence of this view is that since firms' histories and sources of learning differ, the capabilities that firms accumulate also differ. Indeed, industry studies have shown that firms within the same industry usually have many differences that are persistent over time: each firm is unique (Griliches and Mairesse, 1995).

The work on capabilities of early evolutionary economists originally focussed on advanced technologies and firms in industrialized countries. However, other scholars, such as Lall, extended this work into the context of developing countries. In an influential paper, Lall (1992) distinguished between firm-level and country-level capabilities. Firm capabilities include both investment and production capabilities and can be classified according to their degree of complexity, from basic, which involve experience-based tasks, to intermediate, which involve an element of search, to advanced, which are research-based and involve the creation of wholly new products and processes. Firm capabilities also include 'linkage capabilities', the way in which firms learn from and transfer knowledge to the external environment, that is, other organizations and institutions, including customers, suppliers, government agencies and science and technology providers. Countries also have distinctive national capabilities, which are more than the sum of the capabilities of their firms and other organizations because they also include they way economic agents interact and the features of the economic environment, such as the policies, incentives and institutions.

The early work on technological capabilities has been further developed by many scholars and has now entered mainstream thought in the field of science, technology and innovation studies (STI). A useful development of this theorizing is the recognition that industrial sectors have a set of institutions and organizations that differ across sectors and influence the way technological capabilities are accumulated and firms compete. In order to understand an industry's patterns of development and change, it is necessary to study the various agents that influence the accumulation of knowledge and the nature of competition in the industry and the way they interact.

The pharmaceutical sector is a typical example of the distinctiveness of sectoral institutions that shape technological learning and competition. Medicines are usually strictly regulated for their efficacy and safety by government agencies in a way that is unusual in other industries. The structure of demand is also distinctive because of the important role played by the state through the public procurement of essential medicines for the health system and, especially in low-income countries, the

major role played by international donors in the purchase of key medicines. On the supply side, universities also play an important role as providers of skilled labour and scientific knowledge.

Technological capabilities in manufacturing of medicines in Kenya

This section draws on various sources, including firm interview data, in order to give an assessment of the Kenyan technological capabilities in the local production of pharmaceuticals. The technological capabilities of the Kenyan domestic pharmaceutical sector are analysed by looking at various dimensions of the production system in which local manufacturers of pharmaceutical operate.

The analysis starts with the description of the local producers because the firms are at the centre of the industrial system. A good starting point for the assessment of the manufacturers' capabilities is the analysis of the characteristics of their products in terms of quality and technological sophistication, the extent to which they achieve industry standards and their productivity. What firms can achieve, however, also depends on the capabilities of the system of suppliers, customers, regulations and institutions with which they interact, including the educational and financial systems, so these aspects will be included in the analysis.

Industrial structure

Local manufacturing of pharmaceuticals in Kenya is dominated by locally owned firms. In 2014 there were 39 local manufacturing firms with products registered with the Pharmaceuticals and Poisons Board (PPB), the agency that regulates the manufacture and trading of medicines in Kenya. Of these, 34 produced medicines for human consumption, whilst at least five firms produced animal health products. Of the 34 firms, only one producer is a foreign-owned MNC, GSK East Africa, which has not followed the exodus of other MNCs. Although MNCs dominated the local production of pharmaceuticals in Kenya in the 1990s, because of the unattractive economic conditions in Kenya in the 1990s and changes in global supply chains, most of them have moved production facilities to lower cost locations and are only present in Kenya for activities such as marketing and clinical studies (Wamae and Kariuki Kungu, 2014).

However, government policy has provided other incentives for local production by removing import duties and taxes from inputs to

pharmaceutical products, such as APIs, excipients and packaging materials. The situation, however, changed in 2013 when the new VAT act reintroduced taxation for pharmaceutical inputs and only exempted finished products. This decision made locally produced medicines up to 22% more expensive, and the industry put pressure on the government to reverse the decision. This happened in the 2014 Act, but there are still some unresolved issues that are worrying local manufacturers (Wamae et al., 2014).

Studies of the Kenyan supply medicines chain show that Kenya has high margins for distributions, which raise the final price of the medicines to users in spite of fairly low manufacturing costs, in comparison to countries, such as Brazil, India, Indonesia, Kenya, Netherlands, Russia and South Africa. The study shows that the percentage of distribution costs is clearly highest in Kenya (see IMS Institute for Healthcare Informatics, 2014: 11). The high margins are a sign of the market power enjoyed by private distributors, who have a global reach and access to cheap imports, mainly from India.

Products and standards

Kenyan manufacturers are mainly engaging in activities that require basic to moderate technological capabilities, such as formulation activities, that is, converting manufactured bulk substances into final usable forms, and packaging rather than activities at the high end of the technological spectrum, such as R&D aimed at the discovery of new molecules and product development or the production of bulk pharmaceutical substances (APIs). The tablet is the most common dosage form; Kenyan firms also manufacture capsules, topical preparations (creams, gels, ointments or pastes), liquid preparations for oral use (including syrups), injectable infusions (small and large volume parenteral preparations) and ophthalmic formulations. Topical preparations have seen significant growth between 2007 and 2013 (Figure 2.1) (Wamae and Kariuki Kungu, 2014).

Formulations, however, can vary substantially in terms of the technological capabilities required for production. Products such as injectable infusions and ophthalmic formulations require sterilization, which is achieved through a production process that is technologically complex and demanding in terms of meeting standards of safety, efficacy and quality – particularly for injectable infusions. There are three local firms that manufacture injectable infusions and a few others that produce sterile ophthalmic products, including Laboratories & Allied (Wamae and Kariuki Kungu, 2014).

There are also important differences in the technological requirements within the group of non-sterile formulations. Some of the more technologically progressive firms have dedicated laboratories that undertake extensive product development activities with regard to existing products and are developing the capabilities for the production of more technologically sophisticated products. For example, some firms are moving from plain tablets to modified-release and sustained-release tablets. Some firms also engage in active process improvements. Some producers already meet WHO-GMP standards, and are also upgrading their production processes to gain WHO recognition, which could possibly open the door to funding by international donor agencies. One company, Universal Corporation, has already received WHO prequalification for its Lamivudine/Zidovudine anti-retroviral product in 2011, and other firms, such as Cosmos, are aiming to gain pre-qualification in the near future. Other firms are attempting to gain GMP standards with the help of PPB and international agencies such as UNIDO (UNIDO, 2014).

Formal R&D activity (the discovery and product development of new active pharmaceutical ingredients) is in its infancy, with only one firm engaging in R&D. Another firm, Botanical Extract EPZ (or BEEPZ), is the only Kenyan firm developing capabilities for the production of artemisinin, which is used in the production of anti-malarials. BEEPZ is the development of an industrial concern born in 1996 in Tanzania to develop the production of high-quality *artemisia annua* with improved yields and artemisinin content. The project expanded its facilities to produce the raw materials in Kenya and Uganda, and in 2007 BEEPZ commissioned its principal processing facility in the export processing zone (EPZ) in Athi River, Kenya, currently producing non-API-grade artemisinin for export (Botanical Extracts EPZ, 2015). The expansion of production of *artemisia annua* to Kenya and Uganda was possible thanks to grants from the UK Department for International Development (DFID) and the multinational company Novartis, a leading producer of artemisinin-based anti-malarial drugs, which also became a BEEPZ customer in 2009, when the EPZ plant started production (IRIN News Africa, 2015).

There are also three local firms that process some raw materials that are used to manufacture bulk pharmaceutical products. These raw materials are 100% destined for export, as the local capacity for manufacturing active pharmaceutical ingredients remains underdeveloped.

Productivity, capacity utilization and cost efficiency

Unfortunately, it is too difficult to obtain a direct measure of productivity for the various manufacturers, but it is well known that capacity utilization is an important determinant of productivity. Firms that only operate at a low level of capacity utilization are less efficient and can only achieve relatively low levels of productivity.

Annual capacity utilization for the manufacture of most dosage forms averages around 60%. Only injectable infusions experience higher capacity utilization ranging between 85 and 100%. A number of reasons have been identified from interview data. These include: the functioning state of machinery and equipment; delays in sourcing spare parts from abroad and specialized maintenance support from machinery and equipment suppliers; human resource issues and in particular highly specialized skills in some critical areas such as product development; perceptions of locally manufactured products by some market segments; and lack of policy coherence (Wamae and Kariuki Kungu, 2014). Some of these challenges have a direct impact on the competitiveness of locally manufactured products.

The interesting observation is that these factors seem to apply mainly to the supply side of the industry. In other words, limited capacity utilization does not seem to be due to lack of demand. The previous sections showed that local producers only supply a quarter of the domestic market and a very small fraction, less that 1%, of the COMESA medicines market, so there are plenty of opportunities for expansion. Indeed, Kenyan local manufacturers have the twofold challenge of having to increase capacity utilization and very importantly considering options for expanding their total capacity.

On the other hand, once the segments in which local producers operate, which are mainly fairly unsophisticated formulations of essential medicines, are taken into account, it is possible to see that Kenyan manufacturers operate in a very competitive sub-section of the market with many competitors, both domestic and importers, and where prices and therefore profit margins are low because of the low purchasing power of the consumers and the inability to access funding from donors because of lack of WHO prequalification (UNIDO, 2012). So the technological limitations of the manufacturers also contribute to relegating most of them to a narrow and highly competitive segment of the industry where demand for each firm's product might well be constrained in some cases.

Human resources and the educational system

Successful industrial production requires a range of different skills. Local universities, such as Jomo Kenyatta University of Agriculture and Technology, Mount Kenya University and the University of Nairobi, provide graduates with good-quality basic skills and training in pharmacy, engineering and chemistry. Top polytechnics such as the Kenya Medical Training College are good sources for mid-level training. Employees also use foreign universities, for example in the UK, Germany and India. All firms also have compulsory training in-house. However, the internal education system cannot meet all industry requirements, especially as upgrading is needed.

Official reviews (UNIDO, 2012) and interviews suggest that there is a scarcity of pharmacists specialized in industrial pharmacy. The educational system has a high literacy rate and provides people well qualified in clinical pharmacy, but newly qualified employees need extensive training in the industrial aspects of drug production, including specialized training in industrial quality assurance. A key issue is that the teachers were originally trained in clinical pharmacy, so there is not a long tradition of industrial pharmacy in Kenya. University graduates have a good training in basic skills and theory, but many firms make use of training programmes run both internally and externally by international organizations, such as GIZ, Action Medeor and UNIDO. The latter sponsors popular courses such as the industrial pharmacy advanced training course run in Tanzania at the Kilimanjaro School of Pharmacy with the support of US universities (UNIDO, 2015).

Firms use some local training institutions, both public, such as the Kenya Medical Research Institute (KEMRI) and the PPB, and private. For advanced skills, however, they need to bring in experts from abroad, usually from India but also from other countries. Expatriates are expensive but important for quality because they have rare skills and experience in industrial processes. Usually they are offered short-term contracts (two to three years), possibly renewed once but usually not longer because of permit limitations and because new people tend to have more up-to-date skills. Foreign experts are identified through various channels, such as suppliers, agencies, the Web, competitors and international agencies.

Finally, in some cases firms also use their informal networks to send employees to be trained abroad, with India being a popular destination because of the strength of the Indian pharmaceutical industry. So local manufacturers seem to be able to rely on solid internal supply of skills,

although at a fairly basic level, and to access expertise at a global scale even though the latter is subject to intense scrutiny because of its high costs.

Equipment and inputs

The shallow level of the Kenyan industrial sector is an important factor when inputs to production and equipment are considered. Kenya's industry is one of the most developed in East Africa, and local producers can find local suppliers for basic inputs including packaging, with the exception of some more advanced packaging for sterile products, which is procured abroad, for example from China. Some more technologically complex packaging, such as over-pouches for injectables, used to be imported but are now produced locally.

Raw materials for production are mainly imported, due to the lack of producers of APIs and excipients. This dependence on imports is an important issue because it generates possible shortages which might influence production capacity, and additional costs even though pharmaceutical inputs are supposed to be exempted from duties. In addition, Kenyan firms compete with imports produced by vertically integrated companies who also produce APIs, and are likely to price this key ingredient above the competitive level.

Kenya does not have a developed industrial machinery sector, so the main machinery is imported from international suppliers. A popular source of equipment for pharmaceutical production is India followed by China, although language can be a barrier. India's machines have the advantage of being significantly cheaper than those from industrialized countries and basically do the work well enough for tasks that do not require a high level of technological sophistication. Europe (especially Germany and Italy) and other high-income countries are the sources of more advanced and reliable machinery. The choice of suppliers is sometimes dictated by financial considerations: higher-quality machinery might be not only more efficient but also more profitable in the long run. Companies, however, lack the resources for a high upfront investment in European machinery, in spite of the fact that the financial sector in Kenya is the most developed in East Africa.

The dependence on imports of machinery creates additional costs for local firms. Spare parts attract additional costs because imported products need to be checked and to obtain a quality stamp according to rules of the Kenyan Bureau of Standards. Additional inefficiencies are also created by the lags that occur in decisions during the process of import.

Machines are operated by local engineers, who also keep records for GMP inspections, and are usually installed by suppliers who offer a comprehensive package of support including training and maintenance, at least for the first few years of life of the machines.

Some companies are currently looking to automate their production processes. Reduction of labour costs is one of the reasons, but improvement of quality and productivity and reduction of human error and exposure in handling are more important factors.

Knowledge flows, linkage capabilities and innovation

As explained above, capabilities at the industry level depend not only on the capabilities of the various economic agents, such as manufacturers, but also on how effectively the various components of the industrial system interact and promote flows of knowledge. This section, therefore, looks in more detail at the flows of knowledge in the system and how these influence the accumulation of capabilities within firms.

Medicine producers develop their capabilities by acquiring knowledge from the external environment and through experience accumulated through a process of learning-by-doing over time. An important input to the firms' capabilities comes from the education and training activities of its workers, as discussed above. Firms, however, can step up their accumulation of knowledge by explicitly investing in learning. This can happen internally through formal or informal research activities and by acquiring knowledge from other firms – suppliers, customers and even competitors – or research institutions. Most of the firms interviewed mentioned the importance of suppliers as sources of useful knowledge. Suppliers regularly train manufacturers' employees to use their machinery. Furthermore, by coming into contact with many different firms, suppliers gain useful knowledge about the industry and can be used as sources of technological knowledge or to identify people and firms with specific expertise that is useful for a company. Since Kenyan firms use foreign suppliers, they have been able to tap into their suppliers' knowledge networks in order to identify foreign experts to hire, good training programmes and foreign firms where they can send their employees to learn more about advanced industrial technologies: some firms, for example, have mentioned examples of employees sent to be trained in Indian firms.

As mentioned above, firms also gain valuable knowledge by hiring international experts from countries such as India, South Africa and even European countries. Hiring expatriates and sending employees

to train abroad are expensive investments, so firms have schemes in which the trained employees relay the knowledge learnt to their colleagues.

As the innovation literature has pointed out since the work of Von Hippel, firms also learn from the users of their products (Von Hippel, 1982). Some producers have stressed the importance of the feedback collected by their marketing teams. A firm selling sterile injectable products stated that important knowledge was learned from nurses who used their products, and changes were implemented following the nurses' feedback.

Other common channels through which firms learn useful knowledge are exhibitions (also abroad), websites, membership of professional associations and conferences. Manufacturers also learn from each other because employees move between firms or meet and have informal exchanges at training events and seminars. Flows of knowledge also occur through the industry associations, the Federation of Kenyan Pharmaceutical Manufacturers (KFPM) and the Federation of East African Pharmaceutical Manufacturers (EAFPM), which organize training events and other initiatives.

Regulatory agencies also provide firms with valuable knowledge. For example, PPB does not only carry out inspections but also helps manufacturers with advice, especially on issues relating to the acquisition of the GMP standard, including documentation relating to the audits, and on Good Laboratory Practice and Good Distribution Practice. Similarly, the National Quality Control Laboratory (NQCL) offers training and knowledge transfer in the areas of drug testing and medical instrumentation, and Kenya Medical Research Institute (KEMRI) collaborates in the areas of research and training (KEMRI, 2015).

Licensing and joint ventures: the role of government policy

As the previous section has explained, the accumulation of technological capabilities occurs over time, and the current capabilities are influenced by past events. Because of the cumulative nature of technological knowledge, policy initiatives can have a long-lasting impact on the capabilities of firms and industries. In the Kenyan case, there are two examples of policy intervention that can be said to have helped the development of technological capabilities in the industry: the provisions for compulsory licensing in the Trade-Related Aspects of Intellectual Property Rights (TRIPS) negotiations, and the policy of forming parastatal joint ventures with foreign MNCs in order to develop local capabilities based on foreign technology.

In the case of licensing of foreign technology, Kenya campaigned vigorously during the trade negotiations that led to the TRIPS agreement in order to be able to carry out compulsory licensing for some essential medicines. Compulsory licensing means that governments can issue licenses to manufacture medicines that are still protected by patents at more affordable prices than those set by foreign pharmaceutical companies that hold the patents, without receiving the latter's consent. Although in practice there has been no compulsory licensing in Kenya, it can be argued that the threat of compulsory licensing has enabled local firms to reach good licensing agreements with foreign MNCs. According to Garwood (2007), 'Kenya has never issued a compulsory license, but came close to in 2004 before the German pharmaceutical major Boehringer Ingelheim agreed to enter into a voluntary license agreement with Kenyan drug firm Cosmos to produce generic versions of its patented anti-AIDS drug nevirapine'. Cosmos went on to enter another technology transfer agreement with Roche and is now one of the most dynamic Kenyan manufacturers, also aiming to gain WHO prequalification for the production of ARVs. The 'buy local' drive or procurement approach of the 1990s was also significant. It helped to lay a strong basis for the mushrooming of private local manufacturers: thus Cosmos would probably not have had its advantageous licensing position were it not for the 'buy local' move that was in effect very much steeped in ISI thinking.

As the above historical background pointed out, during the import substitution period, the government established ICDC to promote the development of local capabilities partly through parastatal joint ventures with foreign organizations. Joint ventures formed through the 1970s with the Yugoslav government and a German firm are now the precursors of two dynamic Kenyan private firms: Dawa and Infusion Medicare, one of the producers of injectables. Cosmos was also originally formed as a joint venture. Now all three firms are wholly locally owned private firms, and critics of import substitution and ICDC interpret the fact that the joint ventures had to be privatized as a failure of import substitution and ICDC (see, for instance, Himbara, 1993). However, it can be argued that although the parastatal status might have hindered the business development of the joint ventures, ICDC can still be said to be responsible for the creation of organizations that developed local technological capabilities that were later further developed by private capital. Possibly, without the initial policy of forming joint venture, companies like Dawa, Infusion Medicare and Cosmos would not exist today.

The ISI policy involving joint ventures, of course, is not the only way to build industrial capabilities. In more recent years, Kenyan firms have found other ways to draw successfully on foreign capabilities. Two other producers of sterile products followed different strategies: one, facilitated by the assurance of a large government procurement, bought a South African firm outright and transferred the facilities to Kenya, whilst the other, which pursued an export-oriented strategy and is located in an EPZ, assembled a variety of suppliers and contractors to build a new plant with equipment sourced from various countries and drawing on international expertise.

Conclusions

This chapter has provided an outline of the local production of medicines in Kenya, which is the leading manufacturer of pharmaceuticals in East Africa, accounting for half of the local production in COMESA and boosting rising production and exports. The Kenyan pharmaceutical industry is still small in relation to imports into Kenya and the whole of COMESA. However it constitutes a story of successful development of technological capabilities with examples of firms that are upgrading their technology and might be able to become leading players in East Africa, such as Universal, which has achieved enough technological capabilities to be awarded WHO prequalification. Kenya's dynamic private sector and its access to COMESA and EAC are important strengths that suggest good prospects for Kenyan local producers.

However, obstacles and limitations remain, and the analysis in this chapter has shown that Kenyan firms have to upgrade successfully in order to compete effectively against strong imports. Kenyan pharmaceutical producers have not yet been able to access donor funding, with only one firm achieving WHO prequalification so far. Most of the firms also operate in a highly competitive segment of the industry, the production of formulations of essential medicines, which offers low returns and pits them against very efficient imports. There are, however, success stories of firms that have reached significant technological sophistication, as in the case of the producers of injectables, and the analysis paints the picture of an industry integrating in global value chains, with access to global networks of equipment suppliers, foreign experts and training centres.

Still, there is work to be done to improve the regulatory environment, such as making sure that the VAT regulations do not disadvantage local firms, reducing the dependence of local manufacturers on imported raw

materials and promoting upgrading throughout the technologically weaker firms; the current strategy is to progressively move all firms from local to international GMP standards.

It is not straightforward to draw general lessons for the promotion of local production of pharmaceuticals in low-income countries given the messy economic history and diverse patterns of technological accumulation this chapter has presented. It is possible, however, to suggest some possible tentative reasons that might have contributed to the observed successes of Kenyan pharmaceutical production. The chapter has argued that ISI policies, including the use of joint ventures at an early stage of industrialization, followed by gradual liberalization, might have been a positive factor in the accumulation of technological capabilities. Kenyan producers seem also to access global networks that are useful to identify and tap into rare skills and identify good equipment suppliers. The openness of Kenyan manufacturers may also be assisted by India-linked networks of some manufacturers with accumulated family experience in capitalist production from older merchant enterprises (Himbara, 1993).

On the whole, this chapter suggests a positive future for broadening and deepening pharmaceuticals production in Kenya. Despite an international and national context that is often less than helpful, considerable progress has been made in the past few years and capabilities have been established that, while often unseen, are laying the basis for further growth. With a little extra help at the government level, Kenya might soon be a leading African nation in the field.

Notes

1. Research project *Industrial productivity and health sector performance*. The findings, interpretations, conclusions and opinions expressed here are those of the authors and do not necessarily reflect the views or policies of DFID or the UK ESRC, whose financial support is gratefully acknowledged (project ES/J008737/1). This chapter draws on fieldwork undertaken by Watu Wamae and Joan Kariuki Kungu as part of that research project.
2. An earlier version of this figure appears in Wamae and Kariuki Kungu (2014), reworked with permission.

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3

Pharmaceutical Manufacturing Decline in Tanzania: How Possible Is a Turnaround to Growth?

Paula Tibandebage, Samuel Wangwe, Maureen Mackintosh and Phares G.M. Mujinja

Introduction

> "This sector [pharmaceuticals] is going to die… A hundred percent reliance on imports is dangerous." (Tanzanian government official)[1]

As Chapter 1 described, Tanzania has a decades-long history of pharmaceutical production, the sector mirroring fluctuations in Tanzania's post-independence industrial history. By 2004–05, the sector was estimated to be producing pharmaceuticals worth US$32.5 million, supplying around 30% of the local market and exporting about 10% of local production (MoHSW, 2006). The subsequent rise and decline of the sector is analysed in this chapter, locating firms' sources of both market resilience and vulnerability in local patterns of ownership, finance and management, interacting with the internationalization of firms' domestic and regional markets. Finally, the chapter examines the 'turnaround' challenge facing the local industry. Concerned policy makers are aware, as the above quotation shows, of the health sector insecurity inherent in complete reliance on medicines imports.

Methods and sources

The chapter draws on extensive interviewing in 2013–14, some earlier interviews, unpublished research findings and feedback from

involvement of the authors in policy debates in Tanzania.[2] Senior managers in all five pharmaceutical firms producing human medicines for the private and public market that were operating at the time of the research were interviewed. Interviews were conducted with CEOs and/or production managers, using a semi-structured interview schedule that focussed on firms' capabilities to supply the Tanzanian health sector. Interview data are not attributed to specific firms except by agreement; otherwise, firm-specific information is drawn from the public domain and referenced.

In addition, informants and stakeholders associated with the industry were interviewed, including policy makers, regulators, senior actors in business associations and wholesalers in public, non-profit and private sectors. Finally, seven firms producing non-pharmaceutical products relevant to the health sector were also interviewed.

Recent industrial rise and decline in pharmaceuticals

In 2004–05, seven pharmaceutical firms were producing medicines for human consumption in Tanzania (Chapter 1). There were no multinationals, and only one joint venture with an external partner. The years up to 2008–09 then saw substantial investment, upgrading and some consolidation and new entry in the industry: this was an optimistic period in the sector.

Investment and consolidation

The largest firm is Shelys Pharmaceuticals, a pioneering firm developed by the Sumaria group. Sumaria is a successful example of the large, diversified, family-owned conglomerates that dominate Tanzania's large industry sector (Sutton and Olomi, 2012). It is a regional multinational, producing plastics, cement and consumer goods, and moving into renewables. It built up Shelys as a wholly owned firm in Dar es Salaam; in 2003, Sumaria bought Beta Healthcare International, a Kenyan pharmaceutical company, with private equity funding from Aureos Capital, making Shelys Africa Group the largest East African pharmaceutical company at that time. Shelys built and commissioned a new plant for making penicillins in Tanzania in 2008, to international good manufacturing practice (GMP) standards, and at the time was planning diversification including parenterals and anti-retrovirals (ARVs) (Shelys, 2008). In 2008, Sumaria sold 60% of Shelys to Aspen, a South African multinational, allowing private equity to exit.[3]

Three other larger firms were developed by Tanzanian African capital. Interchem Pharmaceuticals, set up in 1989 in Moshi and part-owned by the IPP group of companies that includes large media interests, made substantial investments but closed in 2008. In 1995, the government sold 60% of the equity in two closed government pharmaceutical firms into Tanzanian private family ownership, and each reopened. Keko Pharmaceutical Industries then made substantial investments. Tanzania Pharmaceutical Industries (TPI) began production in 2008 of three first-line anti-retrovirals (ARVs) for HIV, the first such production in Tanzania. With European Union financial support and technical support from Krisana Krasintu of Thailand, TPI was upgrading its production and quality assurance and planning a new GMP-compliant plant for ARV production (Losse et al., 2007). In 2007, Zenufa, a firm with a family-owned parent company based in the Democratic Republic of Congo (DRC), invested in a new plant in Dar es Salaam, aiming for full GMP standards, with initial loan financing from the Belgian Investment Company for Developing Countries.

Also in this period, Tanzansino, a Chinese government–Tanzanian military collaboration, closed for planned major renovation,[4] while two family firms owned and run by Tanzanian pharmacists, Mansoor Daya and AA Pharmaceuticals, were investing and expanding supplies to the local market. Mansoor Daya is the oldest Tanzanian local producer, while AA was started in 2003.

By 2009, Tanzania-based production was supplying an estimated 35% of a local medicines market worth about US$140 million, and rising medicines exports had reached almost US$8 million.[5] A particular strength of the local firms was supply to the rural areas: rural availability relied quite heavily on local manufacturers, and interviews with rural medicines buyers in 2006–07 had found evidence of brand recognition and trust for locally produced medicines, especially those from Shelys (Chaudhuri et al., 2010; Mujinja et al., 2014). In 2009, Tanzanian pharmaceutical production looked like a relative success story.

Recent industrial decline

Yet between 2009 and 2013, this success story turned into rapid decline (Wangwe et al., 2014a). By 2013, just five pharmaceutical firms were operating. The rising trend of medicines exports to 2009 had reversed (Figure 3.1). By 2013, imports of pharmaceuticals had risen to US$286 million on the back of rising donor spending, while medicines exports had fallen to US$1.7 million. Informed local estimates[6] put the local producers' share of the domestic medicines market at under 20%.

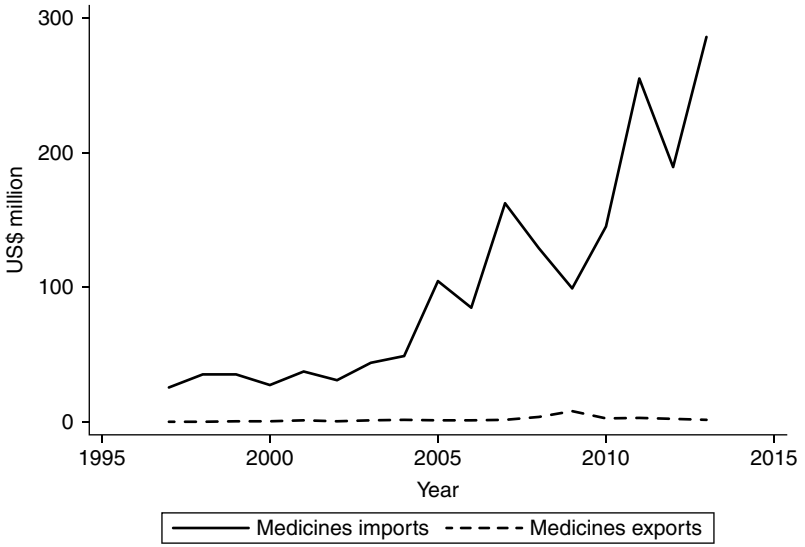

Figure 3.1 The expanding local supply gap: total imports and exports of medicines and blood products (US$ millions)

Source: Drawn from Comtrade data, http://comtrade.un.org/data/, downloaded 5 August 2014.

As the market has expanded, the local firms' share had fallen. Figure 3.1 shows the yawning trade gap.

Data on availability and sources of medicines in the Tanzanian public and private markets confirm this declining trend in local producers' market shares, for a matched sample of medicines and health facilities and shops (Table 3.1).

As the number of producers dropped, the product range narrowed. The only local producer of anti-retrovirals (ARVs) had been closed. All but one of the remaining firms had by 2013 largely ceased to produce basic antibiotics, and the largest firm was moving out of production of many other basic medicines. Local producers' share of public procurement had been falling, and only one local firm was tendering for public sector procurement contracts in 2013–14. A non-profit wholesaler estimated buying locally 'far less than half' than four years previously. A private wholesaler, who in 2010–11 had bought local medicines worth Tshs 1.5–2 billion, was, he said, now buying 'almost nothing, a few syrups'. The resultant decline in the local market share of a number of key essential medicines shows up in the survey data (Table 3.2). A

Table 3.1 Decline in domestic market share of medicines made in Tanzania, 2006–12

	Percent of sample medicines available on day of visit, by country of origin			
Year	**Tanzania**	**Kenya**	**Other**	**Total**
2006	33	14	53	100
2009	21	13	66	100
2012	12	11	78	100

Source: Authors' analysis of WHO/HAI survey data 2006, 2009, 2012.[7]

Table 3.2 Share of local manufactures among specified tracer medicines available in sample outlets, 2006–12

	Local share of available:				
Year	**Amoxicillin capsules**	**Folic acid tablets**	**Albendazole tablets**	**Ciprofloxacin tablets**	**Diclofenac tablets**
2006	79%	79%	81%	40%	45%
2009	74%	27%	33%	32%	26%
2012	13%	51%	43%	24%	4%

Source: Authors' analysis of WHO/HAI survey data 2006, 2009, 2012.

domestic medicines market, worth around US$250 million, had become supplied overwhelmingly from imports paid in dollars.

Industrial strengths and vulnerabilities: explaining sudden decline

The predominance of family ownership with diversified business activity, described above for the pharmaceutical firms, is characteristic of the Tanzanian industrial sector more broadly (Sutton and Olomi, 2012). Diversified family-run businesses have a number of competitive advantages in Tanzania's challenging business environment. Where bank finance is expensive and hard to access, diversified family firms can spread risk and provide access to financing which is both 'patient' (Goodluck, 2014) and also relatively low-cost and flexible. The business structure also reduces transparency and helps to weather crises. Tanzania has a shallow industrial structure: other than agro-processing, manufacturing relies heavily on imported inputs, so firms may integrate

backwards to produce inputs such as packaging. Large diversified firms can gain competitive advantage by addressing in-house some 'institutional voids' (Khanna and Palepu, 1997) in their environment, such as market information sources, skilled labour pools or institutionalized working relations with government.

Some of these competitive strengths can be identified in Tanzanian family-run pharmaceuticals. Where market information is poor and consumers cannot judge quality directly, as in poorly regulated retail medicines markets, local brand trust and recognition is a powerful marketing tool (Khanna and Palepu, 1997). Where the domestic generics market is a firm's core business, investment in building a reliable generics brand benefits both consumers and manufacturer. All the pharmaceutical manufacturers interviewed had relied on capital from other parts of diversified family business, including property and trading. One firm was producing its own bottles, while two relied on overseas companies within a business group for quality assurance of inputs and access to technological information.

However, the vulnerabilities of family-based industrial organization, and of the shallow industrial structure, were also evident in the interviews. Reliance on imported inputs lengthens production schedules and increases quality risks. All firms had problems sourcing good packaging locally, and poor packaging of local products was a common complaint by Tanzanian health sector buyers. The financial and reputational risk associated with quality problems implied reliance on imported blister strips from India. Some firms had found locally bought bottles to be of unreliable quality and had switched to imports. While plastic containers for bulk tablets (sealed first into clean plastic bags) were made locally, the shallow industrial sector constrained improvements in local upstream supply. For example, a shift by pharmaceutical firms from glass to plastic bottles – desirable for safety and supply reasons – required substantial related investments by both pharmaceutical and plastics firms. At root of the problem was the small number of firms and a lack of mutual trust and coordination, posing a major hurdle to mutually beneficial industrial upgrading.

Access to technology and information was also generally constrained. Some firms relied on hard-pressed CEO's visits to trade fairs, and on established suppliers, for technical information, for training and upgrading support, and sometimes for trade credit. Ensuring quality of inputs from Asian suppliers was a constant challenge. Machinery suppliers – predominantly Indian or Chinese – installed, trained and provided spare parts and advice. Two firms had gained external donor support for

technical upgrading and capacity expansion. All trained their own staff and complained of the difficulties of finding and retaining pharmacists and pharmaceutical technicians. This small cluster of Tanzanian pharmaceutical firms apparently collaborated rather little, and benefitted from few spill-overs or linkages between firms.

Changing context and responses

The Tanzania-based industry is operating in a very open market context, where shifts in the relevant international market segments are immediately experienced within Tanzanian domestic and regional markets. Structurally and technologically, several worsening pressures appear to be producing a tipping point. The first relates to size and market positioning. Pharmaceutical firms in Tanzania mainly produce basic essential generic medicines and over-the-counter items such as cough syrups. Economies of scale are limited in basic formulations (Chaudhuri and West, 2014) but are large in active pharmaceutical ingredient (API) production. While small firms can compete, therefore, in formulations, they are at a structural disadvantage to large Indian exporters since they buy small API lots from Asian suppliers, some of whom also produce formulations. As one manufacturer put it, the 'key constraint in this market is demand'. If firms cannot sell sustainably, they cannot grow, and they need their home market as a basis for expansion.

The second pressure is technological and regulatory: firms are forced into a cycle of constant upgrading, both to meet rising international standards that are requirements for different levels of market entry, and to meet competitors' quality standards. Constant upgrading of firms' technological capabilities (Bell and Pavitt, 1993; Lall, 1992) is central to firms' competitive survival in pharmaceuticals, to sustain quality at a competitive price and to retain market access. For all the firms, the technological challenge was framed by Good Manufacturing Practice (GMP) standards.

GMP constitutes a production *culture* to be attained (see also Chapter 12). GMP Guidelines[8] emphasize documentation and validation of the production flow, including effective quality control (independent of production management); high standards of hygiene and preventions of cross-contamination; effective and documented staff training and qualifications; and well-maintained equipment and premises. Our interviewees noted the extent of professional judgement in GMP implementation of, for example, 'adequate' ventilation, 'high' levels of hygiene, risk evaluation drawing on 'experience' and 'well-designed' documentation.

The Tanzania Food and Drug Authority (TFDA) presses for GMP adherence. Tanzanian firms either have attained locally acceptable GMP standards or are working towards them with TFDA support. Manufacturers agreed that TFDA required standards rise over time, just as do the standards achieved by international competitors and the expectations of international buyers. None, when interviewed, had WHO prequalification of individual products to allow them to tender for donor-funded contracts.

All firms reported recent and current substantial investment – relative to their capacity – in technological upgrading. Major investments included new machinery for expanding capacity or for automating processes to improve quality control and lower costs. Other investments included expensive improvements in air handling and plant standards (e.g. door seals and room separation) and production flow reorganization. One firm had just put in a new product line, and another was engaged in an expensive upgrade of tablet quality to produce higher compression. This last firm was aiming, with donor financial and technical support, for WHO product pre-qualification for a combination therapy. Most firms experienced financial stress in achieving these investments, which they saw as essential to stay in business.

A third interconnected pressure comes from donors' tendering processes. Donors such as the Global Fund[9] procure a large share of medicines used in Tanzania (see also Chapter 8). Their large-scale tenders and the market entry requirement of product-by-product WHO prequalification[10] shuts out local firms from markets for HIV, TB and malaria drugs. The effect has been most damaging in anti-malarials. In 2006, about 90% of the then first-line treatment for malaria (sulphadoxine-pyrimethamine [SP]) was sourced locally. From 2007, Tanzania shifted to the more expensive combination artemisinin-lumefantrine (AL) first-line medication. Subsidized supply by the Global Fund and other donors shut out local firms. Two firms developed AL formulations but concluded that pre-qualification (costing an estimated US$150,000) was unlikely to provide market access given the scale and pricing power of Asian competitors. One local firm lost an estimated third of turnover; others also suffered substantial losses.[11]

The final major contextual pressure reported by firms was a recent sharp increase in price competition from imports. This was particularly felt for 'beta lactam' antibiotics such as amoxicillin. These are produced in a separate plant from other medicines to prevent cross-contamination, and all the larger pharmaceutical firms interviewed had such production capability. All confirmed they were becoming increasingly unprofitable.

One has closed its beta lactams plant; another said it would do so 'in a couple of years, unless policy changes'. International tender prices for amoxicillin appear to have flat-lined since 2010 (MSH, 2010, 2013).[12] A local NGO wholesaler was buying at a landed import price well below a local firm's factory gate price. One informant stated some importers' landed prices were below his firm's full materials costs. Since about 78% of materials costs were calculated to be APIs in 2012–13, the latter allegation suggests dumping may be occurring. Local producers who up to 2009 were successfully competing to supply amoxicillin for domestic use had by 2012 largely left the market, as Table 3.2 also confirms.

At the national level, this move up-market leaves the domestic supply of basic essential medicines reliant on imports, which may not be sustainable at current low prices, and which may not reach rural areas as effectively as local supplies (Mujinja et al., 2014). The government official quoted at the beginning of this chapter saw this. Price pressure was also transmitted through private market competition. Around half of the Tanzanian medicines market is private (Chapter 8), and the number of competing wholesalers has been rising.[13] Interviewees contended that margins on private sales and public contracts had been severely squeezed. The financial risk attached to supplying the public sector had also increased, since payment delays by the public procurement agency (Medical Stores Department [MSD]) were increasing, driven partly by 'erratic disbursement' of treasury funding (MSD, 2013: 8; see also MoHSW, 2013). These pressures discouraged local firms from tendering, and MSD officials confirmed that the local share of their procurement was falling.[14]

The larger manufacturers were responding by moving up-market, towards more technologically sophisticated, higher-value products with export potential. All continued to supply some over-the-counter medicines, and some higher-value items such as ciprofloxacin, an anti-infective (Table 3.2). Firms were refocusing on the domestic and regional private market, narrowing their product range and investing in new products for export. Overseas partners could support moves into higher-value products.

This business strategy carries two kinds of risk. At firm level it abandons what one firm called the 'cash cows': the cash-generating basic commodities; this reduced their turnover and liquidity and hence capability to invest. Family firms may find this reduces their survival chances in the medium term. The largest firm, Shelys, had been sold 100% in 2012 to Aspen, the South African multinational firm now part-owned by GSK (Aspen Holdings, 2013). The Aspen annual report

confirms the subsequent change in Shelys' business strategy: pursuit of higher margins by largely moving out of public sector supply (down to 5% of turnover in 2013), refocusing on the private market and dropping low-margin products. Shelys' recent investment has been largely in Kenya (ibid).

At the national level, this move up-market leaves the domestic supply of basic essential medicines reliant on imports, which may not be sustainable at current low prices, and which may not reach rural areas as effectively as local supplies (Mujinja et al., 2014). The government official quoted at the beginning of this chapter saw this trend as a national security issue.

Turnaround strategies: can the pharmaceutical industrial cluster be revived?

> Government policy is totally unfriendly to pharmaceutical manufacturing. (Experienced Tanzanian manufacturer)

Where industrial problems vary by activity, policy must vary too: selective intervention is an essential element of industrial policy. Lall and Wangwe (1997) argued this point nearly 20 years ago; it remains true today that distinct sectoral problems require distinctive sectoral solutions. Pharmaceuticals share characteristics with Tanzania-based industry generally but also face characteristic challenges (see also Chapter 1). Furthermore, some of the firms' problems, as the manufacturer quoted above implies, are policy-based and distinctive to the pharmaceutical and medical supplies sectors. Furthermore, clusters of firms create mutual benefits in terms of knowledge flows and spill-overs (Nadvi and Halder, 2007; Page, 2012; see also Chapter 2), and Tanzania risks losing these benefits as the number of firms falls. Turnaround for this sector needs to be policy-led.

However, a shift to active sector-specific support requires change in the current policy approach, which, as government officials confirmed, currently focuses on policies to influence the general business environment and does not address specific sectoral needs (Wangwe et al., 2014b). The two broad policy challenges are to reverse policies that have the largely unintended consequence of incentivizing imports over local manufacture, and to generate active policy support for the continuous upgrading of technological capabilities essential for local firms to compete in these highly globalized markets.

Sector-specific policy issues

Around half of essential medicines used in Tanzania are obtained via public and non-profit procurement. MSD's public sector procurement gives local firms a 15% price preference in competition with importers when both meet the quality hurdles. The effective preference rate is somewhat lower (one interviewee suggested around 9%), because importers' prices are landed prices at the port, while local firms' price includes delivery to MSD's zonal warehouses.

Manufacturers and other interviewees argued, however, that the procurement and tax regimes in Tanzania specifically disadvantage local firms in pharmaceuticals, as compared to other industrial sectors. The key decision that has generated these disadvantages is the removal of the import duty on all finished formulations. The decision to remove the 10% import duty on pharmaceuticals, applying the East African Community (EAC) Common External Tariff (CET) rate of zero per cent, was announced in the 2009 budget speech.[15] Since then, manufacturers supplying the private domestic market have no protection against finished imports.

Taxes and duties on imported inputs therefore specifically disadvantage local pharmaceutical manufacturers by raising their materials costs of production. The Customs Act 2008, recognizing this disadvantage, stated that where finished goods such as essential medicines are zero-rated for import duties, so are their inputs such as APIs, in order to ensure fair competition for local producers. However, as officials acknowledged, this commitment has proved 'complex' to administer in practice. While APIs are zero-rated, problems arise in identifying other inputs such as additives and excipients; manufacturers complained that highly refined sugar for syrups, for example, paid a high duty but could not be sourced locally. Manufacturers stated that efforts to put together a consolidated list of imported inputs to be zero-rated had not met with a positive response. Requests for zero rating could also be met by harassment and accusations of corruption and favour seeking.

Manufacturers also complained of uncertainty and instability in the tax and duty regime. VAT was payable on many imported inputs, and reimbursement was reported to be slow and often incomplete. Tax rules changed unpredictably. Proposals to impose duty on packaging were reported to have been raised, then withdrawn. 'Uplift', whereby customs officials increased the taxable value where under-invoicing was suspected, was unpredictable and sometimes punitive. Machinery, though exempt from duties in principle, required an import licence which could create

delay, leaving a choice between paying duty or losing cash flow. One interviewee who was considering investing in manufacturing stated that in Tanzania the rules are not as clear as in Kenya, 'where it is clear' what taxes are to be paid.

Pharmaceutical manufacturers identified ways in which contracts to supply the public sector disadvantaged local suppliers. Trade credit rules were an example: an overseas supplier winning a public sector tender would be given a letter of credit. This meant the firm was paid as soon as the goods were delivered to the port, and it could also be used to raise working capital (see Chapter 15). By contrast, local manufacturers were paid only 30 days – or more – in arrears once goods were delivered, leaving working capital to be raised by the firm. If the order is large relative to a firm's capacity, that imposes a large financial burden. Smaller firms said the risk attached to public sector tendering had become unmanageable. One now preferred to supply the public sector via private wholesalers. A wholesaler who won a tender ordered from the manufacturer, who supplied and was paid, thus shifting the tender costs and some other financial costs and risks to the wholesaler.

This last strategy illustrates a more general trend. There appeared, anecdotally, to be a shift in public sector tendering practice towards buying from importers who would 'bundle' imports with (perhaps) some local supplies. Pharmaceutical wholesalers/importers in Tanzania are generally representatives of external, mainly Indian manufacturers. Tanzanian industry, however, has historically strong links to trading capital (Sutton and Olomi, 2012), and some local pharmaceutical manufacturers also import and distribute, with or without repacking. It follows that a policy tilt towards favouring importing over manufacturing may quite rapidly result in a shift towards much higher reliance on imported commodities as traders expand and manufacturers become more 'hybrid' in their activities, expanding more into importing.

Increasing sophistication: the capabilities squeeze

Tanzania has a low level of sophistication in manufacturing, that is, a low share of medium- and high-technology manufacturing within total manufacturing value added (UNIDO/GoT, 2012: 35–36). Its pharmaceutical sector produces products that are relatively unsophisticated by industry standards. However, within Tanzania, pharmaceuticals nevertheless represent a relatively high-technology, skill-intensive industrial activity as compared to much other Tanzanian manufacturing. The recent decline in this sector therefore threatens to reinforce a declining share of sophisticated manufacturing in total manufacturing

value added. Tanzania may be losing technological capabilities at firm level, retreating to a lower level of manufacturing capabilities (Warren-Rodríguez, 2010). In this sense, the apparent crisis in pharmaceuticals identifies a more general problem.

Firms' technological capabilities (Lall, 1992) are core determinants of their ability to compete. Many of the challenges described above concern product and process capabilities: the ability to manage and document the work processes following GMP guidelines, to ensure and be able to demonstrate quality and safety of the final product. For pharmaceutical firms, these capabilities determine their market access, both locally (achieving product registration and sustaining quality when products are tested) and for access to the regional and international markets. All the firms interviewed reflected technological conditions in the international industry, in that they were chasing a moving target, facing constant pressure to upgrade. They also found it hard to sustain technological capabilities over time.

Lall (1992) distinguishes between production capabilities, investment capabilities and linkage capabilities at the firm level (see also Chapter 2). Most pharmaceutical firms interviewed in Tanzania were struggling with all three.

One of the most serious constraints on firms' capabilities in Tanzania is the low level of general and technical education in the country, implying shockingly high levels of innumeracy and illiteracy among production line staff (UNIDO/GoT, 2012: 68). Firms argued that they have more machine downtime than would be true elsewhere, given operators' limited capabilities. Lack of command of English was also a problem as compared, for example, to Kenya, especially when trying to promote people internally. The rigorous rule-following, documentation-centred culture required by GMP is unfamiliar for staff: one CEO wanted to send supervisors abroad so they could get a feel for a GMP factory. The firms all train internally the laboratory pharmacists and chemists they hire, in the equipment and techniques for the factory; they all lose these trained staff both to other firms and especially to NGOs and government, where work conditions are easier. Training is expensive and there is no local pool of skilled labour, constraining a firm, for example, from quickly adding an additional shift. Finally, there is a repeatedly reported problem in obtaining work permits for essential expatriates.

> 'Access to skilled labour is also a problem…. in Tanzania, which is compounded by refusal to grant work permits and where granted, they are expensive'. (Manufacturer)

Investment capabilities, including finance, technological information and management of investment projects, also become more demanding over time, as firms upgrade to meet rising required standards for exports. The large jump in production capabilities required to move from local market standards to international requirements imposed by donors involves investment financing, improvements in internal process operations, replanning factory layouts, retraining, improving factory infrastructure and changing marketing capabilities. This kind of investment can amount to a substantial proportion of a local firm's annual turnover and generally required funding support from outside the business and from non-bank sources. Examples cited in the interviews included financial transfers from other family businesses; external grant funding; a low-cost loan; and a joint venture partner with 'financial muscle', as one firm described it. The joint venture and grant routes to improvement can combine finance and access to technology.

Development of capabilities in production of combination therapies for anti-malarial medication, in the form of two-layer tablets, provides an example. One firm[16] was upgrading, with financial and technical support from Drugs for Neglected Diseases (DNDi), to produce a fixed dose artesunate/amodiaquine combination tablet, primarily for regional export through donor-funded procurement. The formulation was initially produced by Sanofi, in collaboration with DNDi, which then set out to transfer the technology to firms in Africa.[17] To achieve this, the firm must meet WHO-prequalification standards at competitive cost, requiring changes across the production process. DNDi support includes the formulation, technological support and training, new machinery, laboratory upgrading, raw materials for the batches and technical and training support right through to pre-qualification. The firm itself is also investing substantially in quality improvements and cost reductions across the plant. The upgrading therefore benefits the entire plant, with spin-offs in improved tablet production for the local market also.

A second example also relates to combination anti-malarials. Another firm was benefitting from a new formulation available from its parent company, alongside support from its international network to, for example, assure quality of APIs at source. A third firm (currently closed) had benefitted from an EU grant to fund a new turnkey plant to produce anti-retrovirals plant for HIV/AIDS treatment. Without this type of substantial external input, it is hard for the firms in Tanzania to enhance their capabilities sufficiently rapidly to regain access to the regional market for anti-malarials and other medication widely purchased by donors.

External networks and support are thus essential to survival in the race to upgrade and retain or regain market access. The Tanzanian pharmaceutical firms are caught in a capabilities 'squeeze': as process and product standards rise, and as the standards become more binding as requirements for market access, the constraints imposed by the firms' working conditions at home become more severe. Lack of a local skills pool, high and rising energy prices, lack of economies of scale for buying inputs and marketing output, poor transport and business infrastructure and a lack of local linkages – all these constraints have long existed, but have become increasingly binding in the new technological and market environment.

Policy to sustain upgrading and market access in pharmaceuticals: Can it be done?

It requires a change of mind-set for policy makers in Tanzania to turn to prioritizing and actively engaging in selective support of particular industrial sectors. The arguments for prioritizing pharmaceuticals include the national security issues raised at the beginning of this chapter. Loss of national ability to supply one of its population's basic needs increases reliance on exporters, notably from India, who may not be committed to production for this market medium term (Chaudhuri et al., 2010; see also Chapter 6). It may reduce availability and reliable supply especially in rural areas. The decline in the industry is also an element of deindustrialization and cumulative industrial decline, losing valuable skilled and semi-skilled employment opportunities, both in these firms and in upstream suppliers, for example in plastics and packaging firms. Tanzania is also losing opportunities to exploit synergies between health needs and financing and industrial development benefits, as compared to competing countries (see also Chapter 8).

Can this sector be turned around? A turnaround requires two key changes in mind-set and policy behaviour:

- an acceptance of the need for well-designed industrial protection mechanisms, and their effective implementation in stable and clearly explained rules;
- an active and sustained engagement with existing firms and their suppliers, in a determined effort to deepen and strengthen the local pharmaceutical production system.

There is principled opposition by some Tanzanian officials to protection of the market in essential medicines. Duties, argued one official, would

raise prices, so 'people would die'. This echoes emotive WHO and international NGO characterizations of tariffs on medicines imports as taxes that 'target the sick' (Olcay and Laing, 2005), or a 'sick tax'.[18] In practice, however, there appear to be no studies of the tax incidence of import duties on medicines in comparable contexts, though the most important influences on retail prices are likely to be the extent of domestic market competition, the purchasing power of out-of-pocket purchasers and the extent of competition between public or non-profit and private vendors[19] (see also Chapter 6).

It is, however, well established that 'infant industry' protection, to allow local firms to access markets, invest and grow *may* support both industrial growth and increasing industrial competitiveness, so long it is selective and temporary, and associated with incentives for domestic competition and export growth (Lall, 1992: 172). In the East African Community, of which Tanzania is a member, the common external tariff is set at zero for most essential medicines.[20] Tanzania could, without challenging the tariff agreement, institute a 'negative products' list of items that cannot be imported unless local manufacturers are unable to supply reliable quality at an acceptable price.

The key benefit of this change would be to allow local manufacturers to retain and grow their share of the basic essential medicines market. Without this market, the firms lose scale, cost efficiency and cash flow. The negative list would also be a relatively straightforward policy, in contrast to the complex efforts that would be required to identify and effectively exempt all essential inputs to local pharmaceutical production. Reducing or removing VAT on inputs to pharmaceuticals, or at least rapidly reimbursing the tax paid, would also shift the balance of incentives back towards manufacturers, as would raising the preference level above 15% for local suppliers in public procurement of medicines.

Additional practical changes that would shift the balance back towards local production include effective implementation by TFDA of their formal commitment to fast tracking of tests and registrations for local products (which may require additional TFDA resources). Providing trade credit for local suppliers to public procurement, as well as to overseas importers, would also rebalance the incentive structure, as would more timely funding by the Ministry of Finance for procurement by MSD of locally contracted supplies.

All of these policy changes are feasible, and many are implemented by other African countries including Ethiopia and Ghana (see Chapters 4 and 6). However, they would quite sharply shift incentives against the wholesaler/importers who currently manage the bulk of private sector

and substantial elements of public sector medicine supply. The changes would set manufacturing and importing interests against each other to some extent, posing challenges for policy makers.

Active engagement with existing firms in supporting upgrading of technological capabilities, local input sourcing and market access would also assist a shift in policy direction from trading to manufacturing, by engaging government officials more closely in manufacturing affairs. There are examples in Tanzania, outside pharmaceuticals, of success along these lines, such as the sustained consultations with manufacturers that led to the successful initiation of production of long-lasting insecticide treated bed nets. Manufacturing associations could strengthen their engagement with government. Current Tanzanian initiatives to create an active Task Force on Promotion of Local Pharmaceutical Production, including manufacturers, to improve policy and implementation in support of pharmaceutical manufacturing, could greatly enhance government-private sector collaboration.

Supporting continuous industrial upgrading requires a combination of types of support. Government policy can improve external constraints, for example by moderating utility cost increases, and streamlining slow, overlapping and expensive industrial licensing. Government can directly support areas where firms lack incentives and capability to invest themselves, such as industrial and vocation training schemes tailored to the needs of specific sectors, and funding for in-house training. Governments can work with donors to identify and tackle barriers to international market access for local firms. The large government shareholdings in pharmaceuticals, at present managed as passive holdings, could be actively used to support manufacturing improvement, or otherwise sold to support new joint ventures. Government could provide some direct financial support for investment.

The lack of industrial depth in this sector in Tanzania at present implies that government has a role in supplying missing 'public goods' of the type that larger clusters may generate locally: technological and market information; networks and introductions to help to generate joint ventures; active support for upgrading that would be available from consultants in more developed industrial contexts; and timely facilitation of external expertise when required. At present, in the small cluster of pharmaceutical firms, each was creating its own linkages; the mix of competition and beneficial externalities and collaboration characteristic of successful industrial clusters is missing here.

Two government bodies in Tanzania do provide some effective advice appreciated by manufacturers interviewed: the Japanese-supported

Kaizen unit in the Ministry of Industry and the TFDA. The manufacturers interviewed broadly appreciated the TFDA's practical and informed approach. TFDA officials are among the few in government who spend substantial time considering the requirements – and the point of view – of manufacturers. TFDA expertise could be brought into industrial policy implementation, perhaps through secondments, to help in changing the policy culture in support for pharmaceuticals.

Restructuring public procurement to support local firms' domestic market access can also help to stimulate and fund expansion and upgrading. This restructuring may include a policy already under development, to allow longer term contracts where procurement supports new local investment. This was being considered in relation to new investors, but could equally be applied to existing firms requiring longer contracts in order to fund upgrading. Manufacturers of medicines with longer public contracts could then be encouraged to use that stability to support their local suppliers' investments, for example in packaging. Given the shallow industrial structure of pharmaceuticals at present, industrial turnaround will need to address the local supply chain for pharmaceuticals, including local suppliers. Tanzania currently imports large quantities of glass, air, paper and water (bottles, packaging and intravenous fluids) in the pharmaceutical sector; even without any move into producing APIs, upstream improvement of input suppliers, and selective increases in sophistication of technological capabilities could cut industrial and import costs.

Conclusion: staying in the 'moving window'

Sutton (2012) argues that as markets integrate internationally, price competition intensifies and firms respond by investing in quality, producing better quality for a given cost. The net effect is to shift the market 'window' that firms must access upwards over time, dropping out of the window firms that can no longer meet the minimum quality/price ratio required for market entry. Tanzanian firms, facing a combination of a shallow industrial structure with few supportive linkages, a highly liberalized market, a policy 'tilt' towards incentivizing imports, and a largely passive industrial policy approach, have been vulnerable to these rising barriers to domestic and international market entry. The observed industrial fragility – the vulnerability to sudden decline – is not a new industrial phenomenon in Tanzania: for example, a number of the exporting firms that were the subject of an earlier industrial study (Wangwe, 2003) are no longer operating.

This conjuncture urgently requires a more engaged industrial policy. However, the industrial policy literature remains thin on how to sustain continuous engagement between government and manufacturers to support constant upgrading.[21] The small, strategic, but currently shrinking pharmaceutical sector offers a good ground for experimentation in policy renewal, given its perceived strategic importance. Chapter 4, on Ethiopia, provides a comparative case study of an effective set of turnaround policies.

Notes

1. All quotations are from authors' fieldwork in 2012–14, unless otherwise stated.
2. This chapter is based on the research project entitled *Industrial productivity and health sector performance*. The findings, interpretations, conclusions and opinions expressed are those of the authors and do not necessarily reflect the views or policies of DFID or the UK ESRC, whose financial support is gratefully acknowledged (project ES/J008737/1). Particular thanks also to all our interviewees who gave time within very pressured schedules to talk to us at considerable length. Thanks also to Martin Bell, Paul Nightingale and other participants in a SPRU seminar in February 2014, and to participants in a Policy Dialogue workshop in Dar es Salaam in November 2014. The same disclaimer applies.
3. Source: Sumaria Group website: http://www.sumaria.biz/our-businesses/, accessed 6 March 2014.
4. Interview, 2010.
5. Sources: Comtrade data for imports and exports, http://comtrade.un.org/data/, accessed 5 August 2014; NBS (2009) manufacturing survey for pharmaceutical production data.
6. There was no available manufacturing survey later than 2009 at the time of writing.
7. Thanks to Mary Justin-Temu for access to these data; Table 3.1 uses the 2006 sample of facilities and medicines only, for comparability.
8. East African Community Secretariat (nd) *Guidelines on Good Manufacturing Practice for Medicinal Products within the EAC*, Arusha: late draft kindly made available in near-final form by a TFDA official, in 2014.
9. The Global Fund to Fight AIDS, Tuberculosis and Malaria, www.theglobalfund.org, henceforth 'the Global Fund' in this chapter.
10. See http://apps.who.int/prequal/, also Chapter 12.
11. Source: interviewing of firms previously supplying anti-malarials, 2010
12. Median selling prices USD/tablet 0.0171 2010, 0.0173 2013 (MSH 2010, 2013).
13. Sources: TFDA figures for wholesaler numbers cited in Mhamba and Mbirigenda (2010), and interviews.
14. An MSD accountant estimated for us that just 11% by value of MSD's new two-year framework contracts had gone to local firms in 2012–13.
15. Source: URT (2009: 67).

16. This example is reported with permission from the company's CEO.
17. http://www.dndi.org/diseases-projects/portfolio/asaq.html?highlight=WyJ0YW56YW5pYSJd, accessed 23 February 2015.
18. http://www.haiweb.org/medicineprices/29012010/MPM_6.pdf, accessed 23 February 2015.
19. See Waning et al. (2010) for an interesting investigation of non-profit supply and its impact on competition. We have found no studies of import duties' incidence on medicines prices in low- and middle-income countries.
20. The currently available EAC tariff schedule, available from http://www.eac.int/customs/index.php?option=com_content&id=41:common-external-tariff-handbook&Itemid=141, sets antibiotics' import duties at 10%, but this does not appear to be implemented at present in Tanzania.
21. We owe that observation to Martin Bell.

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4

Bringing Industrial and Health Policies Closer: Reviving Pharmaceutical Production in Ethiopia

Tsige Gebre-Mariam, Kedir Tahir and Solomon Gebre-Amanuel

Introduction

Manufacturing of medicines in Ethiopia started in 1964 with the establishment of one joint venture manufacturing company. This company remained the sole producer of medicines throughout the military regime (1974–91). Following the regime change in 1991, several manufacturing plants were established during the period referred to as the 'boom and crash' period, since, for reasons described below, some of the new companies were not successful. To respond to the crisis, the government took a mix of initiatives, simultaneously fulfilling its responsibility for health care improvement and industrial promotion. As a result of policy adjustments and attractive incentives, the environment for investment in pharmaceuticals became conducive, prompting private initiative to engage in industrial investment. Joint ventures that were realized have not only contributed to the pharmaceutical industry; they also effectively transferred skill and technology.

This chapter argues for the importance of integrating the health and industrial policies to foster local pharmaceutical production. We argue that local production of pharmaceuticals is justified from both industrial and health polices standpoints. From an industrial policy standpoint, local pharmaceutical manufacture is usually justified by its benefits for the local economy, such as savings on foreign exchange through

import substitution, employment creation and the development of exports. From a health policy perspective, the rationale for local pharmaceutical manufacture is largely founded on increasing the access to essential medicines. Ethiopia is a country with high disease burden; it therefore considers development of the pharmaceutical industry a strategic endeavour.

The chapter is organized to demonstrate the close interconnections between industrial and health improvement in recent Ethiopian experience. After an overview of the stages of pharmaceutical industrial development in Ethiopia over the last 50 years, the chapter turns to an examination of the context and framework of Ethiopian health policies and the supply of medicines, describing the importance of medicines demand for the industry and industrial supply for health sector development. We describe how the health sector development programme is linked to the provision of essential medicines in the primary health care (PHC) system of the country, and the government's social responsibility in providing medicines to the population.

A key objective of the chapter is to argue, on Ethiopian evidence, that joint ventures in the pharmaceutical industry can be designed as strategic partnerships. It narrates some success stories in terms of technology transfer and upgrading manufacturing plants, and localization of knowledge within Ethiopia, and their roots in a conducive policy environment for private sector investment. A final section examines these developmental aspects of Ethiopian industrial policies. In conclusion we acknowledge the headway Ethiopia has made in manufacturing medicines and identify some issues to be addressed.

In the preparation of this chapter, policy documents, proclamations, regulations, guidelines and literature were reviewed. Key informant interviews were conducted and plant visits undertaken by the authors.

Pharmaceutical industrial development in Ethiopia

Phases of industrial development

The history of pharmaceutical manufacturing in Ethiopia is only half a century old and it may be classified into three periods: the establishment of the Ethiopian Pharmaceutical Manufacturing company (EPHARM), the subsequent boom and crash and the later 'reform and revival' period.

The first pharmaceutical manufacturing plant in Ethiopia, EPHARM was founded in 1964 as a joint venture by the Ethiopian government and the British company, Smith & Nephew. In 1971, Smith & Nephew

was superseded by Teva Jerusalem of Israel. Following the overthrow of the monarchial government by the military in December 1975, the company was nationalized. Due to the socialistic policy of the military regime, private industrial investment generally stagnated and EPHARM remained the sole producer of medicines in the country until 1993. In February 1994, EPHARM was re-established as a public share holding company and recently it was sold to a local investor.

The period 1995 to 2004 experienced the boom and crash. Ten new pharmaceutical plants were established: Asmi Industry PLC, East African Pharmaceuticals (EAP), Addis Pharmaceuticals Factory (APF), ETAB PLC, Pharmacure PLC, BioSol PLC, Life-Line PLC, Fews PLC, Sino-Ethiop Associate (Africa) PLC (SEAA) and Bethelehem PLC. However, the new factories faced daunting challenges, as there were neither policies nor regulatory mechanisms to control dumping of cheaper and substandard products. The prices of local products were not competitive. In addition, most of the new factories were poorly organized and managed. Consequently, four companies were foreclosed for failure to service their loan obligations.

According to the secretary of the Ethiopian Pharmaceuticals and Medical Supplies Manufacturing Association (PMSMA), the production capacities of the majority of the industries at the time was below 50% of their installed capacity. There was a high tariff on raw materials and a chronic shortage of experienced human resources, associated with high turnover of technical staff, shortage of technical manpower, and an absence of any training centre on good manufacturing practices (GMP) and pharmaceutical management. In addition there were no GMP-certified inspectors at the regulatory authority. It was hard to get working capital from banks, there were management problems in the industries, an absence of qualified equipment calibration and maintenance centres, and university-industry linkages were weak.

Established in 1996, East African Pharmaceuticals (EAP) was one of the companies that survived the 'crash' period. EAP was an initiative of British and Sudanese nationals. It had difficulties at the outset when the cost of the investment was driven up due to the decision of Drug Administration and Control Authority (DACA) that EAP should reconstruct its plant to comply with GMP, shortly after it started operation. In 2009, the factory was operating at 30% of its capacity. EAP produces human and veterinary medicines mainly for the local market, although a small portion is exported to Sudan and Somali. Being the only local manufacturing company producing veterinary medicines, EAP enjoys market monopoly. Hence, it is currently considering increasing its

production to meet the market demand. At the time of writing EAP has just achieved a GMP Certificate from the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S).

Established in 1997, Addis Pharmaceuticals Factory (APF) Sh. Co. is the largest pharmaceutical manufacturing plant in Ethiopia. It is located in Adigrat, Tigray Regional State, northern Ethiopia. Though the plant was constructed and equipped with high-tech production facilities, at the start it faced financial and management crisis. In 2009, it acquired a second factory located at Akaki at the outskirts of Addis Ababa, which is dedicated to the manufacturing of large-volume parenterals. APF manufactures about 90 products. It has nine production lines with a capacity to produce 1.2 billion tablets, 19 billion ampoules, 10 million vials, 500,000 capsules, 4 million ointment tubes and 9.6 million bottles of syrup. It has fully equipped laboratories. APF is owned and managed by the Endowment Fund for the Rehabilitation of Tigray (EFFORT).[1]

Sino-Ethiop Associate (Africa) PLC (SEAA) was established in March 2001 as a joint venture between an Ethiopian company, Zaf Pharmaceuticals PLC, and two Chinese companies (China Associate Group and Dandong JINWAN Group). SEAA produces empty hard gelatin capsules and sells them to pharmaceutical factories in Africa and the Middle East. Recently, SEAA completed its expansion project and doubled its production capacity, to 2.4 billion capsules annually. SEAA has recently acquired Certificate of PIC/S conformity. It will be shown later that companies established through joint venture have been generally successful.

The 'reform and revival' period began in 2005. The Ethiopian Pharmaceutical and Medical Supplies Manufacturers Association (EPMSMA) and other key stakeholders appealed to the government for appropriate measures to be taken in support of local manufacturing. To address the crisis the local manufacturers were facing, the government created benefit packages and undertook policy reforms. This improved the business environment, resulting in some new joint ventures.

In 2007, Cadila Pharmaceuticals Ethiopia PLC (CPEL) was established by Cadila Pharmaceuticals Ltd (India) and Almeta Impex PLC (Ethiopia), owning 57% and 43% of the company, respectively. The market size, including easy access from Ethiopia to other East African countries, motivated the investment. All machines and raw materials were imported from India. CEPL has the capacity to manufacture 390 million tablets, 165 million capsules and 1.44 million litres of liquid per annum. In 2011, CEPL acquired a GMP certificate.[2]

Established in 1998, Pharmacure PLC, a Swedish turnkey plant, is an Ethiopian-Saudi investment. It produces large-volume parenterals. Rx Africa (Ethiopia) PLC, an Ethiopian-US joint venture was commissioned in 2007 through the acquisition of a local company called Sunshine Pharmaceuticals. Rx Africa launched 36 products in 2009. Another local manufacturer, Fews PLC, produces syrups.

In 2013, Julphar (Gulf Pharmaceutical Industries) commissioned its pharmaceutical manufacturing facility[3] in Addis Ababa. The facility has the capacity to produce 150 million bottles of suspension and syrup, 500 million tablets and 170 million capsules annually.

One unique local manufacturer is the National Veterinary Institute located in Bishoftu, 40 km south of Addis Ababa. With its well-equipped diagnostic and research laboratories and production plants, the NVI is currently producing 19 R&D-based veterinary bacterial and viral vaccines for both domestic and international markets to more than 25 countries in Africa and the Middle East.

The Ethiopian industry today

Today, the Ethiopian pharmaceutical industry consists of 15 pharmaceutical manufacturers, of which nine produce medicines, one manufactures empty gelatin capsules, and the rest are engaged in producing medical supplies such as syringes, absorbent cottons, gauzes, bandages and sanitary products. Though significant expansion of the industry is taking place, as such the base is not yet well developed, and the companies have relatively low production capacities.

The therapeutic categories of local production include antibiotics, gastrointestinal drugs, central nervous system drugs, cardiovascular drugs, anti-diabetic agents, antihistamines, anthelmintics, analgesics and antipyretics, antiprotozoals, respiratory drugs, dermatological preparations, minerals and vitamins, large-volume parenterals as well as veterinary vaccines. None of the manufacturers produces medicines against tuberculosis, HIV/AIDS and malaria. Since the local manufacturers were not GMP-compliant, they could not make use of the donor funding made available for the procurement of medicines for these diseases. Hence these medicines are being imported from abroad, mainly from Indian manufacturers.

The Ethiopian pharmaceutical industries are small- to medium sized industries. Most use labour-intensive, step-by-step manual manufacturing, with semi-automated production lines. Manufacturers mainly focus on tablets, capsules, powder and liquid preparations. A few produce parenteral preparations, creams and ointments. Production is limited

to secondary manufacturing that involves combining and processing pharmaceutical active ingredients (APIs) and excipients into dosage forms. There is no active pharmaceutical ingredient (API) plant in the country. Almost all input materials (APIs and excipients), including primary packaging materials, are imported, mainly from India and China. According to an interview with the procurement department manager of EPHARM, input materials are purchased in small quantities, at times too small to attract suppliers, and as a result manufactures have no power to negotiate better prices. This situation tends to increase the cost of input materials. Hence, most of the finished products are not competitive as compared to products imported from China and India. Just a few inputs such as sugar (for syrup production), empty hard gelatin capsules and secondary packing materials are locally produced. There are new packaging manufacturers who have begun producing PVC and empty bottles for pharmaceutical use replacing some of the imports (Sutton and Kellow, 2010). Cardboard boxes for bulk packaging are manufactured locally.

Although most of the manufacturers operate below their respective capacities, the capacity utilization of the manufacturers has shown improvement during the 2005–14 period, increasing from a mere 29.3% in 2008 to 79.0% in 2013. This is indicative of the growing market for locally produced pharmaceuticals – an opportunity lying ahead for the sector (CSA, 2014).

As regards quality issues, there are three manufacturers that comply with basic GMP standards, one of whom is to acquire PIC/S Certification soon, while two others are expected to acquire the same in the near future. One of the main issues that must be addressed by local manufacturers is the need to access updated technology. In terms of personnel, however, Ethiopia seems to have sufficient trained pharmacists, though there is a dire need for those with industrial and managerial skills.

Developing and supplying the health sector

This section analyses the interaction of health care development and industrial market development, aiming to show how health and medicines policies influenced the development of the local pharmaceutical industry.

The National Health Policy (NHP) launched in 1993 includes as core elements the development of preventive, promotive and curative health care; assurance of health care accessibility for all segments of the population; and the promotion of private sector and NGO participation

in the health sector (TGE, 1993a). In order to achieve these goals, a 20-year Health Sector Development Programme (HSDP) consisting of a series of five-year rolling programmes was established in 1997/98. The HSDP has been aligned with the wider frameworks of the Plan for Accelerated Development to End Poverty (PASDEP), and a Growth and Transformation Plan (GTP) has been formulated and implemented.

HSDP implementation takes a sector-wide approach encompassing the following components: service delivery and quality of care; health facility rehabilitation and expansion; human resource development; pharmaceutical services; information, education and communication; health sector management and management of information systems; monitoring and evaluation and health care financing.

Over the last two decades the government has been engaged in health facility construction, expansion, rehabilitation, furnishing and equipping. From 2003/04 to 2011, the number of health posts increased from 4,696 to 17,972 and the number of public health centres from 519 to 3,871, while the number of hospitals (public and private) rose from 126 to 194 (FMOH, 2011). Health service coverage increased from 45% in 2001 to 95% by 2011. The rise in health service coverage necessitated an increased demand for pharmaceuticals. Hence, the number of pharmaceutical manufacturers, importer/distributors and retail outlets increased significantly during the same period to serve an expanding market.

Targets set by HSDP IV with respect to pharmaceutical supply and services include increasing the availability of quality pharmaceuticals at an affordable price and in a sustainable manner, and achieving improved rational drug use. In the design of HSDP III and IV, the SWOT analysis made indicated increasing domestic manufacturing capacity of drugs as an opportunity to be explored (FMOH, 2011/12). Recognizing the importance of the supply of pharmaceuticals in the overall health policy, the government decided to increase the availability of essential pharmaceuticals from 75% to 100% and improve the efficiency of regulatory activity (MOFED, 2006). Moreover, the Growth and Transformation Plan (GTP) anticipated increasing the domestic market share of the local pharmaceutical industry from the baseline year 2009/10 share of 15% to the target 50% (MOFED, 2012).

The market for pharmaceuticals in Ethiopia is met through import (purchase and donation) and local production. Local manufacturing still represents less than 15% of the total market for pharmaceutical products. Governmental organizations, private importers, non-government organizations (NGOs) and international agencies such as the UNICEF

and WHO used to participate in the import and distribution of pharmaceuticals. In order to streamline the supply and distribution of essential medicines to the public health care facilities, the former PHARMID was transformed into the Pharmaceutical Fund and Supply Agency (PFSA), as established by Proclamation in 2007 (FDRE, 2007).

Today, local and international procurement for the public health facilities is mainly provided by the PFSA which operates with a revolving fund. PFSA procurement is done through international and local tenders as well as through direct purchasing. The PFSA also receives some pharmaceuticals through donation from sponsors of vertical programmes such as those for ARVs, TB and malaria medication and reproductive health commodities. From its central hub in Addis Ababa and the regional hubs, PFSA distributes medicines and medical supplies directly to health care facilities. Private companies import directly from their respective suppliers and distribute to wholesalers, and these in turn sell to retailers.

The PFSA has designed and implemented different strategies to support local manufacturers of pharmaceuticals and medical supplies. These include the provision of 30% advance payment for the purchase of products won through national bidding and 25% price preference when local manufacturers participate in international bids. Although not yet implemented, a tripartite agreement (PFSA as a collateral, pharmaceutical companies and the Development Bank) has been signed, providing local manufacturers with a loan for 70% of a bid that has been won. Furthermore, to increase local production of pharmaceuticals and medical supplies and create market linkages with consumers, the type and amount of products given priority by the health services have been identified. Based on this, a list of 124 pharmaceuticals and medical supplies produced in the country has been prepared to serve as a guide for the procurement process.

With an estimated population of 95 million in 2014, Ethiopia has the potential to become a significant market for pharmaceutical products in Sub-Saharan Africa. Although the Ethiopian pharmaceutical market grew on average by 20% per annum from 2007 to 2011, it is still rather limited, estimated at around US$500 million, due mainly to low per capita income. Currently, there is slightly higher total health expenditure as a share of GDP, at 4.9% in Ethiopia, as compared to other countries in Africa (excluding South Africa), but the per capita health expenditure remains among the lowest in the region (Wamai, 2009).

Joint ventures and strategic partnerships: fostering technology transfer

The revival of the pharmaceutical industry of Ethiopia after the boom and crash is largely attributed to policy reforms, investment and manufacturing incentive packages. One important phenomenon that stands out is joint ventures. Through the initiative of joint ventures, a foreclosed factory revived, an old factory was upgraded, new factories were established, and enhanced technology transfer included localization of technical knowledge within Ethiopia.

One of the shortcomings of the local manufacturers is that they are organized at the secondary level and hence dependent on foreign companies for raw materials and technology sources. In order to overcome this problem, some local manufacturers established joint ventures as a strategic partnership with foreign companies. These joint venture investors gain access to both local and regional markets, and Ethiopia's cheap labour force, as well as a number of investment incentives that the country offers in exchange for raw materials, know-how, technology transfer and pre-established market networks. This kind of strategic partnership can be considered as a key factor for long-term success. The joint ventures between the Ethiopian company, Zaf Pharmaceuticals PLC, and two Chinese companies, China Associate (group) Co., Ltd and Dandong Jinwan (Group) Co., Ltd (Sino-Ethiop Associate Africa PLC), and between Medtech (Ethiopia) PLC and Gulf Pharmaceuticals Julphar of UAE (Julphar Pharmaceuticals Manufacturing Ethiopia PLC) are based on this principle.

Sino-Ethiop Associate Africa PLC, the sole empty hard gelatin capsules (EHGCs) manufacturer in Africa, was established at the outskirts of Addis Ababa in March 2001 and became operational in June 2003. China Associate (Group) Co., Ltd. is a 35% shareholder of Sino-Ethiop Associate Africa PLC. It is a diversified enterprise engaged in manufacturing of bulk pharmaceuticals and finished formulations and has a trading business. This company has more than ten years of business relationship with the pharmaceutical companies of some African countries, including Ethiopia. Dandong Jinwan (Group) Co., Ltd. is the other partner holding 35% of the shares. It is a diversified enterprise engaged in the production of EHGCs itself and manufacturing of equipment for capsules production. Zaf Pharmaceuticals PLC, engaged in importing of pharmaceuticals, is the Ethiopian counterpart in the joint venture, having 30% of the shares.

The company currently has five automatic capsule production lines to produce EHGCs, with a total capacity of 2.4 billion EHGCs of size 0, size 1 and size 2 per year. The continuous batch system is applied in the production process; as a result, production is not interrupted except during regular preventive maintenance schedule and size part changes. Its capacity utilization is normally more than 95%, operating in three shifts. On average, there are more than 300 production days per year. The company covers 100% of the local EHGCs demand and exports to Sudan, Kenya, Uganda, South Africa, Ghana, Zimbabwe, Democratic Republic of Congo, Yemen and Saudi Arabia, among others.

The company has recently undergone a major expansion that transformed the overall capacity of the company, doubling the annual output. It has also done the civil engineering required to accommodate three more production lines. The director of the company revealed that the expansion has transformed the company in terms of both quality and productivity, including:

- state-of-the-art manufacturing equipment which is automatic and fully synchronized;
- Programmable Logic Controller (PLC) systems: advanced from push-button to touch-screen, enabling easy process monitoring and record keeping;
- heating, ventilation and air conditioning (HVAC) system: programmed based on a one-year study made on the climatic condition of the location in order to improve its overall efficiency;
- water treatment system: use the double-reverse osmosis system along with electro-deionization system that reduced the use of different chemicals and improved the quality of the water; and
- energy utilization: integrated a solar energy source with the existing grid supply.

After the expansion, the manufacturing lines were moved to the new plant, leaving the old facility empty. Although the company is working three shifts at full capacity, it is still unable to meet market demand for EHGCs. It is therefore planning to increase its capacity from five to eight lines at the new plant. Further, the company plans to convert the old facility into a formulation plant for contract manufacturing. The other plan of the company, which is also of interest to the government, is to look into the possibilities of developing gelatin raw materials from cattle bone, which is abundant in the country.

Skills and technology transfer has been extensive. Over a period of ten years, the Chinese technical and managerial staff have been completely replaced by Ethiopian staff (today there is just one Chinese engineer). The technology has been totally transferred (by Dandong Jinwan), signifying the critical role that joint ventures can play in the development of the pharmaceutical industry. According to the general manager of the company, such a smooth transfer was possible due to several complementary reasons, including the trust developed among the partners, the government policy to limit the number of foreign employees in a company, training of personnel locally and abroad, and government insistence that the transfer of skills and technology by partners should take place.

Julphar Pharmaceuticals Manufacturing Ethiopia PLC is another company established as a joint venture. Its vision is to become one of the leading pharmaceutical companies in Africa by the year 2020 with a number of product portfolios. The joint venture is formed between an Ethiopian company, Medtech Pharmaceuticals PLC, that holds 45% of the shares, and a United Arab Emirates (UAE) company, Gulf Pharmaceuticals (Julphar), that holds 55% of the shares. The UAE partner is producer of various pharmaceutical products in the Middle East and in its other subsidiaries in Algeria. Julphar maintains a network of 11 manufacturing plants based in the UAE, with developments under way to open additional facilities in strategic countries such as Saudi Arabia, Ethiopia and Algeria. It supplies its generic pharmaceutical products to the global pharmaceuticals markets. The Ethiopian partner has been exclusively importing and distributing Julphar products and continued to do so for products being produced locally by Julphar Ethiopia as well.[4]

This joint venture transformed a previously bankrupted manufacturing facility, Bethelehem Pharmaceuticals, into a viable, state-of-the-art facility at a cost of about US$9.17 million. Currently, it is running at full capacity and producing and supplying the Ethiopian market with 25 different products (25 million bottles of syrup/suspension, 500 million tablets and 170 million capsules per year). In order to reach the international market, the company has already fulfilled GMP requirements and is expected to be fully certified with PIC/S.

The company has upgraded the facility with new utilities and machineries as per GMP requirements. It has put in place new HVAC system, state-of-the-art and fully automated reverse-osmosis water treatment system, and boilers for generation of pharmaceutical grade steam. Furthermore, to increase its product portfolio and production capacity, a new closed and fully automated oral liquid preparation and filling

line, tablet compression and blistering machines, and ointment filling machines have been installed and made operational. To upgrade the quality control system, Julphar has introduced high-performance liquid and gas chromatography systems and computerized stability chambers. To enhance the quality assurance (QA) system, the company is transferring QA documentation systems such as product dossiers, procedures and validation protocols from the mother company in the Gulf.

According to the country director of Julphar UAE, the joint venture has been highly encouraged by Ethiopian market access and by the investment policy of the government. Accordingly, Julphar has also earmarked an additional investment worth US$50 million to establish an insulin plant. To facilitate the expansion, the government of Ethiopia availed a plot of land for Julphar adjacent to its existing facility. This new investment is the first of its kind in Africa and it aims at making Ethiopia an insulin hub for the growing African insulin demand.[5] This move is heralding the beginning of advanced manufacturing of pharmaceuticals of biological origin in Ethiopia.

To achieve its vision, Julphar Ethiopia PLC is interested in launching new investment in additional plant to produce products like B-lactams and small-volume injectable products. The director reiterated the challenges the company has been facing, including lack of trained and skilled engineers to install and maintain pharmaceutical machineries and facilities and the unavailability of spare parts and consumable materials in the local market. To deal with these challenges, the company has assigned engineers and technicians from the mother company. This arrangement has helped with technology and skill transfer for Ethiopian engineers. To overcome the shortage of trained and skilled manpower in the pharmaceutical industry, the company has made arrangements with local universities for the provision of on-the-job training within its facility and abroad in its mother company. Accordingly, a team of selected students from different universities were fully funded by the company for their stay in Julphar UAE to acquire knowledge and skill in the pharmaceuticals manufacturing sector.[6] From the foregoing it is apparent that integrating health and industry polices is highly beneficial for industrial development, since it can attract and make good use of joint ventures.

Socio-economic policies and the investment environment

The last section referred to the Ethiopian government's incentives for local industry. This section explores those industrial and socio-economic

policies in more depth. The Ethiopian government's industrial policies are developmental in nature, and pharmaceuticals are a key aspect of that broader approach. Consequently, the current investment climate of the country is considered propitious, since the country has several competitive advantages. Ethiopia has sizeable young and educated, trainable human resource and a large number of inexpensive labourers; rapidly developing green energy, as well as modest transportation infrastructure and trade logistics; and duty-free, quota-free access to the US and EU markets under the African Growth and Opportunities Act (Assefa et al., 2013).

Both the National Health Policy (NHP) (TGE, 1993a) and the National Drug Policy (NDP) (TGE, 1993b) emphasize the importance of local pharmaceutical production. The NHP states: 'Availability of drugs, supplies and equipment shall be assured by encouraging national production capability of drugs, vaccines, supplies and equipment by giving appropriate incentives to firms which are engaged in manufacture, research and development' (TGE, 1993a). One of the objectives of the NDP also specifies: 'To develop a domestic drug manufacturing capacity and gradual supply to the export market' (TGE, 1993b). Given the significant headway Ethiopia has made in availing access to PHC for its people, and given the country's ambitious local pharmaceutical manufacturing plans, the NDP is currently being revised to lead GTP II and GTP III.

The regulatory body previously known as DACA was restructured (with greater mandates including improved regulation, and setting standards in health care facilities as well manufacturing companies) and re-established as the Food, Medicine and Healthcare Administration Control Authority (FMHACA) by Proclamation, and has set standards for manufacturing facilities, among others (FDRE, 2009). Even though the primary responsibility of FMHACA is to regulate and control medicines, it has been building the capacity of the local manufacturers in GMP in collaboration with the WHO and the United States Agency for International Development (USAID) programme 'Promoting the Quality of Medicines' and United States Pharmacopeial Convention (PQM/USP).

The other sectoral polices that Ethiopia has put in place that in one way or another have contributed to the overall socio-economic developments (including the local pharmaceutical industry) are trade policies (focusing on business transactions such as the pharmaceutical supply chain), industrial policies (focusing on fostering manufacturing and technology transfer) and investment and labour policies. Since the implementation of the 1991 Trade Policy, Ethiopia has made significant

progress in opening up its economy and notable improvements have been recorded in its international trade.

Industry Policies

Ethiopia's Industry Policy dates from August 2001 and is designed within the framework of a free market economy. The key principles of the strategy include recognition of the role the private sector as an engine of industrial development and facilitation by the government towards that end; an agricultural development-led industrialization strategy; and ultimately export-led industrialization. It focuses on labour-intensive industries and aims to coordinate foreign and domestic investment.

Local pharmaceutical production in developing countries has always been a debatable issue. On one hand, there are opinions that argue against local pharmaceutical production for lack of comparative advantage, including absence of GMP and inadequate drug regulatory systems. These critics are also concerned with the immediate and long-term threats posed by low-quality medicines manufactured by African countries. People on the other side of the debate consider essential medicines as strategic commodities and seek to foster self-reliance and hence local production (Bate, 2008). The Ethiopian industry policy fosters the latter approach.

The investment policy within Ethiopia's industrial policy framework encourages the private sector to invest in almost all areas of economy. The policy does not impose local content, technology transfer (although encouraged) or export performance requirements on foreign investments. Export-oriented sectors receive long-term credit with low interest, export incentives, customs duty privileges and provision of land at competitive rents. The Development Bank of Ethiopia 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. Investors in the manufacturing sector will have customs duty privileges for capital goods and construction materials necessary for the investment, spare parts whose value is not greater than 15% of the total value of the capital goods and tax holiday privileges between two and seven years. There are no restrictions on repatriation of earnings, capital, fees or royalties (EIC, 2014).

Recognizing the role of the private sector in the economy, the government of Ethiopia revised its investment law at least three times between 1992 and 2012. The revisions rendered investment incentives more transparent, attractive and competitive. Major positive changes regarding

foreign investments have also been introduced through Investment Proclamation No.769/2012 and Regulation No. 270/2012, which detail the tax incentives and duty-free privileges for investors.

In general, there are a number of reasons for potential investors to consider Ethiopia as a desirable location for pharmaceutical investment, including factors such as investor-friendly policies, conducive macroeconomic policies and stable foreign exchange rates, a sizeable local market, access to the markets of several African countries through COMESA, preferential trade treatment to the EU, ACP-EU, a favourable export market under the US Generalized System of Preference, abundant and inexpensive skilled and trainable workforce, strategic location with proximity to the lucrative markets of the Middle East, Europe and Asia and attractive incentive packages for investment.

Ethiopia is a member of the World Bank–affiliated Multilateral Investment Guarantee Agency, which gives foreign investors guarantees against non-commercial risks. Ethiopia is a signatory to several bilateral and multilateral investment promotion and protection treaties. Ethiopia has also signed the World Bank Treaty on 'The Convention on Settlement of Investment Disputes between States and Nationals of other States'.

The country's current labour policy is based on Labour Proclamation No. 377/2003 which calls for workers and employers to comply with basic principles of rights and obligations, through co-operative efforts (FDRE, 2004) in conformity with international conventions and other legal commitments to which Ethiopia is a party. Abundance of inexpensive and disciplined labour together with the introduction of the revised labour proclamation is believed to contribute positively towards competition in the industry and other sectors.

Science and technology policies

One of the key indicators of the socio-economic development and technological progress of a country is the contribution of the industrial sector to the economy. The Ethiopian government has recognized that science and technology are the major driving forces behind industrialization. It is taking steps to foster the growth of science, technology and innovation (STI), including the promotion of indigenous knowledge to tackle the country's needs (see also Chapter 7).

The Ministry of Science and Technology (MoST) recently published a document called the 'Green Paper on Science, Technology and Innovation Policy of Ethiopia-Building Competitiveness through Innovation' (MoST, 2012). In this document the pharmaceutical industry has not only been

listed as one of the high-level technology industries but also identified as an area in which efforts will be geared to building domestic technological capability. According to the paper, the pharmaceutical industry is among the National Priority Technology Capability Programmes of Ethiopia.

The national science and technology policy of the country dates from 1993. Although this policy served to provide general directions to guide scientific and technological activities, it was not followed by implementation strategies and programmes aimed at achieving the envisaged policy objectives. It was therefore revised in 2012. The revised policy directives and strategies indicate, among other things, that at least 1.5% of the country's gross national product (GNP) will be allocated annually to support and sustain the different STI activities in all sectors. A centralized innovation fund for R&D activities will be created through a contribution of 1% of the annual profit of all productive and service sectors, and banking and financial institutions will be encouraged through various legal and incentive mechanisms to improve their role of fostering technological innovation (MoST, 2013).

The policy landscape of Ethiopia entered a new phase when the Ethiopian government launched the GTP I (2010/11–2014/15). As the highest national policy framework, the GTP governs Ethiopia's developmental policies, budgets and government organizations, as well as actions of development partners and foreign investors. Among other things, the GTP is tuned to expand infrastructure significantly and increase the role of the manufacturing industry in employment and economic development. The GTP identifies the pharmaceutical industry as a priority sector. 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. The market share of local pharmaceutical producers is targeted to reach 50% by 2015 (MoFED, 2010).

For this set of objectives, regulatory support is essential. As part of the GTP, the FMHACA has been implementing a five-year project which states: 'The main aim of the pharmaceutical industry is substituting essential medicines imported to the country and setting the ground for export of local products by building the capacity of existing pharmaceutical and medical device manufacturers and establishing new ones'. Notwithstanding the responsibilities vested in the authority by Proclamation 661/2009 to ensure the safety, efficacy and quality of

products, the FMHACA together with stakeholders has been exerting efforts to build the technical capacity of local manufacturers.

The FMHACA's ambitious project envisioned 17 local GMP-certified pharmaceutical manufacturers by the end of 2015; at least five pharmaceutical manufacturers pre-qualified by WHO by 2015; seven newly established pharmaceutical manufacturers by the end of 2015; and two newly established pharmaceutical raw materials manufacturers and two newly established traditional medicines manufacturers (FMHCA, 2011). To build the capacities of the local pharmaceutical manufacturers, FMHACA also prepared the Medicine Manufacturing Establishment Directive, and it has made it mandatory for any person engaging in manufacturing medicines to obtain a Certificate of Competence from the Authority (FMHCA, 2013a).

FMHACA, working together with the WHO and USP/PQM and local manufacturers, prepared a five-year GMP Road Map (2013–18). It has assessed and mapped the GMP status of the local manufactures and categorized them into three GMP compliance levels (Level I with up to 50% GMP compliance; Level II with 60–80% GMP compliance; and, Level III with more than 80% GMP compliance). As per their levels, FMHCA and its partners are building the capacity of the local manufacturers for them to be GMP compliant by 2018 (FMHACA, 2013b).

A major scientific and technological project is the establishment of a Regional Bioequivalence Centre (RBEC) in Ethiopia. This presents yet another major opportunity for upgrading. To serve as substitutes, generic products should be bioequivalent or therapeutically equivalent to the originator/comparator products. Consequently, bioequivalence becomes even more crucial for generic products such as medicines for critical use (e.g. anti-retroviral, anti-tubercular), medicines with a narrow margin of safety (e.g. cardiovascular drugs), sustained or modified-release products and medicines with inherent solubility and permeability problems.

To obtain marketing authorization in different countries, manufacturers have to get their products approved and registered by the national drug registration authorities. Under normal circumstances, manufacturers are expected to present product pre-qualification for bioequivalence. However, local regulatory authorities could not enforce bioequivalence testing thus far, because the service fees charged by international contract research organizations are not affordable to the local manufacturers. Hence, the absence of a local bioequivalence testing facility in the subregion has been a big hurdle in the enforcement of the bioequivalence testing requirement of the generic medicines.

To assist local manufacturers, the Regional Bioequivalence Centre Sh. Co. (RBEC) was recently established in Addis Ababa as a public-private partnership. GIZ provided the basic instruments and equipment for the bio-analytic laboratory and technical training to key staff. Addis Ababa University made available laboratory space and furnished offices. Two pharmaceutical manufacturing companies in Kenya (Universal Corporation Ltd and Skylight Chemicals Ltd), one local manufacturer in Ethiopia (Addis Pharmaceutical Factory PLC) and one generic manufacturer in Germany made modest financial contributions to cover the running costs of the Centre until it acquires the WHO prequalification and thereby begins to generate its own revenue. The Centre has a clinical partner, Armauer Hanssen Research Institute, where the clinical studies are being conducted.

Since RBEC is the first of its kind in the Sub-Saharan region (except for South Africa), the centre anticipates an overwhelming demand for BE studies. The Centre will also offer services related to assessment of quality of medicines. In the long run the RBEC would also play key role in clinical trials as well as in pharmaceutical research and development activities aiming at product development and drug discoveries.

The other important entity that has been recently (2013) established by Proclamation is the Food, Beverage and Pharmaceuticals Industry Development Institute, which has the objective of transforming the food, beverage and pharmaceutical industries through accelerated technological development and transfer. Currently, the Institute is preparing a 10-year strategic plan for the development of the pharmaceutical industry.

Conclusion: future pathways and challenges

Ethiopia is making substantial headway in all areas of socio-economic development. It is in the midst of a sustained growth surge that is becoming increasingly broad-based, building on major improvements in educational attainment, improved health outcomes and improved infrastructure capacity (power, transportation and telecommunications). The GTP sets ambitious targets for further improvements in these areas, together with significant reforms aiming to improve local manufacturing capacities (including pharmaceuticals) and trade logistics by rolling out various export-oriented economic programmes (Assefa et al., 2013).

Despite all these achievements, however, there are still outstanding issues to be addressed, such as the low production capacity and

overwhelming dependence on importation of medicines; shortage of qualified management and technical personnel; and inadequate continuing professional development for practising professionals.

Asked about challenges and limitations faced by the local manufacturers, the plant technical manager of EAP reiterated the following: limited working capital of the factories; conflicts of interest with the suppliers of raw materials in India and China (as they are also producers of medicines, so they charge higher prices); paying VAT that is not reimbursed; shortage of foreign currency and hence longer lead time in foreign purchase resulting in price fluctuation and ultimately purchase reorders; small bulk orders with no economy of scale; low manufacturing capacity and hence high production cost; and limited capacity for troubleshooting and management.

Finally, based upon the assessment in this chapter, we suggest the following ways forward.

Strengthen local production: Although some progress has been made over the past few years, the development and local production of medicines is still marginal. Consequently, Ethiopia is relying heavily on imports for medicines and medical supplies. It is therefore crucial to build and strengthen national capacity to manufacture affordable, safe, efficacious, high-quality generic essential medicines which can significantly contribute to the simultaneous achievement of public health and industrial development objectives (MoST, 2012).

Competitive and efficient local pharmaceutical production should be promoted by strengthening local producers' capacity to meet WHO-GMP and WHO prequalification standards, promoting regional and international collaborations and facilitate technology transfer; fostering pooled procurement of raw materials and other inputs.

Establish raw material manufacturing plants: The fact that most raw materials have to be imported has made the local pharmaceutical manufacturers less competitive against imported generic products from Asia. Therefore, looking for alternative local sources of some of the excipients and APIs is one important strategy to improve the competitiveness of the local manufacturers (Gebre-Mariam and Schmidt, 1996, 1998; Gebre-Mariam et al., 1996) (see also Chapter 7). The government should foster such an endeavour.

Build human capital: The availability of adequate, appropriately trained and well-motivated personnel endowed with requisite knowledge, skills and attitude to provide effective and efficient services is of paramount importance for the development of the pharmaceutical industry. Some manufacturers report that local personnel are not adequately trained

to carry out pharmaceutical production and business development. To rectify this, formal pharmaceutical training should be based on the needs of the industry. Strategies should be devised and implemented to update professionals who are in service.

Enhance research and development: R&D on raw materials (APIs and excipients) should be fostered and long-term strategy for their local production should be planned and implemented. Research on product development to make local products competitive should be enhanced. More favourable conditions should be created for the introduction of appropriate technology and know-how to vitalize the industry. To develop the raw material base for the pharmaceutical industry and to enhance the growth of a viable domestic pharmaceutical industry and manufacturing capacities, the government should extend its support to the private sector engaged in raw materials production. Research collaboration between universities, research institutes and local manufacturers should be promoted.

Notes

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1. http://effortinvestments.com/new/index.php/officer, accessed 10 December 2014.
2. http://www.rttnews.com/1687014/cadila-pharma-s-ethiopian-jv-receives-cgmp-certificate.aspx, accessed 10 December 2014.
3. This facility used to belong to 'Bethelehem Pharmaceuticals PLC'. It was foreclosed during the crisis period, the Ethiopian Development Bank sold it out to Julphar, and the latter renovated the plant to meet GMP standards.
4. http://www.julphar.net.
5. http://www.pharmaceutical-technology.com/projects/julphar-manufacturing-facility-addis-ababa/.
6. http://allafrica.com/stories/201501190895.html Ethiopia: Julphar to Build Africa's Largest Injectable Medicine Plant.


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5

South-South Collaboration in Pharmaceuticals: Manufacturing Anti-retroviral Medicines in Mozambique

Giuliano Russo and Lícia de Oliveira

Introduction

Back in 2003, Brazil's and Mozambique's presidents, Luiz Inácio Lula da Silva and Joaquim Chissano, agreed to set up the first pharmaceutical factory in Mozambique, to be entirely owned by the national government. The project – widely known as the Brazil-Mozambican anti-retroviral factory because of its commitment to produce AIDS drugs – still represents the single most expensive and eye-catching project of Brazil's South-South cooperation programme in the health sector.

Part I of this book examines the complexities of African pharmaceutical markets and some practical aspects of setting up and developing pharmaceutical industries in the subcontinent. This chapter's contribution is to present the experience of establishing a pharmaceutical factory in Mozambique through industrial and official development collaboration between two national governments. Uniquely, this is a case study of an attempt to kick-start, through an innovative South-South partnership, pharmaceutical production in a country that previously had none. This chapter therefore discusses an experience sharply distinct from most of the countries' experiences discussed in the book, since they have pharmaceutical industries dating back to the 1950s, and with substantial numbers of firms in their industries.

This chapter draws on multiple sources such as official technical cooperation documents and the published literature on the subject, as well

as on the authors' direct experience of the Mozambican pharmaceutical markets, of Brazil's development cooperation programme and of the factory's implementation project. It aims chiefly to discuss whether foreign lessons about the development of the pharmaceutical sectors can be learned for African countries, and the extent to which similar experiences of industrialization and health policy development can be exported from Brazil to the complex African environment. Two main contributions to the making medicines in Africa debate emerge from the analysis of this case study: one is the absolutely key role of the innovative South-South collaboration to the nascent pharmaceutical industry in Mozambique in terms of both financial subsidy and technical support. The other is that, while the technical collaboration with Brazil remains highly positive, the link to the market in Mozambique seems to have been a major problem, as the health-industry link so fundamental in the Brazilian pharmaceutical development experience seems to have worked less well here, at least in the early years of the project.

After a description of the evolution of the cooperation project and of the collaboration between the two countries to set up a factory in Mozambique, this chapter presents details of the technical investment needed to start such a complex enterprise in a country with a less-than-ideal business environment. The crucial link between the factory and the local as well as regional pharmaceutical markets is then analysed. The chapter ends with a discussion of the issues still hampering the development of the factory in Mozambique, and of the insight to be gained from such an experience, including insights for those countries in the subcontinent with a rather more established pharmaceutical industry.

The Brazil-supported pharmaceutical factory in Mozambique

Official reports show that back in 2003, the initiative to set up a pharmaceutical factory in Mozambique originally had the following stated objectives. It aimed to secure the supply of anti-retroviral medicines (ARVs) for HIV/AIDS treatment in the country, and to jump-start pharmaceutical generics' manufacturing in Mozambique, enabling the fulfilment of the objectives of the national primary care and pharmaceutical policies. It also aimed to reduce the country's dependence on pharmaceutical donations and imports and to contribute to the creation of local capacity for pharmaceutical production and industrial management (de Oliveira, 2013).

Following an informal agreement between the two presidents, diplomatic and international cooperation efforts were stepped up from both the Brazilian and Mozambican governments to iron out the details of the project from 2003 onwards. Figure 5.1 summarizes the long timeline of the project from its inception to 2014.

The Oswaldo Cruz Foundation (Fiocruz) – Brazil's leading public health institution (Roa and Baptista e Silva, 2015) – was appointed in 2004 to conduct the factory's feasibility study. This was completed and approved three years later. *Farmanguinhos* – Fiocruz's pharmaceutical arm, and a key instrumental actor in Brazil's national pharmaceutical policy – was charged with the pharmaceutical technological transfer, technical training and the wider project implementation. These two institutions are directly linked to the Brazilian Ministry of Health and have been credited with playing a pivotal role in the development of domestic

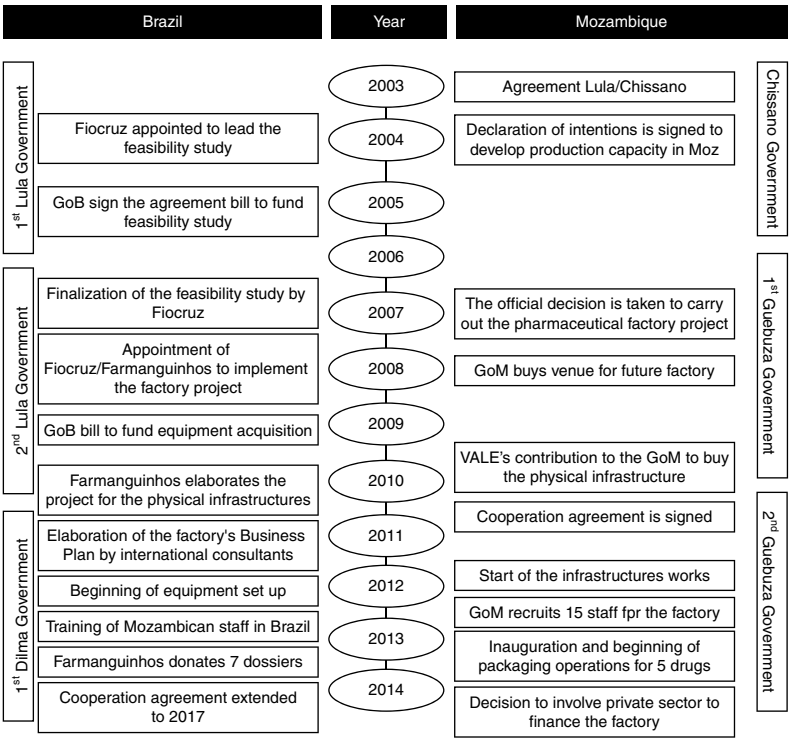

Figure 5.1 Timelines for the implementation of the factory project

Source: drawn by the authors.

pharmaceutical regulation as well as of the pharmaceutical market in Brazil (Flynn, 2008). (Their role is discussed further in Chapter 9). These institutions' early involvement in the factory project in Mozambique was considered instrumental in seeking to replicate that experience back home.

Meanwhile, in the field, a number of cooperation agreements and spending authorizations had to be sought by both the Mozambican and Brazilian sides, as the project was to be funded through multiple sources. The process was lengthy. VALE S.A. – Brazil's largest mining company with ongoing operations in Mozambique – was also recruited by President Lula to support the national government in financing the factory's infrastructure works, which were only finalized in 2012. In the same year, the majority of the pharmaceutical equipment was procured in the international market, donated by *Farmanguinhos*, and shipped to the future factory venue. The government of Mozambique recruited the first 15 local staff in the same year, and *Farmanguinhos* donated the pharmaceutical production technology files and provided the technical assistance required to start production of Nevirapine, Lamivudine, Captopril and Hydrochlorothiazide in 2013 (Russo et al., 2014).

In 2008, the enterprise was officially registered as Mozambique Pharmaceuticals Ltd (*Sociedade Moçambicana de Medicamentos,* SMM), as it planned to extend production beyond anti-retroviral drugs. SMM is owned by the government of Mozambique's State Assets Management Institute (IGEPE), which appoints the executive director and chair of its administrative board from candidates put forward by the Mozambican Ministry of Health (MISAU). In addition to the short-term Brazilian technical assistance necessary for training and setting up operations, four full-time Brazilian consultants in pharmaceutical manufacturing, quality assurance, technical engineering and maintenance have been appointed for the coming years, with the objective of steering the factory towards sustainable production and WHO Quality Certification (Russo et al., 2014).

According to official documents (de Oliveira, 2012), the government of Brazil (GoB) originally agreed to take responsibility for the project's staff training, for procuring equipment and raw materials, for providing technical assistance and for designing the factory and managing the project. Meanwhile the government of Mozambique (GoM) was to be responsible for purchasing the physical infrastructure for the factory, for undertaking rehabilitation works, for funding the factory's recurrent expenditures and for buying the bulk of the factory's pharmaceutical output. The first three-year cooperation agreement was signed in

2011. Extensions of the original 2011 agreement were to be negotiated every three years through official Complementary Agreements (*Ajustes complementares*).

In 2014, procurement contracts were signed by MISAU for the acquisition of locally produced hospital serum bags and imported but locally packaged generic drugs from the factory. Although disruptions were experienced in 2014 in the production lines, a fresh cooperation agreement was signed the same year to extend Brazil's support to the factory until 2017. Towards the end of the same year, following a visit of Mozambican officials to the Brazilian Ministry of Health and Ministry of Foreign Trade, Industry and Development, a decision was taken by IGEPE – the institution in responsible for the factory – to seek capital to finance the factory from the Mozambican banking sector, and at the time of writing this seems to be the path identified for the development of the project in the near future (Figure 5.1). In the process of developing the factory, more than ten years and three presidential terms have elapsed both in Mozambique and Brazil, and administrative, political and foreign affairs details have had to be ironed out across two countries and four different political administrations.

The new pharmaceutical factory is located in Matola City within Mozambique's capital's metropolitan outskirts, on a 20,000-square-metres allotment close to the capital's commercial port and to the South African border. The factory currently engages both in secondary and tertiary pharmaceutical production. That is, it produces its own formulations from imported active pharmaceutical ingredients (APIs) and raw materials, as well as packing imported finished formulations. Twenty-one generic drugs are planned to be produced in the next two years, including ARVs (Nevirapine, Zidovudine and Lamivudine combinations), hypertension drugs (Captopryl and Propanolol) and a list of antibiotics, antimycotics and anti-diabetic compounds specifically requested by the MISAU as currently in wide use in the country's public National Health Service (NHS). Such a list can be expanded on demand to include generic drugs to meet the WHO requirements for ARV treatment and generic formulation to be sold by third parties. All the formulations (pharmaceutical dossiers) belong to *Farmanguinhos* and are transferred for free to MISAU. A laboratory for the control of medicine quality has been already established, equipped to test drugs for efficacy and safety. When fully functional, the laboratory will be capable of providing information on the quality of all the drugs imported into the country and of contributing to the development of new drug testing methodologies.

The technical investment

So far the factory's overall set-up costs have been estimated at US$ 39.6 million (de Oliveira, 2013). Capital investment (land, infrastructures, machinery and implementation of production lines) amounted to approximately 46.5% of overall expenditures and pledged funds, while technological transfers and technical assistance represented a substantial cost item (13.0%), including the value of compounds dossiers for the 21 generic drugs, as well as personnel costs for the expatriate staff who helped setting up the operations. Running costs for the first year (API procurement, training and maintenance) represented 23.7% of present and future expenditures (Table 5. 1).

Although the Brazilian government funded the majority of the project's set up costs (62.7%), the government of Mozambique contributed through buying up land and some existing infrastructure for the establishment of the factory, while a donation from VALE, a Brazilian mining company operating in Mozambique, supported personnel and infrastructure expenditures (Table 5.1).

As Brazil still lacks a comprehensive legal framework to provide funds and procure goods for its international cooperation programme (Cabral, Russo and Weinstock, 2014), funds for the project had to be channelled through the implementing public institutions linked to the Brazilian Ministry of Health – Fiocruz, Fiotec and Farmanguinhos – and through the Brazilian Development Cooperation Agency (ABC), linked to the Ministry of Foreign Affairs (*Itamaraty*). On the Mozambican side, the costly acquisition of the infrastructure from a former hospital serum bags factory (*Final Farmacêutica)* was directly managed by the government, while IGEPE funded the capital rehabilitation and maintenance costs. The donation to the venture by VALE S.A. was expressly solicited by the government of Brazil and channelled through the government of Mozambique Treasury to set up the factory's early production lines and pay for some Brazilian personnel as part of the running costs. With the extension of the cooperation agreement to 2017, both governments agreed to further the funding of the project.

Although according to the business plan the factory would require 88 full-time staff to manufacture at full capacity (24 for direct production, 4 for quality-control-related services, and 18 for management and administration), at the time of writing only 55 had been recruited, and a team of 8 Brazilian technical assistants based in Maputo were still providing key management and technical expertise for the factory's operations. Given the limited development of industrial capabilities in Mozambique,

Table 5.1 Estimated cost of setting up the factory (current US$ million)

Source of funding	Implementing agencies	Activities	Type of expenditures	Spending (to 2013)	Pledged (2017)	Total
Government of Brazil	Fiotec/Fiocruz/MoH of Brazil	Transfer of Technologies; Technical assistance	Technology transfer	6.3	6.7	13.0
	Farmanguinhos/ Fiocruz/MoH of Brazil	Equipment	Capital	4.0	1.0	5.0
		Procurement of raw products	Running costs	1.0	2.0	3.0
	Brazilian Cooperation Agency / Ministry of Foreign Relations (ABC/Itamaraty)	Capacity building	Running costs	0.2	0.5	0.7
Government of Mozambique	GoM	Purchase of land and infrastructure from Final Farmacêutica Lda	Capital	8.0		8.0
	IGEPE	Maintenance of infrastructures	Running costs	2.0	2.0	4.0
		Development of existing infrastructure	Capital	1.4		1.4
VALE S.A.	Support to the GoM for the project	Setting up production lines	Capital	4.0		4.0
	Support to the GoM for personnel expenses	Payment of Brazilian technical director for 4 years	Running costs	0.250*	0.250*	0.5*
Total				**27.2**	**12.5**	**39.6**

Note: *SMM Accounting Report SMM.

Sources: Respective implementing agencies, unless otherwise stated.

technical personnel as well as senior managers for the new factory had to be either summoned from the Brazilian public sector or recruited in the local market and provided for extra training abroad.

In terms of technological transfer, until March 2015, *Farmanguinhos* had donated for free 10 out of 21 technological dossiers for the production of specific pharmaceuticals, to include results from pharmaceutical equivalence tests, quality control procedures for APIs and other ingredients, manufacturing process specifications and test failure reports. The next steps for technological production are still under way and include:

- adaptation of the Brazilian dossiers to the MISAU's specifications;
- training local personnel to the local production of the pharmaceutical dossier;
- assisting production for the drugs' first three pilot batches, following production as well as commercialization of the products;
- establishing a pharmacovigilance system.

In terms of pharmaceutical production equipment, 18 high-tech pieces have been procured internationally by *Fiocruz/Farmanguinhos* and donated by Brazilian cooperation. This included main production line equipment such as compression, coating and blender machines, packing equipment – blisters, labelling and capping machines – as well as quality and in-process control equipment – tablets' hardness and dissolution testers, chromatography and centrifuges. Given the total absence of up-to-date manufacturing machinery in the infrastructures inherited from *Final Farmacêutica*, basic non-specific equipment such as water purification machines also had to be brought in.

The machines presently installed in the factory in Maputo have an estimated market value of US$4 million, with an additional list of equipment worth approximately US$1 million to be procured and bought by 2017. All the machines were purchased by *Farmanguinhos/Fiocruz* through international tenders and donated to the government of Mozambique, including installation services and personnel training for its use and maintenance. SMM technical personnel were all trained in Brazil on the use of the specific machines, and on-site ongoing technical assistance is provided for specific manufacturing.

The company and the market

This section details a key – and often overlooked – aspect of the Brazil-Mozambique collaboration to produce pharmaceuticals: the link to

the market. A feasibility study was conducted in 2007 looking at the likely costs of setting up the factory in Maputo and its specific production capacity for ARVs, but it failed to analyse the market conditions in Mozambique and in the wider Sub-Saharan region (Fiotec/Fiocruz, 2007).

Mozambique's pharmaceutical policy in the 1970s and 1980s focussed on procuring and using generic drugs, to extract the best possible value from its drugs budget (Barker, 1983). However, as Mozambique became after Independence one of the world's largest recipients of health-aid funds, international finance for drugs began to be handled, first through an externally managed Drugs Common Fund (Pavignani and Durão, 1999), and subsequently through an MoH-managed Sector Wide Approach common fund agreement (PROSAUDE). Currently, with the global push for AIDS fight and the introduction of anti-retroviral treatment (ART) in 2003, the country is enjoying a considerable injection of AIDS funds, with anti-retroviral drugs procured in the international market by organizations such as the Global Fund, the World Bank and USAID.

In 2012, the national drugs market in Mozambique was estimated to be worth approximately US$140 million in terms of the value of drugs imported (COWI, 2012), which represented a drugs expenditure of US$5.55 per capita. Eighty-five per cent of the total market value was represented by public sector imports, mostly funded by external funds and donations, some of them managed by the local Ministry of Health through the sector budget support fund, PROSAUDE (CMAM, 2011). In recent years public drugs expenditures have gone from US$78 million in 2004 to US$122 million in 2012 (Table 5.2), the increase being driven by in-kind AIDS drugs donations that rose from the original US$4 million to the current US$49 million in eight years (COWI, 2012).

As shown in Table 5.2, AIDS drugs represent the largest single item of the national public pharmaceutical expenditures, and enter the country exclusively as in-kind donations procured and managed directly by foreign organizations. Public funds pay for roughly a quarter of the overall public sector drug expenditures, with North-America-based organizations (USAID, Supply Management Systems and the Clinton Health Access Initiative) contributing to purchase 67% of all the public sector drugs procured in the country. In this respect, the local funding environment appears still to represent a critical limitation for pharmaceutical production in Mozambique. Given the typical consumer's limited ability to pay, and the relatively small size of the local private

Table 5.2 Public sector drug import value, by source and type of health programme (2012 US$)

Health programme and associated drugs	Internal and external funds managed by MISAU (drug pool and state budget)	In-kind donations	Total
Hospital drugs	11,861,471	1,200,883	13,062,354
Primary care drug kits	8,708,824	0	8,708,824
Community health	3,870,588	7,217,900	11,088,488
STD and HIV-SIDA	0	48,750,977	48,750,977
TB	0	249,550	249,550
Malaria	0	24,124,599	24,124,599
Blood banks	967,647	0	967,647
Oral health	290,294	0	290,294
Surgical supplies	10,111,912	0	10,111,912
Laboratory supplies	2,497,000	0	2,497,000
Imaging devices and supplies	1,741,765	0	1,741,765
Total	40,049,500	81,543,908	121,593,408

Source: CMAM, 2012.

sector, selling to the public sector is obviously the only way for local producers to go to scale and access a local market worth in excess of US$140 million. However, the lack of flexibility of the international drugs financing environment is pointed to by many as a key limiting factor for the development of local production of pharmaceuticals in the country; even if locally produced drugs were made available at competitive prices, the manner in which external funds for AIDS drugs are currently regulated would stand in the way of procuring, or offering preferential procurement terms to buy, locally produced drugs. As a side effect, free internationally procured ARVs also end up crowding out the local private sector, which is traditionally a key customer for locally produced goods (Herzer and Grimm, 2012; Rajan and Subramanian, 2011).

Little consolidated data exist about the private pharmaceutical market in Mozambique. Some estimates put it at approximately US$20 million, calculated on the basis of the drugs value declared on the import documents submitted to the pharmaceutical department in 2012 (COWI, 2012). Although 54 private importers are officially registered

in Mozambique, a 2010 study found that the private sector is highly concentrated, with the four largest firms handling more than 50% of the drugs imported (Russo and McPake, 2010).

As for the regional market, according to some industry pundits (IMS, 2012), with its 10.6% yearly growth rate by volume, Africa is the world's fastest-growing pharmaceutical market after Asia, and is estimated to reach a value of US$30 billion next year. With specific reference to the ARVs market in the Southern African Development Community, the SMM business plan estimated in 2012 that a sufficiently homogeneous regional demand for ARVs existed for SMM to serve. Previous studies of the regional market (COWI, 2012) suggested that across the neighbouring countries of Mozambique, Tanzania, Zambia and Zimbabwe, AIDS treatment lines were relatively similar and reliant on standard Lamivudine-Zidovudine-Nevirapine combinations. This would have implied access to sizeable market for HIV/AIDS drugs of approximately 6 million treatment doses per year across the four countries. However, there is little recognition in SMM's viability study and subsequent business plans of the complexity of those markets, of the possible regional and international competition to be faced, as well as of their regulation and of the role played by national governments in supporting the local industry.

Currently, SMM's business plan expects to sell its products in the Mozambican market in the short term, particularly to the NHS. It aims to sell into the regional pharmaceutical market only in the medium term, once the required certifications are obtained to allow the firm to compete in international tenders (COWI, 2012; SMM and Farmanguinhos, 2013). SMM unit prices, listed in Table 5.3, reflect the initial production costs calculated on the basis of APIs imported from Brazil. As production goes to scale and APIs are bought in from the global competitive market, SMM is projecting lower selling prices reflecting the lower API costs. SMM also enjoys most of the standard preferential policy interventions already adopted in the East Africa Community: an ad hoc tax exemption regulation on imported APIs and other manufacturing product and a preferential buying regime from the government, according to which, when procuring drugs for the National Health care Service, the National Drugs Acquisition Agency is required to give preference to locally produced drugs as long they are no more than 15% more expensive than the products of their international competitors.

The prices listed in Table 5.3 represent SMM's factory gate selling prices for public procurement; a comparison with the Management Science for Health international median reference prices for procurement is

also shown. It is worth noting that although in the same price range, SMM prices for ARVs, particularly those involving Lamivudine, appear to compare less favourably with international reference prices than do those for the other generic drugs (Table 5.3).

The factory's business plan predicted wholesale selling price levels at which the factory would break even, on the basis of the cost structure model used for the production of ARVs in Brazil's state pharmaceutical factories adapted to the Mozambican context (Pinheiro et al., 2006). Although SMM drugs face higher costs because of Mozambique's burdensome import duties on non-API production materials, as well as high maintenance costs, according to the factory's business plan these will be offset by lower capital costs and smaller operating margins, typical of a state-owned company (MacDonald and Yamey, 2001).

Table 5.3 Unit price for selected SMM drugs (US$)

Product	Package (Units)	SMM's selling price to the NHS (US$)	MSH* median price (US$)
Amoxicillin caps 500 mg cx c/500	500	0.0502	0.0313
Glibenclamide tab 5 mg cx c/500	500	0.0035	0.0042
Hydrochlorothiazide tab 50 mg cx c/500	500	0.0047	0.0050
Metronidazole tab 250 mg cx c/1000	1000	0.0116	0.0061
Prednisone tab 5 mg cx c/500	500	0.0077	0.0108
Lamivudine 150 mg 60 tab – 3TC	60	0.1152	0.0508
Lamivudine 150 + Zidovudine 300 mg 60 tab	60	0.4354	0.1714
Lamivudine 150 mg + Zidovudine 300 mg + Nevirapine 200 mg	60	0.2754	0.1654
Lamivudine 30 mg + Zidovudine 60 mg + Nevirapine 50 mg	60	0.1015	0.0726
Nevirapine 200 mg 60 tab – AD	60	0.0849	0.0611

Note: *Management Science for Health Drug Price Database.

Source: SMM.

According to the factory's business plan, SMM furthermore will be able to sell its products at prices comparable to those from the international market, thanks to savings in the initial investment in infrastructures and equipment, donated by the Brazilian cooperation, and in national transport charges and taxes, which are particularly favourable to business in Mozambique, since the original tax rate on chemical products was scrapped. In comparison to the typical cost structure for ARVs (Pinheiro et al., 2006), SMM's production costs will be largely driven by active pharmaceutical ingredients' (APIs) import prices, and less by taxes, profit margins, research and development and local production mark-ups (SMM and Farmanguinhos, 2013).

The South–South collaboration in context

'Emerging donors' and 'South-South cooperation' are terms usually referring to providers of development assistance and forms of cooperation that have recently become prominent in the international aid architecture, due to a recent expansion in resources allocated to development cooperation with poor countries (Manning, 2006). Thanks to their recent economic growth, emerging economies like China, India and Brazil are boosting their cooperation programmes (Brautigam, 2009; Cabral, 2010), and according to one estimate, the volume of aid from emerging donors reached between US$9.5 billion and US$12 billion in 2006, corresponding approximately to 8–10% of total aid flows. The recent literature on the subjects shows that some common features among these emerging aid players are discernible. One of the most salient is the emphasis on horizontal (South-South) cooperation between developing countries and the principle of non-interference in the internal affairs of recipient countries. Related to this aspect, emerging donors tend to have no policy-related conditionality, such as standards of governance and macroeconomic requirements, and fewer procedural conditions, such as counterpart funding or separate bank accounts, relative to traditional donors. More controversially, there is a more evident and openly acknowledged association between commercial interests, geo-strategic objectives and development cooperation than is the case for traditional donors (Kragelund, 2008).

Brazil's overall cooperation programme is still relatively small, estimated to be worth between US$350 million and US$1 billion per year, with a substantial component of support to international organizations and humanitarian assistance and a smaller proportion directed to technical cooperation projects (IPEA, 2011). South-South relations play an

important part in Brazil's strategy of diversification of diplomatic and economic relations, and technical cooperation provides an expedient way of taking forward such an agenda. Brazil's South-South technical cooperation programme has as key features the emphasis on exchange of experiences between equal partners (or 'horizontal cooperation', as it is usually referred to), respect for the partner country's sovereignty and non-conditionality of support, with a dominant but not exclusive geographical focus on Latin American and Portuguese-speaking African countries and on the agriculture, education and health sectors (Cabral, Russo and Weinstock, 2014).

Government figures put the value of Brazilian technical health cooperation at approximately US$12 million between 2006 and 2009. However, recent independent reports estimated that Brazil spent between US$12 million and US$14 million in technical health cooperation projects in Portuguese-speaking African countries alone for the same period (Russo, Cabral and Ferrinho, 2013). Brazil's health-sector-specific characteristics and claimed principles suggest some important departures from the ways in which development cooperation has been traditionally practised. A key feature of Brazil's cooperation is that it is openly driven by foreign policy goals, and development cooperation is seen as instrumental in promoting Brazil's image and interests abroad. Brazil openly adopts the notion of 'health diplomacy' for its health projects (Roa and Baptista e Silva, 2015), implying that health development cooperation can be informed by international health objectives, following the recognition that national health problems need to be dealt with in the global health arena. Brazilian cooperation officials also dispute the use of the term 'aid' to define their work, as that would impose industrialised countries' 'world views, agendas and pre-defined objectives' (Buss, 2011). Instead, 'horizontal partnership' is Brazil's preferred terminology to indicate the wish to draw on principles of non-interference and mutual advantage. Brazilian projects are also claimed to promote 'structural cooperation in health', a concept defined by some as building local capacity for development (Buss, 2011). It begins from the premise that health cooperation should focus on integrating human resources for health and institutional development, developing local capacity to avoid dependency from foreign expertise and promoting internal collaboration between local health institutions to elaborate their own health system development agenda.

As for the relation between national business interests and cooperation goals, Brazilian cooperation in health openly claims to be inspired by the concept of the 'health-industrial complex for health development',

according to which individual countries need to invest in the national health care industry and R&D capacity if they want to develop their health systems (see also Chapter 9). Such an emphasis on self-sufficiency is also aimed at avoiding costly dependency on foreign health care technologies (Gadelha, 2006). This approach happens to be particularly relevant for the pharmaceutical and biotechnology business in Brazil, as, besides being worth approximately US$24.5 billion in 2012, these two sectors are considered to be instrumental in the implementation of the Brazilian Unified Healthcare System's objectives of free and equitable access to health care services (Gadelha et al., 2013). Brazil's position on HIV/AIDS drugs appears in line with its support for strong government involvement in the provision of health care services, underpinned by a constitutional framework that establishes a universal citizen right to health and places a duty of health care provision on the state. The growing roles of the Brazil's Ministry of Health research and training agency, *Fiocruz*, and its pharmaceutical arm, *Farmanguinhos*, influential government institutions behind the development of the ARV industry in Brazil as well as in the factory project in Mozambique, are exemplifications of the strength of this paradigm of state-led health development (see Chapter 9).

Local production of pharmaceuticals: issues raised by the case study

In contrast to the experiences described in other chapters, the Maputo factory story provides a case study of an attempt to kick-start, through an innovative South-South partnership, pharmaceutical production in a country that previously had none. Our narrative of development and implementation of the project has shown the key role of the innovative South-South collaboration for the nascent pharmaceutical industry in Mozambique in terms of both financial subsidy and technical support. However, while the technical collaboration with Brazil remains highly positive, the link to health markets in Mozambique seems to have been a major problem, as the health-industry link so fundamental in the Brazilian pharmaceutical development experience seems to have worked less well here, at least for these early years.

The experience of the Brazil-Mozambique collaboration details the challenges of starting up such a complex enterprise from scratch, in an environment often lacking the basic infrastructural pillars for industry development. Human resources were identified as the single most important bottleneck for SMM development. As the majority of the

staff recruited locally had to be sent for training abroad, some of those employed have been poached by competing businesses in wholesaling and retailing, and highly specialized positions in the factory are still covered by expatriate staff. Although personnel with middle-management skills should be already supplied by the local labour market, experienced executives with a track record of management in comparable industries are acutely lacking in Mozambique, given the country's relatively recent history of industrial development.

Mozambique's particular industrial environment was recognized as another factor hampering the development of the pharmaceutical factory. In comparison to other African countries with a more established industry, Mozambique seems to be lacking a critical mass of suppliers, products and services needed for the development of a competitive pharmaceutical business. All the primary products needed for Maputo factory's manufacturing are, up to now, imported from Brazil; all the basic maintenance and technical services are contracted to South African firms, and resorting to lower cost Indian and Chinese equipment has not been an option, given the limited equipment maintenance services provided by such suppliers in Mozambique.

Strengthening the government's current quality control of pharmaceutical manufacturing processes and final products is needed, as this was also reported to be a hurdle for the long-term development of pharmaceutical manufacturing in Mozambique. A lack of quality regulation *de facto* allows competitors to employ cheaper substandard machinery in pharmaceutical production and produce substandard – and, crucially, cheaper – generic products. The factory's case study shows that lack of effective quality regulation ends up benefitting those importers of non-branded generics for whom an ability to cut costs and offer wildly discounted generics represents the core of their market strategy in Mozambique.

This experience, however, also identifies a path to local industry development based on foreign assistance but also on national governments' willingness to support local procurement of drugs (Russo and Banda, forthcoming). As is already well known in those African countries with a more established pharmaceutical industry, this case study reaffirms that only through preferential pricing and reduced profit margins can local medicine production be competitive in Mozambique, but that the spill-over information-related benefits from local production can be substantial for epidemiological surveillance as well as for governments' price negotiations (Russo et al., 2014). However, a number of points of discussion are raised by this case study on the

feasibility, sustainability and opportunity of local pharmaceutical production in Africa.

At the time of writing, the factory's sustainability after the likely end of Brazil's support in 2017 remains an issue. Brazil's original objective was to provide MISAU with enough production capacity to carry out its medicine policies; however, the GoM's appointment of IGEPE, together with the conspicuous absence of references to the factory in MISAU's policy documents, seem to signal a more pronounced interest in the factory's contribution to the country's industrial assets rather than to its public health goals. To this respect, the GoM will have to decide whether it is still in its interest to keep the factory as a public enterprise, or to attempt a privatization with a degree of public sector involvement, in the way similar experiences developed in Uganda and South Africa (Rajagopal, 2013; World News, 2013).

Finally, this case study raises questions about the suitability of foreign health policy and production models to the African context. If Brazil's original plan was to help Mozambique to replicate its own domestic experience in the AIDS fight and in pharmaceutical production, the implementation of this factory project exposed Brazil's limited familiarity with the development cooperation conundrum, but also the relevance of the differences between the two contexts (Russo et al., 2014). If some of the holdups in the project could be attributed to the relative lack of experience of Brazilian civil servants borrowed from their domestic duties to implement a cooperation project in the African continent, this case study probably shows that solutions that have proved effective elsewhere are hard to replicate in Mozambique for more than just one reason.

First, there is evidence from this experience that MISAU's engagement with the project and enthusiasm for using the factory as an implementation tool for its own national drug policy has not been the same as that which motivated the creation of public pharmaceutical laboratories in Brazil in the past decades (Russo et al., 2014; Flynn, 2010). Second, in stark contrast to what happens in the Brazilian pharmaceutical market, the majority of medicines in Mozambique are imported and paid for by the international community, so it is easy to understand why the government of Mozambique failed to see short-term gains in acquiring national production capacity and paying for something – ARV drugs –already provided for free. Finally, the human capital and manufacturing environment fundamentals that made possible the development of the pharmaceutical industry in Brazil are, in all likelihood, not yet in place in Mozambique. As a result, setting up a factory project already tested

back home became highly cumbersome in a context where lack of skills, funds and services is the norm rather than the exception (Cabral, Russo and Weinstock, 2014).

Conclusion

Contrasting with other chapters in Part I that discuss very different experiences in African countries with a more established pharmaceutical industry, the present chapter has presented an original experience of developing local manufacturing from scratch through collaboration between two national governments. By describing the decade-long process through which Brazil and Mozambique cooperated to set up *Sociedade Moçambicana de Medicamentos* in Maputo, we aimed to illustrate the complexity of shoring up such an ambitious development cooperation project. Our analysis suggests that national and regional demand may justify SMM's production of ARVs and other generic drugs, but that public purchase of drugs remains essential to guarantee the sustainability of the business. We have also highlighted the differences between the two settings, Mozambique and Brazil, and have drawn attention to the possible risks involved in putting emphasis on the development of an enterprise without linking up adequately with local pharmaceutical markets. We believe that such an experience offers an insight into the complexities of developing pharmaceutical manufacturing operations in Sub-Saharan Africa, and into the options that the international community has to support it. The hope is that this will contribute to advancing the debate on local pharmaceutical manufacturing and on paths to its development.


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6

Can Foreign Firms Promote Local Production of Pharmaceuticals in Africa?

Sudip Chaudhuri

Introduction

African countries, particularly the smaller ones, suffer from various disadvantages that prevent local producers from serving a substantial proportion of their domestic markets for pharmaceuticals. How to take care of these disadvantages to promote local production and to reduce dependence on imports is an important political and economic issue in Africa today. Most of the countries with developed industries have used foreign investments and technology in the process of their development. Is a similar trend likely in Africa? Are foreign companies likely to invest there to undertake manufacturing of pharmaceuticals? Can they be induced to do so? The objective of this chapter is to understand the prospects for foreign direct investment (FDI) in the pharmaceutical industry in Sub-Saharan Africa, particularly in smaller countries such as Ghana.

The foreign firms which are active in Africa can be broadly classified between the multinational corporations (MNCs) and the Indian generic companies. These two types of firms are quite different in terms of background and behaviour, and in the next section some of these differences are briefly outlined. The environment for pharmaceutical production and manufacturing is changing quite rapidly, both in Africa and abroad, and that is having an impact on the behaviour of both the MNCs and the Indian companies. The chapter first focuses on the MNCs and discusses the implications for the pharmaceutical markets in Africa. It then focuses on the Indian companies. We will see in the discussion that follows that on their own initiative, Indian companies may not be very

keen to undertake investments for manufacturing in Africa. But given a conducive environment, they may not be averse to initiating manufacturing in Africa on a greater scale. The final section of the chapter takes up the case of Ghana, a relatively small African country. After a brief introduction to the structure of pharmaceutical market and industry in Ghana, the chapter analyses some policies which may be undertaken to promote local production, particularly in order to induce foreign firms to invest in Ghana.

MNCs, generics companies and the international pharmaceutical industry

Traditionally, pharmaceutical companies are classified between a small number of big MNCs that do research and development (R&D) for new drugs and aim to get these patented, and a large number of smaller generics companies that manufacture products that are not patented or products for which patents have expired. The MNCs are exceptionally large in size. The head offices are located in developed countries, mainly in the US, the UK, Switzerland, France, and Germany. They operate all over the world. The largest pharmaceutical MNC, Novartis (headquarters: Basel, Switzerland) reported US$46 billion in pharmaceutical sales in 2013. Each of the other top five MNCs – Pfizer (US), Roche (Switzerland), Sanofi (France), Merck (US) and GlaxoSmithKline (UK) – individually had sales worth more than the entire pharmaceutical market of the Middle East and Africa in 2013.[1]

The patent system and marketing power are at the root of the worldwide dominance of the MNCs. Naturally, for the products patented by the MNCs, they enjoy a monopoly status. They also use an elaborate marketing infrastructure to maintain dominant market shares even after patents expire. Even when the product is protected through patents, the MNCs promote their drugs under brand names, that is, through trademarks, rather than under generic names, which are commonly used in scientific literature. They continue using these brand names and try to take advantage of continuing brand loyalty when generic companies enter the market after the expiry of patents.

Traditionally MNCs have relied for their growth on patented drugs, and have focussed mainly on the large developed country markets. The largest pharmaceutical market is in US (US$343 billion), and this together with Western Europe (US$241.4 billion) and Japan (US$129.5 billion) accounted for about two-thirds of the global pharmaceutical market of US$1,052.1 billion in 2012 (BMI Espicom, 2013).

Like most other countries in the world, India after independence initially recognized product patent protection in pharmaceuticals, and the MNCs dominated the Indian market too. However, the abolition of product patents in 1972 eliminated the monopoly status that the MNCs enjoyed until then. Indian firms started manufacturing and marketing the latest drugs and were able to dislodge the MNCs from their position of dominance in the domestic market. India became self-reliant in drugs. The country furthermore emerged as a major player in the global pharmaceutical industry, receiving worldwide recognition as a low-cost producer of high-quality drugs. India now supplies medicines not only to other developing countries such as those in Africa but also to developed countries such as the United States.

The Indian pharmaceutical industry is highly heterogeneous. Most of the firms are small in size and operate only in the domestic market or in other developing countries. But some of the companies are large and not only compete with these small firms in these markets but also are active in regulated markets in developed countries. Two companies from India – Sun Pharmaceuticals (rank 48) and Ranbaxy (rank 50) – are among the 50 largest pharmaceutical companies in the world.[2] With the acquisition of Ranbaxy in 2014, Sun Pharmaceuticals will make a significant jump in the rankings. Other major Indian companies include Dr Reddys Laboratories, Cipla, Lupin, Glenmark and Cadila Healthcare. The larger Indian companies not only manufacture drugs in India and export these to different parts of the world. They have also started acquiring companies abroad to expand their manufacturing and marketing operations.

The changing marketing strategy of MNCs in Africa

Due to colonial or other links, some of the MNCs, for example GlaxoSmithKline (Glaxo as the firm then was known), had offices in some African countries. But as the MNCs started focusing more on the larger and more lucrative developed country markets, the African markets, especially in small countries, became less and less important for them and they started closing down their offices. Of course, their products were still available, but these imports were managed by their agents – local importers/distributors.

In recent years, however, the MNCs are returning to Africa and are focusing more on the subcontinent. Both push and pull factors are in operation. The most important push factor is that developed country markets have become less attractive, and the main pull factor is the

better growth prospects in Africa (Mckinsey and Company, 2013; Tempest, 2011).

The cost of developing new drugs has gone up, but the introduction of new patented drugs in the market has slowed down. Earlier, as mentioned above, because of the steady flow of new patented drugs, the MNCs focussed mainly on the large markets for patented medicines in high-income countries. But in view of the declining productivity of R&D, MNCs can no longer afford to ignore the generics markets. Their turn to generics markets includes not only the patent-expired markets in the high-income countries but also the generics markets in emerging economies. The centres of economic activity are changing, with most of the growth expected to come from emerging markets (Mckinsey and Company, 2013).

Among emerging markets, Africa is still relatively small. The combined size of the market of the top ten African countries is about US$14 billion, compared to US$343 billion in the US and US$129 billion in Japan (Table 6.1). However, the future growth is expected to take place in emerging countries, including in Africa, rather than in the developed countries. It has been estimated that between 2012 and 2018, major developed country pharmaceutical markets will remain stagnant (as in Japan and the UK), increase marginally (as in the US), decline marginally (as in Germany and France) and decline significantly (as in Italy and Spain). In contrast, the top ten African countries are expected to grow at 11% annually (Table 6.1). Quite understandably, therefore, while preparing their strategies for future, the MNCs are focusing more on the emerging countries, including in Africa.

The major drivers of growth in pharmaceutical markets in Africa have included increased disease burdens, particularly HIV/AIDS. The private markets have been expanded by developments in health insurance schemes, and some countries' health systems have seen large investments in public health. Political stability and rapid economic development, improving business climate, a maturing regulatory environment and increased confidence in generic products have all also contributed to market expansion (African Union and UNIDO, 2012; Mckinsey and Company, 2013).

The changes are having a variety of different impacts on the behaviour of the MNCs in Africa. The MNCs are no longer relying only on their agents. They have started opening offices and staffing these with their own employees. Marketing expenses for brand promotion have risen. To push up their sales they have also started offering credit facilities. Another notable development is that the MNCs are toning up their

Table 6.1 Anticipated trends in global pharmaceutical markets

Country	Market size 2012 (US$ billion)	Estimated market size 2018 (US$ billion)	Anticipated annual growth rate*, 2012–2018 (%)
Emerging markets			
China	82	164	12
Russia	22	39	10
India	16	28	10
Brazil	27	39	7
Africa**	14	26	11
Developed markets			
US	343	360	1
Japan	129	129	0
Germany	49	47	–1
France	43	41	–1
UK	38	38	0
Canada	26	25	–1
Italy	28	22	–4
Spain	23	16	–6

Note: * Compound annual rate of growth
** South Africa, Algeria, Egypt, Morocco, Tunisia, Sudan, Nigeria, Libya, Ivory Coast and Kenya.

Source: Mckinsey and Company, 2013.

distribution networks. They have started using the services of specialized supply chain organizations such as Imperial Health Sciences. The latter has operations in South Africa, Kenya, Ghana, Nigeria and Malawi, where medicines are received, stored and distributed in countries across Africa.

Perhaps the most significant development of all is that MNCs have started introducing new brands to compete in the generic markets. As mentioned above, when MNCs market new patented drugs, they sell these in brand names and continue to do so even after the patents expire. The patented drugs in monopoly markets are high priced. For patent-expired products too, the MNCs participate in the higher end of the market that has more limited competition. Even after the patents expire, the firms typically continue to use the same brands and continue to charge a very high price.

This strategy on the part of the MNCs has, in fact, helped the Indian generic companies. The large Indian companies typically adopt the strategy of charging a price lower than that of the MNCs to enter and

grow market share in the patent-expired products. Armed with lower prices and active brand promotion, Indian companies such as Cipla, Ranbaxy, Sun Pharmaceuticals, Cadila and Glenmark have been able to dominate the markets in many products.

Particularly for Sub-Saharan African countries, India is the predominant supplier. In Tanzania, for example, the Indian generics company Cipla was the second-largest company in the retail market in 2010 with a market share of 16%, next only to the local firm, Shelys (21% market share), and ahead of MNCs such as Novartis (10%) and GSK (6%). Among the other notable Indian participants are companies such as Ranbaxy (8%), Sun Pharmaceuticals, Unichem Laboratories, Cadila Glenmark and Ajanta Pharma (Frost and Sullivan, 2010: 151; 2012: 81–83). As in most African countries, local firms in Tanzania manufacture a relatively simple list of formulations such as simple antibiotics, cough and cold preparations, analgesics antipyretics, sedatives, nutraceuticals, anthelmintics and anti-malarials (see Chapter 3; Chaudhuri et al., 2010). For technologically more sophisticated formulations, the competition is mainly between the MNCs and the Indian companies.

The MNCs are now increasingly trying to make their presence felt in these generic markets. They are reluctant to dilute their innovator brand by lowering the price to compete against generic products. There is a brand loyalty associated with innovator products and there is a price-insensitive market segment where MNCs continue to sell despite high prices and despite the availability of cheaper generic products. To enlarge their market, the MNCs are introducing new brands and selling these at prices significantly lower than their innovator brands. The dual-brand strategy enables them to be present not only in the price-insensitive segment of the market but also in the price-sensitive segment.

The most active MNC in this game is GSK. The innovator brand for their anthelmintic drug, albendazole, is Zentel. They have introduced a new brand for the same product, named Alzental. Another example is the antibiotic amoxicillin/clavulanate. The GSK innovator brand is Augmentin. They also sell the same product in the brand name Clavulin to compete against similar-sounding generic brands such as, for example, Clavam of India's generics company Alkem. These MNC generic brands are priced significantly below the innovator price, often 50% or less. These are still priced above the brands of generic companies. But with the price differential much smaller and their better reputation, the MNCs hope to prevent the slide in their sales in the generics markets.

Now that they have started competing on prices, the matter of costs has become important. Another important trend observed is that the

MNCs are trying to get their generic products manufactured in cheaper locations. The Ghanaian company LaGray has entered into an agreement with Sandoz, the generic arm of Novartis. The former will manufacture products to be marketed in their brand names by the latter. India offers an even cheaper location. MNCs such as GSK, AstraZeneca and Abbott have entered into supply agreements with Indian companies such as Dr Reddys, Aurobindo, Cadila Healthcare and Torrent. Dr Reddys, for example, will supply about 100 branded formulations to GSK for marketing in different emerging markets including in Africa. These deals enable the MNCs to get access to low-cost reliable products without undergoing the lengthy process of getting regulatory approvals in different markets and without incurring any capital expenditure for setting up manufacturing plants. The Indian companies gain by having access to the formidable marketing resources of the MNCs (Chaudhuri, 2012).

However, what these trends indicate is that although MNCs are targeting African markets, they are unlikely to make any significant investments to manufacture drugs in Africa, at least not in the near future.

Indian generic companies in the African market

European countries, mainly France, Germany and Switzerland, are the most important suppliers for some relatively large North African countries such as Algeria, Morocco and Egypt (UNCOMTRADE). But for Sub-Saharan Africa, India is the predominant supplier of medicines. As Table 6.2 shows, in 2012 India contributed more than 50% of the formulations imports in Uganda and Mozambique and more than 40% in Nigeria, Ghana and Rwanda. Its share was also substantial in countries such as Ethiopia, Tanzania and Zimbabwe. If we could exclude the imports of high-priced patented medicines and focus only on generics, India's contribution to Africa would be much larger than Table 6.2 suggests. Where drugs are purchased from multiple sources, as for example for ARVs, India has turned out to be the dominant supplier, accounting for more than two-thirds of Africa's imports (Chaudhuri, 2008).

Indian generic companies exporting medicines to Africa can be classified into two broad categories: those which are active also in the regulated markets in developed countries such as the United States, and those which are not yet present in these markets. The larger and more reputed companies belong to the first category. These more dynamic Indian

Table 6.2 Indian share of pharmaceutical formulations imports into Africa, 2012

Country	Total imports, US$ million	Imports from India (%)
Uganda	204	57.6
Mozambique	50	52.6
Nigeria	263	43.7
Ghana	126	42.7
Rwanda	55	40.4
Ethiopia	154	39.3
United Rep. of Tanzania	161	36.8
Zimbabwe	170	36.6
Mauritius	103	34.7
Burundi	42	33.3
Cameroon	168	25.0
Botswana	124	23.1
Niger	44	21.3
Côte d'Ivoire	259	19.1
Madagascar	49	18.9
South Africa	1,890	15.9
Namibia	142	13.1
Mauritania	15	10.4
Togo	68	6.2
Senegal	167	4.5
Mali	142	4.1
Morocco	360	3.6
Algeria	1,879	2.6
Cabo Verde	8	1.3
Egypt	1,498	0.5
Total (25 countries)	8,139	13.7

Source: Calculated from UNCOMTRADE database (http://comtrade.un.org).

generic companies have been more interested in the patent-expired markets in high-income countries such as the US and in Europe because of the larger markets and better prices realized. Prices achieved are higher in these markets because regulatory requirements to enter these markets are stricter and so entry is more difficult. The Indian companies active in the African markets also primarily target the markets where entry barriers are higher and hence competition is less strong. These companies promote their products through brands and their main competitors are the MNCs (and also generics companies from other countries). As mentioned above, these companies often try to enter and grow in these markets by charging a price lower than that of the innovator MNC. The

smaller Indian companies are more active in over-the-counter medicines and in markets for simple products where they compete mainly against the local manufacturers and other smaller generic companies.

The changing composition of Indian companies

The composition of Indian generic companies is however changing in Africa. With improvements in the regulatory environment in Africa, the not so quality-conscious Indian companies are increasingly finding it difficult to operate there. Allegations have been made from time to time that some Indian companies have taken advantage of the regulatory environment in India and in Africa to export poor-quality drugs. In fact, it has been a very common complaint in Africa that India has not been taking initiatives to regulate the quality of drugs exported. This is now changing. Due to the efforts of the government in India and also some steps taken in some African countries, the quality standards have improved. Most African countries, for example, do not permit imports into their countries from India without a Certificate of Pharmaceutical Product (COPP). This is given by the drug control administration in India to units that qualify for the WHO-GMP standard. This standard is stricter than Schedule M, the Indian version of GMP, and hence exporters are required to satisfy higher standards than in the domestic market.

Like the MNCs, the more serious Indian players are also getting more involved in Africa. Here too both push and pull factors are in operation. An important push factor arises from the fact that earlier expectations of huge gains in the patent-expired markets in large markets such as in the United States have not materialized. Those markets have turned out to be very competitive, despite some value-added market segments where competition can be limited and where gains are still substantial.[3] However, with the declining R&D productivity and a reduced flow of new patented drugs in the market, the MNCs are aggressively trying to make the entry of generic companies more difficult in these markets.

The better regulatory environment in Africa has improved the attractiveness of the market for the larger Indian companies and is acting as an important pull factor there. Perhaps more important is the anticipated future growth in the pharmaceutical market in Africa. The African market is still relatively small for Indian companies. Africa accounts for about 15% of India's exports (Table 6.3). But Africa is an expanding market for India. The growth of India's pharmaceutical exports has been quite spectacular, and Africa has been able to increase its share from about 10% in 1994–95 to 15% in 2011–12. The growth of the African market has in fact been faster than all other regions except America

Table 6.3 India's Pharmaceutical exports

	1994–95	1994–95	2011–12	2011–12
	(Rs million)	(%)	(Rs million)	(%)
Europe	10,663	42.4	90,964.35	29.6
America	3,661	14.6	90,147.29	29.3
Asia	7,941	31.6	77,886.87	25.3
Africa	2,676	10.7	45,280.45	14.7
Oceania	182	0.7	2,949.168	1.0
Others	0	0	368.29	0.1
Total	25,123	100	307,596.4	100.0

Source: India's Directorate General of Commercial Intelligence and Statistics (DGCI&S) trade data, accessed from the 'India Trades' database of the Centre for Monitoring Indian Economy.

(Table 6.3). In 1994–95, just Nigeria and Kenya accounted for about 50% of India's exports to Africa, and the share of top five countries was nearly three-quarters of the total. However India's exports now are more diversified. Among the countries which are relatively more important are Ghana, Benin, Sudan, Angola, Malawi and Cameroon.[4]

Are Indian companies likely to invest in manufacturing in Africa?

It is clear that Indian companies will continue to play a very active role in the African markets. Indeed, because of the factors mentioned above, they are likely to expand their operations there. Some Indian companies have already been actively involved in foreign direct investments (FDI) in Africa. Notable examples are Cadila in Ethiopia, Cipla in Uganda and South Africa and Ranbaxy in Nigeria. Other Indian companies too may be involved in the future in setting up manufacturing plants in Africa. But are Indian companies in general likely to be involved in any significant scale in investing in Africa? R Modi, chief of the Indian company Cadila, mentioned during his presentation at the African Pharmaceutical Summit in Hammamet, Tunisia, on 23–24 September 2013 that profit has not been the main motivation for Cadila's investments in Ethiopia. It is possible that beyond narrow financial reasons, some Indian companies will invest in Africa. But if Africa is to benefit in any significant way from Indian companies to further develop the industry there, what is required is more systematic investments. Unless Indian companies find Africa commercially attractive, it will be difficult to sustain such investments.

Unless the policy environment changes in Africa, the indications are that Indian companies in general will continue to find exporting a better option than investing in Africa. The main reasons are the following.

Perhaps most importantly, Indian companies essentially face a free trade regime in Africa. Some countries impose tariffs on imports of finished formulations. Some countries have a restricted list, as in Ghana, as discussed below. But in general, imports are not otherwise controlled or prohibited. This implies that from the Indian firms' point of view, it is easier to export than to undertake direct investments. Export activity does not involve huge investment, nor is it risky. Lately, as just discussed, African countries are trying to improve their drug registration and regulatory systems, but traditionally it has been very easy to enter most of the African markets.

The most common model followed by Indian firms is for the Indian exporters to tie up with local importers/distributors. In some African countries, this trade is dominated by people of Indian origin, so that linking up with traders is not a difficult proposition in these countries. Again in comparison to China, the main competitor in Africa, India has the advantage of more exposure to the English language, which is understood and used in many African countries. The main role of the Indian company is therefore restricted to getting the product registered and manufacturing and supplying to local partners. This hardly requires much investment: Indian companies do not create separate plants for the African markets. They use their existing capacity – often excess capacity – for the purposes. It is also practically riskless. Many exporters insist on advance payment. Even where the medicines are supplied on credit, at worst the Indian company will lose money for that consignment, and then they can stop supplying medicines in the future.

Investments abroad, on the other hand, involve more risks. It is very important for foreign investors to be assured of the safety of their investments. Africa is now politically much more stable. But foreign investors seem to expect some proactive steps on the part of the government to instill confidence that their money will be safe and that, if necessary, they can take money out of the country. There are also risks related to volatility of foreign exchange rates. Perhaps most important, the local partnerships required for direct investments carry higher risks. Export activities of Indian companies are carried out through local partners, as mentioned above, and in such cases the roles are clearly defined and risks are fewer. In case of joint ventures, however, the success of the company will depend much more on the local partners. The question of reliability of partners becomes more important in the case of investments abroad,

since substantial investments would be involved and it is not easy to get rid of undesirable partners.

It follows that it is still quite a challenge to undertake manufacturing activities in Africa. Most of these countries suffer from various disadvantages, discussed in the preceding chapters. They include lack of technical know-how and trained manpower in the local African labour markets and the low levels of development of support industries including suppliers of APIs, other materials and machinery. Production costs may be higher than in India because input costs and utility costs are higher, and also because productivity may be lower. In some smaller countries, the market is considered too small for profitable operations.[5] It is therefore much easier for Indian companies to manufacture in India and then to serve the African markets through exports.

This current status and set of perceptions can however be changed through policy interventions. Left to themselves, foreign firms may not be keen to invest. But if proper conditions are created, if the above-mentioned issues and factors are taken care of, then they might be induced to do so. If the experience of other countries is any guide, then neither the inflows of FDI nor the benefits from FDI result from a passive open-door FDI policy (Lall and Narula, 2004; Chang, 2004). What is required is an active industrial policy.

The last section of this chapter develops this argument for the case of Ghana.[6] It discusses how foreign firms can help to develop a local pharmaceutical industry, and how they can be induced to contribute to promote local production.

Ghana, industrial policy and foreign direct investment

Ghana is a relatively small African country. The size of its total formulations market was estimated at about US$329 million in 2012 (BMI, 2013: 16). There are about 38 pharmaceutical manufacturing units in Ghana of which about 20 are actively involved in manufacturing formulations. Only one company, LaGray, started manufacturing an API (erythromycin) for their own use in formulation manufacturing. Local production caters to about 30% of the market, with the remaining 70% of demand being met from imports. Some of the local firms, for example Kama and Ernest Chemists, are involved in both manufacturing and importing.

India is a major source of Ghanaian imports not only of formulations but also of the APIs and other materials required for the local production of formulations. Out of the 30% of the market which is supplied by local

manufacturers, 25% are over-the-counter (OTC) medications and the remaining 5% are simple prescription formulations. About two-thirds of drug purchase in Ghana are financed through out-of-pocket expenditure, the remaining being financed through public procurement, donor-funded purchases and reimbursement by the National Health Insurance scheme. Ghana has an elaborate drug distribution system dominated by importers/distributors/wholesalers. The branded generics segment of the market is large, and both imported products and locally manufactured generic products are sold as brands. Local manufacturers are actively involved in sales promotion, particularly for OTC items.

The Ghanaian government has put in place a number of policies that have helped the local industry to grow to attain its present status. Among these policies, one of the most important steps taken to promote the pharmaceutical industry was to ban the imports of finished formulations of 14 widely used products including ampicillin, tetracycline, chlordiazepoxide, indomethacin, paracetamol, aspirin and diazepam. Domestic formulations manufacturing has also benefitted substantially from the industrial protection provided by combination of zero import duties on materials and machinery required for formulations production with 10% import duty on imports of finished formulations. Another important advantage that domestic formulations manufacturers have been enjoying was the refunding of the 15% VAT imposed on all materials and machinery required for formulations production. However, in 2013, the government has withdrawn this benefit, as has also happened elsewhere (see Chapter 2).

Like other countries discussed in this book, Ghana also offers a 15% price preference for domestic suppliers in public procurement. This has also helped manufacturers, though the system has not always functioned properly. Local manufacturers complain that the procurement system is not very transparent, and especially when the government buys at regional and local levels there is suspicion that the 15% advantage is often not provided. The government does not reveal the prices at which it actually procures. Perhaps if such information is made public the situation will improve.

Industrial policy in Ghana

What can be done to further increase the share of local production in the Ghanaian domestic market? What is fundamentally important for promoting an industry is to put in place policies to provide access to three key aspects of business activity: finance, technology and markets.

This section first discusses the problems of finance and technology in the context of Ghana. It then explores the ways in which a policy of ensuring a larger market for local producers can prompt FDI to assist the development of the pharmaceutical industry in Africa.

Under the conditions in which they operate, the local firms hardly earn adequate profits to plough back into investments. Furthermore, the rate of interest charged by banks in Ghana is exorbitant, often exceeding 30% per annum. As shown below, to set up Good Manufacturing Practice (GMP)-compliant manufacturing plants, to develop products for getting regulatory approval and for marketing these products, huge funds are required. Taking loans at such high interest rates is simply not a viable option, so that exploring other funding options is vital. The more resourceful foreign firms with access to diverse sources of funding offer one of the possible policy options.

Technology, furthermore, is a fundamental constraint in Africa today. When pharmaceutical manufacturing started in Ghana, technical requirements were simpler and technology was often arranged through informal channels. The promoters of local companies such as Amponsah Efah, LaGray and Pharmanova are themselves technologists, and they have used their knowledge and contacts to set up small-scale plants. But the technological scenario in recent years has changed fundamentally. Current requirements are significantly tougher. If local manufacturing in Ghana is to make a significant difference to the industry, then technical knowledge and expertise need to be available qualitatively and quantitatively on a big scale.

The first technological requirement is that the manufacturing plants need to be GMP compliant. To set up a GMP-compliant plant, significant additional costs, particularly investment costs, have to be incurred. Moreover, the products manufactured need to be approved for marketing by the local drug control administration. The companies are required to undertake various types of studies (e.g. bioequivalence studies) and to generate data and submit dossiers to the drug control authorities. Marketing approval is granted after various types of review by the latter, including chemistry review, bioequivalence review and after-plant inspection.

The technical knowledge required to set up and run GMP-compliant plants and to develop products for getting regulatory approvals for marketing are not widely available in Ghana and other African countries. It is vitally important to arrange this if the local industry is to develop.

A possible solution is to use the technological resources of foreign firms for the purpose. Manufacturing operations by Western MNCs are carried out in quite a different environment, while the situation in India is much closer to that in Africa. Pharmaceutical technical knowledge is furthermore highly diffused in India, so if Indian companies invest in Africa, then a major constraint will be lifted.

Furthermore, as Chapter 5 has emphasized, market access and serving the local market effectively are essential elements of business success. If the African governments can initiate policies to substantially limit the access of foreign firms to the domestic market, then Indian (or other foreign) companies will lose out unless they undertake investments in Africa to cater to that market. Where the loss is substantial, as in the cases of larger countries or regional markets, chances of FDI will be much higher. How can a country manage its domestic market to induce foreign firms to invest?

Policy makers in developing countries often are reluctant to impose import controls on the grounds that such an action may lead to shortages and/or lack of import competition may lead to higher prices. But this need not necessarily be the case, as Ghana shows. The products on its banned list are manufactured adequately in the country, and the country did not suffer from shortages after the policy was imposed. Lack of import competition has not resulted in higher prices. Importantly, import competition has been replaced by domestic competition, leading to competitive prices in the domestic market.

To explore the question of pricing further, Table 6.4 compares the retail prices of selected products in India and Ghana. The products include some of those which are manufactured in Ghana, for example ciprofloxacin, paracetamol, amlodipine, diazepam, metformin and also some of those that are not currently manufactured in Ghana, for example anastrazole, granisetron, losartan, rabeprazole and rosuvastatin. As Table 6.4 shows, the extent of price differentials between India and Ghana is quite different, depending on whether these products are manufactured in Ghana or not. For the products not manufactured in Ghana, the price differentials are significantly larger. For the products manufactured in Ghana, not only is the price differential much narrower – less than 1.5 times – but it is in fact the case that for three products, Ghanaian prices are lower than those in India. These include diazepam and paracetamol, which are products reserved for local manufacturers. Thus Table 6.4 suggests that local production in Ghana has contributed to affordability.

Table 6.4 Comparison of retail formulations prices in India and Ghana

	India: Median price in INR (1 tablet) 2013	Ghana: Median price in INR (1 tablet) 2011	Ghana/India price ratio: Col(3)/col(2)
Tablets manufactured in Ghana			
1. Ciprofloxacin, 500 mg	6.18	9.11	1.5
2. Amlodipine, 5 mg	2.36	3.64	1.5
3. Metformin, 500 mg	1.46	1.52	1.0
4. Diazepam, 5 mg	2.90	0.30	0.1
5. Paracetamol, 500 mg	1.14	0.30	0.3
6. Diclofenac, 50 mg	1.43	1.82	1.3
7. Lisinopril, 5 mg	4.58	6.07	1.3
8. Atorvastatin, 10 mg	8.60	9.11	1.1
9. Cetirizine Hcl, 10 mg	3.10	3.04	1.0
10. Metronidazole, 200 mg	0.39	0.61	1.6
Tablets not yet manufactured in Ghana			
1. Anastrazole, 1 mg	48.50	182.10	3.8
2. Cepacitabine, 500 mg	150.05	267.08	1.8
3. Granisetron, 1 mg	14.05	409.73	29.2
4. Itraconazole, 100 mg	47.50	182.10	3.8
5. Losartan, 50 mg	5.65	12.14	2.1
6. Rabeprazole, 20 mg	2.75	75.88	27.6
7. Risperidone, 2 mg	3.80	75.88	20.0
8. Rosuvastatin, 20 mg	20.36	69.81	3.4
9. Tindazole, 500 mg	5.52	69.81	12.7
10. Sertraline, 100 mg	6.3	98.64	15.7

Sources: 1. For Indian prices in col (2): median prices of retail brands accounting for 1% or more of the market. Market share data have been obtained from the *Sales audit data* of AIOCD Pharmasofttech AWACS Pvt. Ltd (AIOCD-AWACS), a pharmaceutical market research company; Price data have been obtained from CIMS (2013).

2. For Ghana prices in col (3): 'Medicines List', February 2011 of the Ghana National Health Insurance Scheme (http://www.nhis.gov.gh/_Uploads/dbsAttachedFiles/1(3).pdf). Prices in Ghana cedis (GHC) have been converted to Indian rupee (INR) using the annual average exchange rates for 2011 from www.oanda.com. The list specifies the maximum prices at which the medicines purchased at the retail level are reimbursable. Pricing data are collected from manufacturers, wholesale distributors, private pharmacies, government, mission and private health facilities and the median prices are set as the maximum price reimbursable under the insurance scheme.

3. Since the Ghana prices refer to 2011 whereas the Indian prices refer to 2013, depending on the extent to which Ghana prices have gone up since 2011, the price differential in fact may be larger than the figures show.

If the number of products on the banned list is increased, and if free flow of imports into the economy is controlled, then not only will domestic producers find a larger market. Import restrictions may also induce foreign firms exporting to the country to undertake manufacturing within the country.

Imports can also be controlled in several other ways. Ghana has introduced a National Health Insurance Scheme (NHIS), which covers about half the population. About 40% of the funds paid out by health insurance are for medicines. The NHIS-funded formulations market has therefore emerged as a major market segment in Ghana accounting for about 23% of the market (Seiter and Gyansa-Lutterodt, 2009: 19). The NHIS has expanded since that 2009 study, and the share of insurance-funded medicine purchase has risen. The substantial bargaining power of the NHIS agency can thus be used to enlarge the domestic market. The NHIS does not currently differentiate in its procurement between medicines according to whether they are manufactured locally or imported. However, after allowing some time for capacities to develop, NHIS reimbursement could be restricted to locally manufactured products. Since the prices to be reimbursed are being fixed by NHIS in any case, the possibility of such actions leading to higher prices will not arise.

A further policy option available is to use the instrument of government procurement. So far as the institutional market is concerned, the only benefit the local manufacturers receive is the 15% price preference, and that too, as noted above, does not operate properly. An important flexibility that the World Trade Organization (WTO) provides concerns public procurement. The WTO Agreement on Government Procurement (GPA) is a plurilateral agreement which is applicable only to the member countries which have signed the GPA. African countries, including Ghana, have not yet joined the GPA.[7]

Public procurement of drugs (and other goods) in Ghana is currently guided by the provisions of the Public Procurement Act. This provides for three types of competitive tendering: international, national and restricted. 'International tendering' means that organizations responding need not necessarily be located in Ghana. 'National tendering' means that the tendering can be restricted to organizations located in Ghana, but the organizations need not be manufacturers. They can be importers located in Ghana.

A simple step that could be initiated in Ghana for the further development of the pharmaceutical industry is to introduce tendering restricted to local manufacturers. This might be a two-stage tendering process: a technical evaluation and then evaluation of the financial bid. At the first stage of technical evaluation, tenders may be accepted only from those local manufacturers that are GMP-compliant and that have the manufacturing capacities to satisfy the procurement requirements. The financial bid may be restricted to the companies which qualify in the technical evaluation. Based on the widely used International Reference Prices,[8] maximum purchase prices may be also specified. This

will ensure a larger domestic market for local manufacturers, and hence a more attractive market for FDI, without compromising on prices.

Conclusion

This chapter can be appropriately concluded with a quotation from the Chairman of an Indian company currently exporting pharmaceuticals to Africa. He summarized the prospects of FDI in Africa. He told us during an interview that if imported products including those from India are freely available in Africa, then it is difficult to induce Indian companies to go to Africa and set up plants. But if local production is somewhat protected, and if this is supplemented with few steps to take care of the disadvantages of local production in Africa including some incentives, for example some income tax benefits particularly in initial years and infrastructure support (land, water, roads, electricity), then the prospects of FDI from India will be brighter. In fact, his company will be willing to explore the possibility actively.

Notes

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1. Wasem Noor, 'Pharm Exec's Pharma 50 2014', 9 June 2014 (accessed 17 April 2014 from http://www.pharmexec.com/pharm-execs-pharma-50–2014?id=&sk=&date=&&pageID=2); BMI Espison, 2013.
2. See note 1 above.
3. For example, after the expiry of the basic patent for a chemical, generics companies that can successfully challenge some of the secondary patents can prevent other generic companies from entering the market for a limited period of time, gaining substantial additional value-added.
4. Source: as in Table 6.3.
5. See Guimer et al. (2004); Kaplan and Laing (2005); Losse et al. (2007); Chaudhuri et al. (2010); Abbott (2011); Moon (2011); UNCTAD (2011); African Union and UNIDO (2012); Chaudhuri and West (2014) for further insights into local production in Africa.
6. The case study on Ghana relies to a great extent on the information collected through interviews while doing studies for UNIDO, Vienna and UNDP, New York.
7. Mostly developed countries are currently members of GPA; for the list of those who have joined, see https://www.wto.org/english/tratop_e/gproc_e/memobs_e.htm

8. Management Sciences for Health (MSH), *International Drug Price Indicator Guide* (annual) http://apps.who.int/medicinedocs/documents/s19968en/s19968en.pdf, accessed 20 April 2015.


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7

Raising the Technological Level: The Scope for API, Excipients, and Biologicals Manufacture in Africa

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Introduction

This chapter discusses raising the technological scope for locally manufacturing active pharmaceutical ingredients (APIs), excipients and biologicals in Africa – a hitherto nascent industry. It also discusses African drug development and manufacturing through the standardized use of 'reverse pharmacology' to bring new treatments for neglected diseases to the point of regulatory approvals. Currently there is very modest production of APIs on the African continent, although a few significant projects exist,[1] (such as LaGray in Ghana and Fine Chemicals in South Africa), or are in the planning stages.[2] Generic producers in India and China supply nearly all of the APIs used in African pharmaceutical manufacturing. Most African companies cannot afford the heavy investment and research and development activities required for API production.

Two strategies are suggested to help to address these issues: first, the introduction of technology transfer (product development) packages at centres of excellence, with each package being transferred to several manufacturers; second, the use of 'leap-frogging' technologies to reduce capital investment, minimize the environmental footprint and enhance competitiveness. Leap-frogging technologies have the advantage that Africa can skip technology and investment legacy issues. Leap-frogging technologies can also narrow the gap between rich and poor economies in drug discovery/development and pharmaceutical manufacturing by