Part III

Industrial Policies and Health Needs

The last chapter of Part II framed the development policy challenge of aligning industrial and health goals as 'problem-solving'. This last section of the book draws on case studies and experience to address some of these major policy challenges.

The section starts with a problem health policy makers grapple with across the world: how to control prices of medicines. While most high-income countries closely manage medicines pricing in the context of universalist health systems, most developing countries have low levels of control. Chapter 11 describes an important effort to change this situation in South Africa, a country grappling with the legacy of an inherited and profoundly inegalitarian two-tier health system. The author draws lessons for both policy and process in other African contexts.

A second major industrial policy issue with huge health consequences is the definition and enforcement of quality standards in pharmaceutical manufacturing. Manufacturers and health care providers alike have a shared interest in ensuring the industry grows without compromising public health safety. Standards are both a key technical issue and an arena for international debate on procurement and regulatory strategies. Chapter 12 argues for stronger local African initiative in defining, regulating and harmonizing quality standards.

Procurement of medicines operates as implicit industrial policy, and Part II argued that it is understudied. Chapter 13 investigates innovative approaches, drawing on high-income country initiatives in valuing and pricing innovator medicines for lessons applicable in lower-resource contexts. The chapter picks up from Chapter 11 the issue of price negotiation and its discussion links to Chapter 14, which addresses more broadly the interaction between industry and government through biopharmaceutical business associations.

Chapter 13 also opens up the key issue of business finance for industrial development, a theme addressed further in Chapter 15. Chapter 15 brings together a number of different threads in the book by discussing finance and incentives to support the development of national pharmaceutical industries. The chapter identifies a convergence of thought and initiative recently generated across the African continent for the development of policy incentives for industrial development for health benefit.

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11

Policies to Control Prices of Medicines: Does the South African Experience Have Lessons for Other African Countries?

Skhumbuzo Ngozwana

Introduction

Despite the heightened interest in the African pharmaceutical market, there are constraints and challenges that continue to affect access to medicines. One of the key constraints is the high prices of medicines. In the private sector, wholesale and retail mark-ups have been found to range from 2% to 380% and from 10% to 552%, respectively (Cameron et al., 2011). A later study found wholesaler mark-ups between 25% and 50% (IMS Health, 2014a; 2014b), and retail mark-ups between 25% and 500% (Rosen and Rickwood, 2014). Local manufacturers and importers alike have expressed concern over the high mark-ups in the distribution chain, as the exorbitant prices are believed to limit patients' access and sales.

African governments are all grappling with the issue of high medicine prices. Coupled with the increasing momentum for developing local pharmaceutical industries, the issue of medicine prices and how to contain them will come into sharp focus for policy makers. African policy makers are also acutely aware of measures employed by other countries around the world to contain runaway health care costs, and specifically pharmaceutical expenditure. Although price controls are important policy instruments, they are very controversial. The South African experience with pharmaceutical price controls may therefore be a useful case study to inform other African countries' interventions.

This chapter presents the South African experience with the single exit price (SEP) regulations which were enacted to deal with these distortions and to replace the mark-up-based retail pricing systems with fixed professional fees in order ultimately to reduce the price to patient.

Pharmaceutical price control options

Governments have moved to control prices, first, because the innovative pharmaceutical industry has historically been dominated by monopolies, creating the tendency to price products at a premium. Medicines are also different from any other consumer goods in that patient is often price-insensitive, given that the doctor prescribes and a third party pays for the drugs. Furthermore, many consumers and health care professionals equate a higher-priced product with quality, and conversely see a lower-priced product as inferior, resulting in the ready acceptance to prescribe, dispense or ask for high-priced products. The challenge for governments therefore is how to institute proper controls to ensure that medicines are priced fairly and that access is not constrained by high prices.

The literature on pharmaceutical price controls identifies three distinct ways in which expenditure can be controlled: direct controls on the prices of medicines across various levels in the distribution chain; through demand-side measures including financial and reimbursement systems; and finally by influencing demand through the implementation of demand-side measures.

Price controls at the level of the manufacturer

The most difficult step in price controls is arriving at a reasonable or fair price for a medicine. The literature on price controls and the tools employed are mostly from high-income countries. These include the cost-plus method, profit caps, comparative pricing, direct price negotiations and pharmaco-economic evaluations, or a combination of these tools. The cost-plus pricing model is difficult to employ in a country where most suppliers are subsidiaries of international companies or importers of products from other markets. In this scenario, experience shows that it is very difficult to obtain accurate and reliable data to arrive at a determination of real costs and profits.

The second method of price controls, using profit caps, is employed in, for example, the United Kingdom through the Pharmaceutical Price Regulation Scheme (PPRS), whereby the government negotiates a reasonable profit with companies for products sold to the National Health

Service. This method too faces difficulties with arriving at accurate costs and profits when dealing especially with subsidiaries of international companies and importers.

The third method is comparative pricing, comparing prices of products in other markets with local market prices. Complexities include varying dosage forms, strengths and trade names, and the fact that the margins and mark-ups allowed to players in the chain differ across territories. The Netherlands, for example, sets maximum permissible prices using the average wholesale price of similar products in a basket of countries including Belgium, Germany, France and the United Kingdom. It is reported that upon its introduction in 1996, Dutch pharmaceutical prices dropped by an average 20% (Rietveld and Haaijer-Ruskamp, 2002).

The fourth commonly used tool involves direct price negotiations between buyers and pharmaceutical companies. In France, the government directly controls prices through negotiations before a product is launched. Finally, pharmaco-economic evaluations are used by regulators to attempt to arrive at a fair price, taking into consideration the societal costs of the disease and the costs of other treatments. Through economic modelling, the direct and indirect benefits of the drug are calculated and compared with alternative therapies. Pharmaco-economic evaluations are used extensively in the UK, Netherlands, Canada and Australia, among other markets (see also Chapter 13).

Price controls at the wholesale and pharmacy level

Wholesaler margins are controlled through setting either a maximum margin or a maximum price at which wholesalers can sell on to retail pharmacy. Margins in retail pharmacy can be controlled by setting a fixed percentage mark-up to the wholesale price of each medicine, by setting a maximum over all mark-up, or finally by tiered mark-ups where the percentage mark-up reduces as the price of the product increases. The fixed-margin system is widely used in Europe, with margins for prescription drugs normally around 30%, whilst over-the-counter products are freed from price controls. Although margins are fixed, wholesalers may still be able to negotiate discounts and thus increase their profits. The tiered structure is intended to create disincentives for dispensing more expensive products.

Some countries, including China, have a system of price controls that differentiates between imported and locally produced products (Bao, 2000). The Chinese system also differentiates based on drug classes: basic therapeutic and preventive drugs acquired in large volumes, class 1

anti-psychotics, anaesthetic agents, contraceptives and other special classes.

Other measures to influence prices

There are other demand-side measures that can influence prices and expenditure. These include positive and negative lists, reference prices, co-payments, parallel importation, and generic substitution, as well as education of health care professionals and the public. A negative list of products that are not reimbursed forces companies to lower prices in order to gain a listing on the positive list. Similarly, reference prices, which are used to benchmark products in the same therapeutic category that are assigned a certain price cap, and related demand-side measures such as co-payments, are meant to force patients to opt for the cheaper medicines. Generic substitution and closely related educational measures to educate health care professionals and patients about the quality and benefits of generic medicine are other demand-side measures that have been employed to lower medicine expenditure.

The basis of the South African price control regime

Implications of the two-tier South African health care system

When the first democratic government in South Africa came into power in April 1994, it inherited a two-tier health care system (private and public) reflective of the country's divided history. These two tiers have widely differing resources and access medicines via different channels. The private health care tier is a well-resourced private insurance-based world-class platform which serves an estimated 15% of the population (Council for Medical Schemes, 2014). The private pharmaceutical market is valued at $4.1 billion (IMS Health, 2014b) and is supplied with medicines by about 130 manufacturers and importers supplying 5,000 product lines.

The second tier, the public sector health care system, serves the remaining 85% of the population. It is under-resourced, with chronic staff shortages, a quadruple burden of disease and systemic lack of funding. Public sector supplies are obtained through tenders administered by the Central Procurement Unit of the Department of Health. It is supplied with 2,400 product lines by an estimated 90 manufacturers and importers, at an estimated value of $1 billion a year in 2014.[1]

Besides these deep divisions, the democratic government faced spiralling health care costs and an increasingly exclusionary health care

system, in which those who served the poor and marginalized were paying more for medicines than those in the affluent areas who were more likely to benefit from price and volume discounts, rebates, bonuses and other incentives. The pricing of medicines had historically been left to market forces, so companies were free to price their products as they wished, to offer bonuses and deals, discounts and rebates, and to discriminate among clients on the basis of volume of purchases and other considerations. The government therefore decided to intervene to correct the distortions.

Despite the large literature on pharmaceutical price controls in highly developed markets with well-developed health insurance schemes and universal coverage (Rietveld and Haaijer-Ruskamp, 2002), there was little from the developing world with similar health care systems to South Africa with a significant portion of patients without health care insurance and with considerable out-of-pocket expenditure on health care and medicines.

The government was also aware of developments internationally, where high medicines prices were receiving global attention from governments and consumers alike. Further, they were acutely aware that price controls have to be enacted in such a way that they still create headroom for market forces to work to exert further downward pressure on pricing. In trying to come up with mechanisms to control prices, the government looked to emulate countries that had successfully introduced controls and managed to reduce, contain and sustain medicine expenditure.

A further challenge faced by South Africa was the huge fragmentation of the distribution channel, unlike the Western world where there are a few distributors and wholesalers controlling the entire distribution chain, and hence enjoying economies of scale. So the choice of policy options to contain drug costs would have to take into consideration the country's unique health care structure.

The South African rationale for price controls

The government believed that medicines were public utility goods, and not mere commodities, and that it could no longer allow a situation where companies priced their products as they pleased. This was reinforced by their view that the prevailing drug prices in South Africa were inflated artificially through the elaborate system of bonuses, discounts, rebates and other perverse incentives systems that led to the dispensing of more expensive drugs, and irrational use of drugs. These perverse incentives, the state alleged, added an additional 50% to the final cost

of the drug. The Department of Health claimed that South Africa was among the world's top five most expensive medicine markets.

The Department of Health's position was strongly challenged by the Pharmaceutical Manufacturers Association (PMA) of South Africa, who held the claims were devoid of truth and based on an unfair comparison. The PMA held that the Department of Health was trying to influence the public and create the impression that the pharmaceutical industry was responsible for the high medicine costs, in order to introduce measures to control the industry. To circumvent this, the PMA approached the office of the Public Protector to make a determination whether the statements made by the Department of Health, perceived as laying the groundwork for price controls, were factual.

A key contention was that the Department had compared prices of products sold in the South African retail sector with prices of multi-source products sold by a prominent global NGO, the International Dispensary Association, which supplies developing countries with generics bought internationally in bulk. The PMA's position was that the department was using an untenable comparison to justify the introduction of medicine registration and pricing reform in South Africa, whilst ignoring the fact that patient prices were often double the ex-manufacturer prices, and that various studies had indicated that South African prices were on par with international prices.

Despite the PMA's efforts to block the reforms, the government made clear that they would immediately take measures to correct the disparities and distortions. In this regard, a number of key government policies – legislative and regulatory provisions – were enacted. The next section reviews the constitutional mandate that led to the interventions.

Constitutional enablers of the National Drug Policy

On 8 May 1996, the democratically elected parliament adopted the new Constitution of the Republic of South Africa.[2] This enshrined a Bill of Rights. Section 27 underpinned the legislative and regulatory processes that would follow in reforming the health sector; it read:

> Section 27 (1) (a); everyone has the right to have access to healthcare services, including reproductive health.
>
> Section 27 (2): the state must take all reasonable legislative and other measures within its available resources, to achieve the progressive realisation of each of these rights.

Informed by this provision in the constitution, and acutely aware of the urgency to address the imbalances of the past, to create a new and equitable health care system with universal access to affordable quality health care for all, and ensure the progressive realization of Section 27, the government introduced a number of policy papers which would drive far-reaching regulatory and legislative reforms. The most important was the National Drug Policy (NDP) of 1996. The NDP had far-reaching implications, laying the basis for the Single Exit Price (SEP) regulations discussed below.

National Drug Policy

The NDP (Department of Health, 1996) was aimed broadly at increasing access to safe, affordable quality medicines for all South Africans, and laid the foundation for all the subsequent legislative and regulative revisions and amendments. Specifically, the NDP's objective was '[t]o promote the availability of safe and effective drugs at the lowest possible cost'. The NDP intended to rationalize the pricing structure of drugs and included the following to realize that aim:

- the appointment of a Pricing Committee;
- introducing total transparency in the pricing structure of pharmaceutical manufacturers, wholesalers and dispensers of drugs;
- introducing a non-discriminatory pricing system;
- replacing the wholesale and retail percentage-based mark-up system with a fixed professional fee;
- regulating price increases.

The far-reaching aims of the NDP found expression in the amendment to the Medicines and Related Substances Control Act 101 of 1965. The new Act 90 of 1997 introduced, among others, sections dealing with bonuses and samples (18 A and B), the ethical marketing of pharmaceuticals (18C), generic substitution (22F) and the creation of the Pricing Committee and enactment of the single exit price regulations (22G).

The Medicines and Related Substances Act

Before the introduction of the SEP regulations, the South African pharmaceutical market was dominated by innovator brands, with very little generic penetration. Medicines were promoted directly to doctors and pharmacists, who often received samples, bonuses and many other incentives to drive the prescription or dispensing of particular drugs. These practices led to doctors often prescribing more expensive drugs.

The amended Medicines Act made provisions for the parallel importation of medicines into South Africa by others other than the patent holder (15C), the prohibition of bonusing, rebates and any other incentive scheme (18A), prohibition of sampling of medicines (18B), mandatory generic substitution (22F) and the formation of a Pricing Committee and the clauses governing its mandate[3] (22G), namely that:

(1) The Minister shall appoint such persons as he or she may deem fit to be members of a committee to be known as the pricing committee.
(2) The minister may, on the recommendation of the Pricing Committee make regulations
    (a) on the introduction of a transparent pricing system for all medicines and scheduled substances sold in the republic
    (b) on an appropriate dispensing fee to be charged by a pharmacists or person licensed in terms of Section 22 C (1) (a).
(3) The transparent pricing system contemplated in sub-section (2) (a) shall include a single exit price which shall be the only price at which manufacturers shall sell medicines and scheduled substances to any person other than the state.

The provisions contained in the amendment to the Medicines and Related Substances Control Act 101 of 1965 were immediately challenged in court by the Pharmaceutical Manufacturers Association of South Africa (PMA), who felt that the Department had overreached itself in drafting the act. Although the PMA withdrew its court challenge in 2001 following an international outcry and mounting international and civil society pressure, the regulations pertaining to a Transparent Pricing System for Medicines and Scheduled Substances[4] only came into effect on 2 May 2004.

The Single Exit Price regulations

South Africa's attempt to control prices at wholesale level has elements of a fixed professional fee but with a fixed maximum, based on a tiered scale that considers the price of the product. At retail pharmacy level, the professional fees are also fixed, on a tiered system that endeavours to promote the dispensing of cheaper products. Over-the-counter products are exempted from controls, but pharmacists cannot benefit from discounts as they do in Europe.

The SEP was defined by the regulations as a composite of the manufacturer's exit price, plus the distribution or logistics fee and a 14% value

added tax (VAT). The SEP thereby derived would be the one and only price at which wholesalers, pharmacies and other people allowed to dispense in terms of Section 22C (1) (a) could sell the medicine in South Africa, irrespective of the volumes purchased. The SEP would control pricing throughout the pharmaceutical value chain, setting dispensing fees for pharmacists and logistics fees for wholesalers and distributors.

The final price to the end user would include the SEP and the professional (dispensing fee) for the service rendered. Whilst companies would have the freedom to set initial prices, the pricing committee would decide on an annual price increase in accordance with a methodology in the SEP regulations.

Whilst the introduction of the SEP was widely criticized and seen as an anti-private-sector move by the new democratic government, the high prices of medicines had received attention previously from government commissions under the National Party. The three previous commissions – the Snyman Commission (1962), the Steenkamp Commission (1978) and the Browne Commission (1985) – had also made recommendations including curbing excessive medicine promotions, generic substitution, issuing of compulsory licences, calling for the state to participate in the supply of medicines through a tender system and for the state to investigate the introduction of price controls.

Setting the regulations

The Minister of Health appointed a pricing committee with representation from the Departments of Trade and Industry and Finance and the Competition Commission. The committee had pharmacists, lawyers, health economists, pharmaco-economists, academics and consumer representatives, but no industry representation. Their mandate was to establish a new regime of total transparency in the pricing structure of all prescription medicines and over-the-counter products. The committee would also set up regulations for logistics and dispensing fees, international benchmarking of pharmaceuticals and pharmaco-economic evaluation of medicines.

The government stated that, when fully implemented, it expected the SEP regulations to reduce the prices of medicines by 40–70%. In line with the regulations, effective 2 August 2004 and for a year thereafter, the price of medicines would not be higher than 50% of the 'Blue Book' manufacturer net price.[5] The Blue Book was a well-known industry publication that supplied the pharmaceutical industry and health care sector with independent and accurate price lists. The government held that the manufacturer net price listed in the Blue Book was inflated to

cater for the complex systems of bonuses, rebates and other incentives at play in the industry, in order to allow the retail chains to acquire drugs at below 50% of the listed Blue Book price.

The SEP regulation 8 allowed for a manufacturer to set their single exit price, which could only be raised once on an annual basis, whilst temporary price reductions were allowed as often as the manufacturer wanted to make them for competitive reasons. The SEP could be increased only once a year based on a predetermined formula[6] that incorporated, among others, the Consumer Price Index (CPI) and Producer Price Index (PPI) for the preceding year; changes in the rates of foreign exchange and purchasing power parity; and the need to ensure the availability, affordability and quality of medicines. The currencies considered are the US Dollar and the Euro, as most South African pharmaceutical companies purchase products and inputs of production from abroad with these two currencies.

The final increase as per formula is calculated as follows:

API Formula = *70% CPI (historical) + 15% (Rand/Dollar variance) + 15% (Rand/Euro variance)*

The exchange rate split of 15% US$ and 15% Euro was based on data provided by the Department of Trade and Industry and data on pharmaceutical imports.

Although this formula has been applied from the beginning, the actual price increases granted by the MoH have displayed a degree of discretion, and the timing has often been delayed, in some cases by up to five months.

Manufacturers can also apply for increases above the formula-based increases, to assist manufacturers and importers to compensate for exchange-rate-related increases in the prices of production inputs or finished products imported from principals overseas. The exceptional circumstances under which the minister would authorize such an increase were adverse financial, operational and other consequences for the manufacturer; adverse effects on the availability of the medicine in South Africa should the increase not be granted; the nature of the disease the medicine was registered for; resultant adverse effects on public health; and lastly, to ensure that the constitutional obligations were not abrogated.

Finally, the Director General of the Department of Health could inform the public if she or he felt that the single exit price of a medicine was unreasonable. Manufacturers and importers were required to inform

the Director General six months before the registration of a medicine the intended SEP, the countries where the product was sold and how much it was selling for, the costs of manufacturing, and the marketing and selling costs of the product.

At inception, the regulations stipulated the maximum professional fees that could be added to the single exit price by various players in the distribution chain.

Controversies and challenges

The SEP regulations were immediately challenged in court by various organizations. The pharmacy groups contended that the fees were not sufficient for them to survive, and that the stipulated professional fees threatened the survival of many independent pharmacies. Further, the Pharmaceutical Society of South Africa (PSSA), a large retail pharmacy chain, New Click (Pty) Ltd, and others argued that the Department had overreached itself in promulgating the regulations. The Cape High Court found in favour of the state and dismissed the case, although the dissenting judgment[7] held that it was difficult to understand how the SEP was arrived at; that the logistics fee regulations were contradictory and at odds with other legislation; and that the dispensing fee had been based 'on no more than a thumb suck' and a simplistic 'one size fits all' approach. The PSSA, New Clicks and others appealed the Cape High Court ruling, and the case went to the Supreme Court of Appeal where the Cape High Court decision was overturned.

The Supreme Court of Appeal, in overturning the decision of the Cape High Court, made this finding[8]:

> The order of the court below is set aside and replaced with the following order in each application:
>
> (a) The 'Regulations relating to a Transparent Pricing System for Medicines and Scheduled Substances' as published in GN R553 on 30 April 2004 are declared invalid and of no force and effect.

The state in turn appealed, and the case went all the way to the Constitutional Court, which ruled that the Department had indeed acted within the law, but ordered the Department to go back to the drawing board and review the professional fees.

The Department of Health adjusted the proposed dispensing fee to 26% of SEP to a maximum of R26. This proposal was immediately

rejected by the Pharmaceutical Society of South Africa, once again on the grounds that it was insufficient and would cause unnecessary hardship to their members and eventual closure of pharmacies. The PSSA proposed a tiered dispensing fee system with average fees of R37, a proposal that found no favour with the Department of Health.

Following these court challenges and negotiations between the various parties, the dispensing fee and the logistic fees have gone through various iterations, and have now been finalized. The June dispensing fee was first published in March 2006, and was immediately rejected by pharmacists. This was then replaced with a new proposal of June 2009. More discussions and consultations followed, and the last iteration was published in June 2014 (Table 11.1). The table shows the complex calculations of the permitted fee for each band of the SEP, at the various revision dates.

The proposed dispensing fees were revised upwards over time as pharmacists complained that their business would be unsustainable (Table 11.1). The lowest tier has stayed below R100 (US$8.50) and the fixed fee was reduced, but the dispensing fee has been revised upwards with the adjustment of the percentage of the total medicine price. In the top tier of products above R799.85 (US$67.80), the fee has also been adjusted upwards through a revision of both the fixed component and the percentage of the medicine price

Logistics fee

Prior to publication of the logistics fee regulation, wholesalers and manufacturers negotiated the logistics fee independently, and there were reports of widely varying logistics fees, with some companies paying in the high double digits. Innovator companies with patent-protected products that wholesalers were desperate to stock would often pay in the low single digits, whilst some did not pay any logistics fees at all. This position put the generic pharmaceutical industry at a distinct disadvantage, as wholesalers would often squeeze generic companies for bigger logistics fees to make up for the loss with innovator companies. The government finally moved to regulate the logistics fee, and in March 2011 published the first draft regulations for Logistics Fees (LF). The second iteration was published in September 2012 following negotiations and discussions with providers of logistical services. The fee involves four tiers, with a LF of 8% of the ex-manufacturer price excluding VAT + R3 ($0.25) for items less that R100 (US$ 8.50), and a LF of R54 (US$4.58) for items exceeding R1,000.00 (US$84)

Table 11.1 Pharmacy dispensing fee: fee in rands (R) plus permitted mark-up (%), by band of SEP in rands (R) and date of publication of schedule

Date of publication of fee schedule				
03/2006	**06/2009**	**12/2010**	**09/2013**	**06/2014**
SEP < R77.00 R7.00 + 28% of SEP	**SEP < R100.00** R6.00 + 36% of SEP	**SEP < R75.00** R6.00 + 46% of SEP	**SEP < R81.00** R6.30 + 46% of SEP	**SEP not > R 85.70** R 6.95 + 46% of SEP
SEP = R75.00 < R 150.00 R 23 + 7% of SEP	**SEP = R100.00 < R 250.00** R 32 + 10% of SEP	**SEP = R75.00 < R 200.00** R 15.75 + 33% of SEP	**SEP = R81.00 < R 216.00** R 16 + 33% of SEP	**SEP R 85.70 < R228.53** R18.55 + 33% of SEP
SEP > R150.00 < R250.00 R 26 + 5% of SEP	**SEP > R150.00 < R1000.00** R 45 + 5% of SEP	**SEP > R200.00 < R700.00** R 51 + 15% of SEP	**SEP > R216.00 < R756.00** R 55 + 15% of SEP	**SEP > 228.53 < R799.85** R59.00 + 15% of SEP
SEP > R 250.00 R 31 + 3% of SEP	**SEP > R 1000.00** R 65 + 3% of SEP	**SEP > R 700.00** R 121 + 5% of SEP	**SEP > R 756.00** R 131 + 5% of SEP	**SEP > R799.85** R 140 + 5% of sep

Source: Government Gazettes, various years, extracted by author.

Despite representations from wholesalers and support from the generics industry for the logistics fee to include a minimum fee and a fixed cap, the department rejected that application on the grounds that having a fixed minimum would be anti-competitive. It published the final logistics fee with only a fixed cap. Manufacturers and importers would be free to negotiate a fee up to the capped level with wholesalers. The regulations also stipulated that where the current logistics fee exceeds the current caps, manufactures and providers of logistical services must negotiate to reduce the fee within 60 days of publication of final logistics fees. The regulations, however, allowed the minister to authorize a manufacturer or importer to increase the logistics fee in exceptional circumstances.

Experience with the Single Exit Price regulations to date

Price increases under the regulations

Table 11.2 below captures the experience with the SEP to date. It shows the quantum as determined by the SEP methodology and the eventual increase granted by the Minister.

It is clear from the table that the minister has not always adhered to the formula, and has exercised discretion in granting increases – a sore point for the industry.

Although the industry has complained about the low increases from inception, experience shows that since the introduction of the SEP, they have not always taken the full increase granted. In fact, temporary price reductions have been taken frequently within the period of an

Table 11.2 SEP increases since the implementation of the SEP (%)

Year	SEP calculation as per methodology (%)	SEP granted by the Minister (%)	Variance
2004/05 & 2006/07	2.60 2.60	5.20	N/A
2008	8.40	6.50	–1.90
2009	12.12	13.2	+1.08
2010	9.90	7.40	–2.50
2011	–2.10	0.00	N/A
2012	6.90	2.14	–4.76
2013	8.20	5.80	–2.40
2014	8.90	5.80	–3.10

Source: National Department of Health, Pharmaceutical Task Group, author analysis.

SEP increase. This has largely been for competitive reasons, and at times motivated by the need to sell short dated stock before it expires.

A further justifiable complaint is that the Department of Health delays the increases, so companies lose out. For example, in 2010, there was a five-month delay between the increase and the time that companies could take the increase. These delays occurred as a consequence of the 'application' process introduced, and decisions to accept applications only from 1 April. Given the 30-day approval process, the earliest companies can take an increase is 1 May, which leaves companies with just seven months to enjoy the price increase. Besides these delays, there were also frequent rejections due to such matters as formatting issues on the SEP increase application template, Department of Health database discrepancies and missing documentation.

SEP impact on prices

The experience of South Africa with price controls demonstrates that, contrary to popular opinion, the Department of Health conceptualized a regime based on global practice and tried to blend a number of instruments with a good historical record of effectiveness in other countries.

In terms of controls at the manufacturer level, in attempting to arrive at a fair ex-manufacturer price, and considering the complexities of setting a fair price in a predominantly import based industry, the government settled arbitrarily on 50% of the Blue Book price on the basis that prices were inflated by the same figure to make up for the incentives, bonuses, sampling and other perversities in the system. The price negotiation component between companies and government has only been recently employed for state procurement, where besides published reference prices, the Central Procurement Unit can and does directly negotiate prices with manufactures, especially if they are not too far from the reference prices listed. At the same time, elements of comparative pricing were built into the regulations through the International Benchmarking provisions wherein South African prices would be compared to a basket of prices in five countries including Canada, Australia, New Zealand and Spain. Similarly, pharmaco-economic evaluations were also built into the regulations, although these and comparative pricing through benchmarking have yet to be finalized.

When it comes to other measures to control prices, South Africa has not adopted positive and negative lists, whilst experience with demand-side measures such as reference prices, co-payments, and generic substitution and education of health care professionals and the public is mixed. Private health care insurance schemes all have reference pricing

systems in place, and accompanying co-payments if patients elect to use more expensive products outside the formulary and reference prices. Government enacted provisions for mandatory generic substitution, and although this and other measures have seen generic usage increase from the mid-20% in 2002 to around 60% by volume (IMS Health, 2014a), there is still scope for more growth. To this extent, the government can do more to educate patients about the safety, quality and efficacy of generic medicines, as well as the benefits for patients and health systems. This is an area that still requires much work.

There is general acceptance that the introduction of the SEP regime has resulted in a downward impact on the prices of medicines. The graph in Figure 11.1 is drawn from data from the Council of Medical Schemes, which publishes an annual report detailing, among other things, total health care expenditure in the private sector, and looks at the contribution of the various players.

The Department of Health reported savings of 19%, made up of 25–50% for generic medicine prices and 12% for originator medicines.[9] IMS Health reported an average drop in medicine prices of 24% between June 2003 and June 2006 (Vokes, 2007) since the introduction of the SEP. Similarly, Emsley and Booysen (2004) reported that the introduction of the SEP had resulted in a reduction of 36.7% in the prices of quetiapine and 13% for haloperidol. Admittedly, that paper was published a few months after the introduction of the SEP, so it is

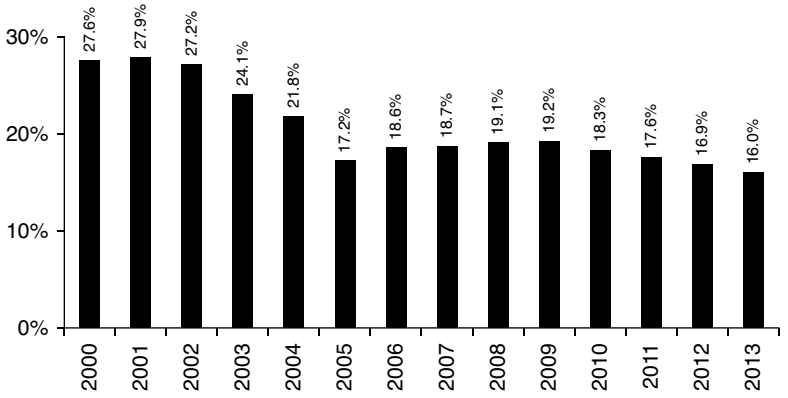

Figure 11.1 Medicine contribution to total private health care costs

Source: Drawn by the author from data from Council for Medical Schemes (2014).

not clear if the reductions have been sustained. Further evidence of the impact of SEP on prices was reported by Steyn et al. (2007), who demonstrated that the SEP regime had reduced the average cost of anti-diabetic medicines by around 29.6%. Finally, the biggest private health insurance company, Discovery Medical Aid, reported: 'Because of the single exit price legislation, these drug price reductions benefit all users in the private healthcare system. Conservative estimates suggest total annual savings of about R 319 million per year are achieved for the scheme in medicine expenditure' (DHMS, 2012).

The media and other parties have also reported extensively on the impact of these price regulations. For example, the *Mail and Guardian*, South Africa's leading weekly newspaper, reported on 26 February 2008: 'The introduction of medicine pricing regulations a few years ago resulted in a 20% drop in prices, and savings of over R 2.3 billion on medicines'.

Other reports and theses, especially looking at the impact of the SEP on the pharmacy profession, and occasionally on the patient, do however offer a different view of the impact. They describe a profession decimated by the regulations, with multiple closures of pharmacies, especially in rural areas. Although critically important and requiring further critical academic enquiry, they are outside the scope of this chapter. There is also anecdotal evidence that the early gains made may be slowly eroding as the contribution of medicines to overall health care costs continues to creep up, albeit slowly. Whether this is purely a factor of the SEP policies starting to fall short, or because of increased medicines usage, or the impact of pseudo-generics which tend to crowd out true generics and inflate prices, or other factors, requires further study.

SEP impact on manufacturers and access to medicines

It is accepted internationally that the entry of generics significantly widens access to medicines, and the size (volume) of the market often expands after patent expiry. The impact of the SEP regime on access to medicines is an area that still requires further investigation.

The reference prices are normally set with the first generic entrants and often undergo revisions with further entry. In certain instances, the revisions have been quite dramatic, leading to wholesale price decreases, further lowering the price of the drug and indirectly promoting access. The case of simvastatin is instructive. Simvastatin is highly genericized, with the first generic product launched in 2002 by Adcock Ingram. Adcock remained the clear market leader despite other generic alternatives. In 2009, Michol, a new simvastatin generic entrant, came in at a

very low SEP, and as a consequence the prices of a pack of 30 simvastatin tablets dropped from over R120 to around R25. Arguably, the effect of this would have been to increase access by patients, especially those who pay out of pocket for package deals that include consultation fees and medicines from family practitioners.

The impact of the SEP has also come through in capping prices through private medical schemes' reference pricing systems. All the private medical insurance schemes have their own reference pricing systems to set the maximum price a scheme will pay for a generic drug. The effect has been to force newly launched generics to price below the reference price, and in some instances to compel the innovator to drop their prices or face the risk of their products facing co-payments. Similarly, if, for competitive reasons, a generic manufacturer drops prices drastically and sets a new reference price, other companies are forced to follow suit or face the prospect of co-payments, which will deter patients.

Impact on manufacturers

Manufacturers have complained that the SEP regime has put the sector under pressure, as the SEP increases are insufficient to offset the effect of the weaker Rand, coupled with wage and utilities inflation. This leads to reduced earnings and threatens the commercial viability of some product lines. Given that most companies import both the active pharmaceutical ingredients and other raw materials from overseas, the weakening of the Rand in a price-controlled environment leads to significantly higher cost of goods sold, without the recourse to increase prices to offset that. This is particularly so because although the regulations have a mechanism for extraordinary prices increases, companies complain that the process is onerous, hugely bureaucratic and difficult to access. These pressures have led to some manufacturers discussing discontinuation of some products. Recently, it was reported that Fresenius Kabi had withdrawn one product, Voluven, from the market, although the company stated that the withdrawal was not related to cost pressures (Bateman, 2014).

Delays are also a major problem for manufacturers. When a company applies for an SEP for a new product, or informs the Department of an SEP price adjustment, the Department 'approves' and then notifies price vendors such as Medikredit. The product is then allocated a NAPPI (billing) code, after which it can be sold on the South African market. Companies complain that delays in assessing the SEP applications and informing vendors delays market access for new products, and in the case especially of first-to-market generics, restricts and denies patients access to cheaper products. Although the regulations envisaged that the

SEP would be agreed within 48 hours of notifying the Department of Health, the process has evolved to one of 'approval', and delays of up to a month are not uncommon.

The potential closure of independent community pharmacies in rural and remote areas, mentioned above, may clearly reduce access. The Pharmaceutical Society of South Africa opposed the SEP regulations and the dispensing fees on the basis that they threatened the viability of independent community pharmacy. Since the early court challenges, there have been widespread reports that some community pharmacies did go into bankruptcy. The Pharmaceutical Society of South Africa reports that many small town and rural pharmacies have closed (PSSA, 2014) negatively affecting access. Dodd (2007) demonstrated that independent pharmacies saw net profits fall, that the price controls could push some pharmacies into bankruptcy and that closure of pharmacies in remote and rural areas would render the distribution of medicines economically unviable and thus affect access.

Some contend, furthermore, that the SEP regime has the unintended consequence of keeping prices higher than they would otherwise have been. They argue that late entrants often find it impossible to offer discounts on the prevailing prices, given that medical schemes will still reimburse up to the level of the reference price, so there is no incentive for pharmacists to offer the lower-priced product. This is compounded by the fact that the dispensing fee is calculated as a percentage of the price of the drug, inadvertently incentivizing pharmacists to dispense the highest-priced generic as long as it is within the reference price band.

Finally, it is argued that the SEP regime creates a disincentive for new entrants to offer lower entry prices. Some experts believe that because companies know that they will struggle to get price increases (Medical Chronical, 2012) sufficient to offset inflationary pressures and Rand weakness, among other challenges, they deliberately set high prices from the outset, possibly reducing access. The proponents of this view note that medicine prices in South Africa are artificially inflated, and higher in comparison to the same products in other countries.

Conclusion: are there lessons for other African countries?

South Africa embarked on the SEP path exactly a decade ago, informed by the realization that, as public utility goods, medicine prices could not be left to the vagaries of the market. In that time, there has been much acrimony, public disagreements in the media and other public spaces

between the main protagonists. Throughout all of this, the Department of Health, backed by the government and the ruling party, as well as public health and patient advocates, held firm. There have been threats of court cases, and many actual court cases, which have invariably led to iterations of the dispensing and logistics fees. What has emerged, though, is that through proper consultation and a willingness to open up and present the evidence base for positions held on various issues, it is possible to move towards negotiated positions. The first critical lesson for those who would want to embark on the price regulation route, therefore, is the absolute necessity of having clear and unambiguous political support for reform. Without this, there is no hope for success.

The second key lesson from South Africa's journey with price regulations is the necessity of involving all key stakeholders in the process very early on. Governments and policy makers must take the private sector into their confidence and clearly and firmly explain the rationale for their decisions, ensuring that all views and all aspects are taken into consideration beforehand. Arguably, if the South African Department of Health had embarked on an exercise with the pharmacy profession, escorted by reputable independent and honest brokers, to arrive at a reasonable and evidence-based dispensing fee, there would have been no need for court cases, nor for the time spent in the last couple of years on endless consultations and the various iterations of the dispensing fee.

Third, it is imperative to collect the evidence base to guide policy decisions to be taken before embarking on a price reform process. This means making a full and thorough assessment of the entire distribution chain and finding the factors at play with each of the stakeholders. In the South African example, the R26/26% dispensing regime was no danger to the big retail chains, but threatened the survival of the small community pharmacy.

Fourth, it is imperative to make both the interpretation and implementation of any regulatory processes as simple as possible. The complexity that crept into the South African SEP regime and the bureaucratization of the process only served to make the pricing regime more unpopular. A measure of predictability and certainty around the application and approval process, the time periods for taking the increases and so forth would have lessened the tension between industry and the regulators.

Finally, although the SEP regime seems to have had a positive impact on prices, it is clear that supply-side measures on their own have only limited impact. It is thus critical for those governments that intend to regulate prices to devote equal attention to the demand side. This can be

done, among other methods, through massive patient education about the benefits of generic medicines, the incentivization of health care professionals to prescribe or dispense the cheapest products – above and beyond the dispensing fee – and the need to adopt generic prescribing across the board.

Notes

1. National Department of Health, South Africa – Tender analysis by author, from data accessed in December 2014 at http://www.doh.gov.za/mpc3.php.
2. The Constitution of the Republic of South African – 'Everyone has the right to have access to – a) health care services, including reproductive health care'. Section 27 (1) (b) of the Constitution further mandates the state to, 'take reasonable legislative and other measures, within its available resources to achieve the progressive realisation of the right'.
3. The Medicines and Related Substances Control Act 101 of 1965 as amended.
4. Department of Health. Regulations Relating to a Transparent Pricing System for Medicines and Scheduled Substances. GG No R 553 30 April 2004.
5. Department of Health. Regulations Relating to a Transparent Pricing System for Medicines and Scheduled Substances. GG No R 553 30 April 2004.
6. National Department of Health – Regulations relating to a transparent pricing system for medicines and scheduled substances made in terms of Section 22G of the Medicines and Related Substances Act, 1965 (Act No 101 of 1965).
7. *New Clicks South Africa (Pty) Ltd v Tshabalala-Msimang and Another NNO*; *Pharmaceutical Society of South Africa and Others v Tshabalala-Msimang and Another*.
8. The Supreme Court of Appeal of South Africa – In the matter between The Pharmaceutical Society of South Africa AND Others and the Minister of Health and ANOTHER, New Clicks South Africa (Pty) Ltd and Dr Manto Tshabalala-Msimang and ANOTHER, Case No 542/04 & 543/04.
9. A presentation by the Department of Health on Medicine price regulation – the South African experience (2009).

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12

Pharmaceutical Standards in Africa: The Road to Improvement and Their Role in Technological Capability Upgrading

Geoffrey Banda, Julius Mugwagwa, Dinar Kale and Margareth Ndomondo-Sigonda

Introduction

This chapter discusses standards, an elusive term and concept. For the African pharmaceutical sector especially, the term is used by the manufacturing sector, regulators, technical experts, procurement agencies, health system actors and policy makers to mean different things. There is a dearth of systematic studies that address what standards are, their classification and the logic behind their set-up and operation, and this has contributed to a huge asymmetry in understanding. The socio-economic, technical and political issues and how they have an impact on local production and industry development, including their effects on access to markets, have also not been systematically explored.

A common understanding of standards, their classifications and development, is important as the continent implements the African Union's Pharmaceutical Manufacturing Plan of Action (see also Chapter 15). Even more important is the need for African technical experts, regulators and policy makers to realize that standards and their development in the pharmaceutical sector is a process under their control. They can drive agenda setting and design realistic and context-sensitive road maps which align local industry development without compromising public health safety. The ability of policy makers to take a critical approach to the meaning and use of standards in the African pharmaceutical sector is an important enabler for designing road maps.

In this chapter we set up some of the issues that need further debate. We deconstruct standards and classify them into two groups; technically based standards and organizational or institutionally based standards. Technically based standards cover product, process, plant and environmental aspects. Organizational or institutionally based standards are those which are important for creating market confidence in firms' output through assuring the credibility and legitimacy of products, quality, production, distribution and recall processes. This credibility and legitimacy arises from physical inspections of production and distribution facilities, and the availability and examination of documentation and data management processes – administrative activities essential for endorsement, certification and accreditation.

We argue that this perspective helps to build an understanding of which types of standards are 'mutable'[1] – that is, judgement-based standards such as inspection, certification and accreditation for which capability building and improvement is a gradual process. By contrast, standards which cannot be compromised are those which deal directly with patient and public health safety concerns, namely quality, safety and efficacy of medicines. Such distinctions aid technical and policy people in designing and implementing appropriate interventions and road maps for technological capability and standards upgrading which do not compromise locally manufactured medicines' quality, safety and efficacy. These distinctions also help in crafting responsive, context-sensitive standards and compliance development processes that do not impose unnecessarily high costs or regulatory barriers on existing local industry. Our discussion of standards is informed by extensive literature searches, fieldwork in India, Kenya, Zimbabwe and South Africa where we interviewed technical experts in 2014, and interaction with regulatory and compliance experts in the UK.

A brief historical perspective

The history of standards in the pharmaceutical industry is traceable to adverse events in patient safety, and one of the notable failures was the 1950–60s thalidomide disaster (Grabowski et al., 1978), in which a morning sickness pill containing thalidomide taken by pregnant mothers resulted in newborns with severe birth defects. The disaster catalysed stringent drug approval and monitoring processes, necessitating the passing of the Kefauver-Harris Drug Amendments Act in 1962 which called for proof of safety and efficacy in the approval process, approvals that now use animal testing and clinical trials that can take

up to 12 years. The logic for the development of stringent regulation was that there was a need for an independent government regulatory agency to ensure public health whose goals were not compromised by commercial interests of pharmaceutical companies (Abraham, 2002). All stages of the drug life cycle are regulated from drug discovery to release of the drug on the market (Harper et al., 2007). Table 12.1 summarizes five key stages in the life cycle of a pharmaceutical drug, and the regulatory requirements or standards pertinent for each stage.

For drug discovery, the key guideline is good laboratory practice (GLP), and for phase 1 to 3 clinical trials the guideline is good clinical practice (GCP). When the drug moves to the production phase, good manufacturing practice (GMP) becomes the guiding regulatory requirement, followed by good distribution practice guideline for distribution covering traceability of medicines (systematic identification of products) to aid in organized defective product recall from the market. For post-market surveillance, pharmacovigilance is the regulatory requirement. In addition, there is a wide range of other regulatory requirements at

Table 12.1 Drug life cycle stages and regulatory requirements

Drug life cycle stage	**Regulatory requirements/Guidelines**
Drug discovery	Good laboratory practice (GLP): these guidelines focus on toxicological safety and protection of the test subject
Clinical trials (phases 1, 2, 3)	Good clinical practice (GCP): these guidelines consider product efficacy and safety evaluation, as well as individual protection and safety during testing
Manufacturing	Good manufacturing practice (GMP): these guidelines are concerned with assuring a manufactured product's quality, safety and efficacy, for both the product and the patient. The process aims to build in quality and ensure quality standards.
Distribution	Good distribution practice: these guidelines deal with storage, transportation and traceability for product recall.
Post-market surveillance	Pharmacovigilance: Sometimes called phase 4, this is monitoring of the product after market authorisation to check for any adverse events or product failure in all respects.

Source: Adapted from Harper et al. (2007) and Muller et al. (1996).

supranational and national levels, inspired by public health concerns and safeguards against drug disasters, to address trade and market entry obligations (Immel, 2001).

The situation is less complex and expensive for generic medicines, which are modelled on branded drugs, since proof of safety and efficacy has already been demonstrated for the branded drug. The generic drug producer needs at the minimum to demonstrate the equivalence of the drug for approval and it does not go through rigorous clinical trials. The bulk of medicines produced in Africa are generics, and consequently the standards that we will discuss in this chapter focus on generics manufacture. We do not cover standards in drug discovery and clinical trials.

While the first set of GMP guidelines for manufacturing, processing, packing or holding finished pharmaceuticals was introduced by the US Food and Drug Administration (FDA) in 1963 (Immel, 2000), the WHO has spearheaded the standards-setting process since the late 1960s, coming up with several amendments and extensions to the guidelines. In this chapter we focus on good manufacturing practice (GMP), defined by the WHO (2004) as the part of quality assurance that ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by market authorization. Many countries, including India, Kenya and South Africa, have developed their own GMP guidelines based on the WHO guidelines. The WHO is thus a global technical agency responsible for setting standards and normative guidance and for establishing best practice, all of which are implemented through national drug regulatory authorities (DRAs) and other relevant institutions. There is criticism, however, that the WHO sets standards for all its member states regardless of the level of development. There is also some questioning of the way in which the WHO has shifted from a solely advisory body (technical assistance included) towards acting as a regulatory body after it began pre-qualifications of pharmaceutical products for developing countries. WHO prequalification has acted as a catalyst for upgrading facilities in developing countries, but its stringent requirements have also been an impediment to market access to global donor-funded medicines purchase, in particularly for HIV/AIDS, TB and anti-malarial drugs.

Standards, their establishment and assurance

A standard can be viewed broadly as a consensus between different agents to do certain key activities according to agreed-upon rules (Nickerson and Muehlen, 2006). This is a definition of standards as a process: a

common and agreed understanding of the rules of the game and how it is played, which resonates with the definition of institutions. These standards, therefore, operate on the back of strong institutional and organizational arrangements empowered to certify compliance with set rules through proclamations or a tightly controlled allocation of insignia or certification. Independent validation from a third party is critical for building confidence of other stakeholders who lack inside information or the means to gather credible information to make informed decisions. Standards therefore provide consumers with a basis for making informed consumption decisions and manufacturers with a benchmark of best practice (Nadvi, 1999) and hence a competitive tool.

A technology standard, on the other hand, is defined as 'a set of specifications to which all elements of products, processes, formats or procedures under its jurisdiction must conform' (Tassey, 2000: 58). This form of standards has been credited with the standardization that has significantly reduced manufacturing costs through economies of scale achieved by mass-production of similar or 'standard' components (Katz and Shapiro, 1985; Farrell and Saloner, 1986). It is argued that the presence of standards reduces uncertainty by providing actors with a framework that enables widespread diffusion of a technology (Rosenberg, 1976), as well as a modular approach to the production process where components can be manufactured by different producers.

Organizational or institutionally based standards interact with technology standards through the processes of data or process interrogation against set norms, validation, acceptance and certification. Thus certification and/or accreditation of products or firms affirm that accepted best practice (norms), 'standardized' and imbued with accountability, has been used at various stages in a product's design, development, manufacture, distribution and disposal. Specifically for the pharmaceutical sector, inspection, validation, certification, accreditation and regulation provide a system of traceability and accountability. This is done through detailed verification of quality-dependent procedures through internal and independent audits, quality training of personnel and constant monitoring of quality performance measures (Nadvi, 1999), as well as market performance and rectification in cases of failure.

Government departments, regulatory agencies, pharmaceutical companies' industry associations and other stakeholders play key roles in the design, implementation and refinement of policies and standards governing the sector. The credibility of a standard setting and monitoring process depends on the representativeness of the political process, how well it exploits existing technical knowledge, matches

context of application, and how committed participants are to the issue at hand (Fischhoff, 1984). These processes inherently reflect different interests, power structures and the resources of different stakeholders. Consequently and at the heart of this discussion, low-income countries tend to typically be 'standard takers' rather than 'standard makers', with the responsibility for implementation, monitoring and enforcement of the standards resting with the national governments (Stephenson, 1997), which in many African settings are resource-constrained. It is with this background to technical and organizational/institutional standards that we argue that African technical and policy organs need to gain a confident understanding that designing and implementing a road map to improving standards in the pharmaceutical value chain is something that is and should be under their control.

Standards as tools for competition and pressure to improve

The significance of standards has grown over time and they have come to represent an important locus of collective strategy (Astley and Fombrun, 1983) within which the 'rules of the game' are set (Jain, 2012). For many producers and service providers in both the global North and South, compliance with international standards can add a competitive edge and form a necessary condition to access niche markets (Nadvi, 1999). More recent research emphasizes that standards provide opportunities and incentives for low-income countries to modernize local industry and strengthen supply of quality products (Jaffe and Henson, 2004; World Bank, 2005). This growing evidence base suggests that in low-income countries standards can link upgrading local industrial capabilities with supply of medicines and hence better local health service quality and inclusiveness (Nadvi and Waltring, 2002).

It has been argued that good-quality and affordable pharmaceutical products, whether imported or locally produced, depend largely on the outcome of standards-based competition (Narayanan and Chen, 2012). In the international trade literature, research suggests standards can be non-tariff barriers to trade (Stephenson, 1997; Wilson and Abiola, 2003), with regards to labour (Maskus et al., 2004; Maskus and Wilson, 2001) and environmental standards (Anderson, 1996; Anders and Caswell, 2009). These barriers emanate from inadequate provision of finance, local governance and regulatory structures. Kaplinsky et al. (2011) considered how standards such as hazard analysis critical control points (HACCP) and International Standards Organisation (ISO) are used as non-tariff barriers, especially for resource-constrained

countries. Supporting this assertion, a growing body of literature shows that without financial and technological support for domestic manufacturers, standards create significant cost and international market entry barriers (EC, 1997; Nadvi, 1999; Stephenson 1997).

International procurement practices and requirements of donors often enforce higher pharmaceutical quality standards than stipulated by national regulatory authorities. Implementation of these higher standards by local firms and achieving certification requires investment in people, equipment and changes in production organization as well as management practices – a costly exercise. Multiple accreditation caused by the need for local, regional and international certification such as WHO pre-qualification has direct negative bottom-line impact. One African firm reported during fieldwork that a WHO pre-qualification inspection can cost as much as US$100,000, a large financial burden especially if accreditation and certification is not supported by success with global health and international medicine supply tenders. As a result, some local industrialists have questioned the logic of solving national-level institutional failure at supranational level. They argue that it is better to strengthen local regulatory authorities or take the harmonization route by solving the institutional challenges at national or regional level. These criticisms inform our critical discussion of standards, what they are and how road maps for improving standards and industry capabilities can be crafted.

The need to deconstruct standards

A respondent from Kenya on being asked what standards were, remarked as follows: 'this is where we have a problem ... the word "standard" is misused both at global and national levels'. Such a remark underscores the need to deconstruct standards and classify them. He went on to describe what he considered to be standards, such as the guideline that describes good manufacturing practice (GMP) (which he termed a standard in itself), facility standards and personnel standards, as some of the key issues to be considered. In this section we discuss consecutively the two types of standards identified above: technical standards and institutional or organizational-based standards

Technical and process standards

GMP guidelines are intended to be a set of minimum standards, covering recommendations on quality management, personnel, production facilities and equipment, documentation and records, production and

in-process controls, packaging and identification labelling, storage and distribution, laboratory controls, validation, complaints and recalls, and contract manufacturers (WHO, 2004). The diverse range of issues covered by GMP guidelines not only makes them a key and central lens for our discussion of pharmaceutical standards but also highlights why these guidelines are one of the most contested yet key drivers of the pharmaceutical industry. Under GMP we have chosen to focus on four standards that emerged as key in our research. Two of these standards (product and process) were classified as those which should not be compromised because of their direct relationship with patient and public health safety. The GMP process is critical for ensuring product quality, safety and efficacy. As noted in Chapter 3, GMP standards constitute a 'production culture' interwoven with professional judgement as regulators decide on what is deemed adequate especially for processes and facility standards.

Product and process standards

There was consensus among the multinational and local pharmaceutical manufacturers interviewed on the fact that product and process standards cannot be compromised. These they argued, should be the same wherever medicines are produced in the world. These standards are engineered in such a way that quality is built in and checked for at various stages and the evidence meticulously documented. The suppliers of raw materials have their facilities, processes and products vetted, and on receipt, raw materials are sampled and subjected to specific physical, chemical and biological tests. Raw materials are carefully stored ensuring avoidance of cross-contamination. There is a clear and documented chain of custody, traceability and accountability that is established along the whole process. In many African countries the production pharmacist is ultimately responsible and accountable for the release of batches of products after compliance with product and process standards as well as quality control tests. The quality control tests cover chemical, physical and biological characteristics of the product and avoiding contamination in the same three areas. Some of the tests, for example for tablets, include microbial tests, hardness and how well the tablet dissolves.

The drivers of product and quality standards are people, the production equipment and laboratory equipment. Improving standards therefore requires in many instances equipment and skills upgrading. For example, a Zimbabwean firm improved ingredient drying in the wet granulation tablet-making process by investing in a high-capacity fluid bed dryer. They also invested in automatic capsule-filling machines to improve standards and productivity. On the question of whether

technical standards change there were diverse opinions in the interviews. Some respondents argued that technical standards do not change, whereas some regulators reported that technical standards have become more stringent with time. One interesting perspective came from a technical expert who when asked by researchers in Tanzania whether very stringent GMP is necessary, argued that for infusions and injectables (parenterals), it was essential that they have to be sterile because they go straight into the bloodstream. However, he said, for tablets, the minimum safe requirements are different because they go into the stomach. Yet, he argued, current requirements are that they should be 'almost sterile', a standard hard to attain for manufacturers in Tanzania, and more stringent than essential good hygienic standards using good SOPs (standard operating procedures).

It is insights or perspectives such as these that need to be debated by those responsible for designing the road maps for upgrading standards in all their forms for the pharmaceutical sector. Our discussion, however, does not delve into the technicalities of GMP and the specific tests and indicators of quality. Our intention is to spark debate. In separate conversations, UK compliance experts acknowledge that there are different interpretations of GMP. What the US FDA means by GMP compliant is not necessarily what Europe's EMA means by GMP compliant and by extension what different African countries mean by GMP compliance. This argument resonates with the standards of the regulators as referred to by a Kenyan technical expert. It therefore becomes difficult according to the Kenyan expert to bring into one country a product produced in another, hence the African regulatory harmonization efforts described later in this chapter.

Facility and personnel standards

Another set of standards that technical experts in Kenya identified are facility and personnel standards. These encompass environmental and structural standards for buildings and health, educational and technical standards for personnel (which are often assumed). One Kenyan respondent remarked that '[facility standards] – that's where the problem of Africa lies'. He reported that facility standards are assumed but not clearly enunciated by regulators, and are especially problematic for old production facilities that have to be refurbished. A Kenyan respondent said, for example, that the WHO talks of 'competent people and suitable premises' in its requirements for pre-qualification – which, however, leaves a lot of room for different interpretations. Facility standards are linked to environmental standards and determine air quality and

freedom from contamination through physical separation. Personnel standards include technical know-how, hygiene standards (medical check-ups included) and administrative skills as discussed later. Thus personnel standards cover diverse skills sets depending on functions, which might include but are not limited to analytical and organic chemistry, microbiology, plant engineering, production, pharmacovigilance, quality assurance and research and development. Facility and personnel standards formed the class of standards for which improvement, according to the technical experts we interviewed, should be approached in a gradual and cumulative manner. In Tanzania, regulators reported that they know that the firms are growing and they give them 'timelines' for improvement. These are the classes of standards that we classify as being mutable.

Organizational/institutional aspects of standards

The supply of medicines and other medical products into the health delivery systems is intensively regulated and governed by strict product, process, marketing and institutional standards. The need for regulation comes from information asymmetry between the producers on one side and patients and clinicians on the other side. Patients cannot assess safety or observe quality and efficacy of medicines on their own, and neither can the medical practitioners who decide on their behalf (Harper, 2007). This is where regulatory bodies come in, by seeking evidence of compliance with guidelines, rules and regulations to give credibility and legitimacy to organizations inspected. Accreditation and certification are an institutionally based regime of standards that are built on and meant to validate the technical, process, facility and personnel standards as reflected in the various guidelines such as GLP, GCP, GMP, Good Distribution Practice and pharmacovigilance.

The challenge for Africa rests in skills shortages at the regulator and among compliance managers at firms. As the firm operates, it records data which must be managed and produced as evidence to the regulators (inspectors). This process requires someone with a technical background who also is conversant with data management and documentation. The regulators in addition to the physical inspections also analyse documents and check against the set norms. As discussed earlier, this is where the judgement of the assessor (regulator) comes into play. These standards are of an organizational and institutional nature and are dominated by soft issues of training and retaining human capital.

These institutional/organizational standards tend to be resource-driven and path dependent. Their evolution depends in part on historical

legacies of national institutions, industrial capabilities and tertiary training that included practice-based polytechnic training. South Africa and Zimbabwe as a result have relatively well-developed medicines regulatory systems. For South Africa the main piece of legislation shaping pharmaceutical standards is the Medicines and Related Substances Control Act (1965) and its various amendments. The Medicines Control Council (MCC), a public sector body tasked with regulating pharmaceutical products in South Africa has eleven expert committees, which evaluate the safety and efficacy of a drug submitted for approval and they inform the decisions of the MCC. Apart from the Registrar of Medicines, all members of the MCC committees are engaged on a part-time basis, including the evaluators, who are often in full-time employment elsewhere. There is, however, concern on such a heavy reliance on external expertise.

The Medicines Control Council (MCC) comprises four units, inspectorate and law enforcement, operations and administration, clinical and medicines registration. These units perform an administrative and coordinating role, facilitating the work of the expert committees. The MCC works within, and is influenced by, the public sector institutional context, as well as serving as the local competent authority for monitoring implementation of requirements from agencies such as the WHO, FDA and ICH in pharmaceutical manufacturers operating in South Africa. In terms of skills, respondents in South Africa also identified loss of regulatory skills especially at regulatory bodies as a key challenge. They reported that it took a long time to train a competent regulatory person, especially those with industrial experience, and as a result they are perpetually in training mode. The firms also reported that they face the same skills training and retention problems.

Harmonization to upgrade regulatory standards

An interesting issue identified by experts in the Kenyan pharmaceutical industry was the issue of the 'standard' of the regulatory bodies themselves. Different countries have different regulatory capacities and capabilities. Highly resource-limited countries do not have the same capacity and capabilities as resource-rich countries. As a result, manufacturers fear that accreditation by one country does not equate to the same level of stringency as accreditation by another. Interviewees reported that some countries in the East African region had few regulatory pharmacists who looked at dossiers and at the same time had to do factory inspections – an impossible task.

These realities are some of the catalysts for regional medicines harmonization initiatives such as the African Medicines Regulatory

Harmonisation (AMRH) initiative led by the New Partnership for Africa's Development (NEPAD). In recognition of regulatory capacity limitations for some countries and its consequent socio-economic impact, NEPAD Agency undertook, in collaboration with partners[2] to initiate the African Medicines Regulatory Harmonization (AMRH) Programme since 2009. The AMRH initiative is part and parcel of the implementation of the African Union Pharmaceutical Manufacturing Plan for Africa (PMPA) (see Chapter 15) and aims to facilitate access to quality, safe and efficacious medicines to the African people by working through the existing political structures, and the regional economic communities (RECs).

In particular, the initiative aims to catalyse the establishment of effective national, regional and continental medicines regulatory agencies, and has made significant progress since 2009 in Eastern, Western and Southern Africa towards transparent, efficient and effective regulatory systems that provide assurance of faster approval of medical products and technologies that meet internationally acceptable standards of quality, safety and efficacy. Some of the key aspects focussed on are harmonized guidelines for registration of medicines, good manufacturing practice (GMP) inspection guidelines, quality management systems (QMS) and information management system (IMS).

Through NEPAD Agency's coordination, the East African Community (EAC) successfully launched the Medicines Regulatory Harmonization (MRH) programme in March 2012, and is now at implementation stage with substantial progress made in the endorsement of the harmonized guidelines for registration of medicines, good manufacturing practice (GMP) inspection guidelines, quality management systems (QMS) and information management systems (IMS). The NEPAD Agency has undertaken to expand the AMRH programme to other RECs beginning with the Economic Community of West African States (ECOWAS) through its health agency, the West African Health Agency (WAHO) in collaboration with the West African Economic and Monetary Union (UEMOA). The MRH Programme for West Africa was launched on 2 February 2015. Progress has also been made on implementation of the programme in the Southern African Development Community and central African regions.

Cost implications of standards

Regulation raises numerous questions concerning compliance costs in relation to benefits obtained, transaction costs associated with regulatory administration and enforcement, and unanticipated or unwanted responses on the part of the regulated industry. Regulations may have

high individual compliance costs, which are compounded by the fact that organizations are simultaneously attempting to comply with other, possibly conflicting regulations. When regulatory standards or mechanisms conflict, they may prevent one another from achieving their intended benefit. Increasing legislative controls in highly complex, and heavily regulated arenas such as health care can lead to 'regulatory inflation' rather than enhanced compliance. Moreover, the risks of compliance failures and regulatory inflation are heightened in the field of healthcare because jurisdiction is often fragmented and operates at multiple layers from global to local levels (Mugwagwa et al., 2015).

The consensus from South African respondents with respect to standards was that innovation, technological capability upgrading and health delivery were cost-sensitive processes, and that while adopting and keeping standards came at a cost, higher costs were being incurred from policy and regulatory uncertainties on the one hand and inefficient quality assurance systems on the other. Trying to curb costs today by compromising on standards would lead to 'fewer drugs to treat current and future generations', but taming the policy and regulatory jungle to ensure cost-effective and sustainable compliance with standards would be good for companies, regulators and patients in the short and long runs. Multiple accreditation has direct bottom-line impact.

The Kenyan standards and upgrading road map

Respondents in Kenya were in general agreement that product and process standards are necessary and that they should be seen as 'minimum regulatory expectations' required to manufacture a product that meets specific needs, that is, fits the purpose for which it is made. Kenya has developed a road map for upgrading standards. They acknowledge that it is a gradual process requiring multi-sectoral coordination and concerted efforts. In an interview, an industry expert involved in designing and developing the road map for the country said:

> So we came up and said you must solve the problem, but it's not a small one … we looked at the whole scenario and came up with seven key areas

which are detailed below as direct quotes:

1. You must have a road map for the local industry to improve because you cannot shut down any one of them because they have been producing.

2. You must have a system where you check the quality of the product on the market and remove the ones which are not performing and remain with those which are performing well.
3. You must have someone overseeing the market and industry and that is the regulator, you must incentivize the capacity and improve its capacity.
4. Whereas the industry is trying to achieve the standards, it's going to cost money, so you should look for a way where they can get the money.
5. You must provide the incentives for the time the industry is improving, they must not improve and lose their market, so you must protect it and come up with incentives that will help them.
6. You must come up with a strategy for capacity building of human [skills], their capacity to undertake this both in the regulatory and in the private sector
7. There are those items which are essential for the industry to place their products on the market, but not one single company can do it alone, so you must put them together and see how they can be shared, and this is what you call the support services or shared platform.

Recognizing that they could not do all seven activities at once, they prioritized the first initiative. They developed the road map, and by mid-2014 the technical aspect had been completed and they were waiting for the narrative part of the document, endorsements and final launch. A concerted effort to involve industry, regulators and the Ministry of Industrialization was made during the process of developing the road map (Technical Expert, Kenya, 2014). The technical expert through his networks brought together the ministers for health and industrialization in a joint meeting to discuss the road map.

Money for upgrading processes and standards

Kenya realized that the process of upgrading production facilities and machinery would impose financing constraints on affected firms. The fourth point in the strategy above deals with the need to facilitate funds availability. To that end they engaged the Kenyan Bankers Association, who informed them of their fears about funding pharmaceuticals production. According to the pharmaceutical industry respondent, the bankers said: 'We are risk-based institutions, we go only where there is less risk, but in pharmaceuticals the risks are so high that we dare not'. This statement points to issues of finance capability on the part of banks (see Chapter 15). Reinforcing the challenge of finance capability,

one respondent cited an example of a Development Bank which refused to fund a quality control laboratory because they said they could not demonstrate what would come out of the laboratory. The pharmaceutical technical expert argued that the bank failed to see the overall picture and how the quality control laboratory would result in better production processes and products. The bankers themselves acknowledged that they lack a deep appreciation of the industry dynamics:

> We have never got an expert who we can trust to go there [pharmaceutical industry] and do an evaluation; and I said to them then I should become a banker. (Technical expert, Kenyan pharmaceutical sector, 2014)

Efforts are under way to bring industrialists and bankers together to try and bridge the gap in knowledge about the sector and hence improve risk analysis. Kenya's road map, however, evidences a purposive and integrated approach to improving standards and upgrading facilities. In interviews the technical experts acknowledged that this would be a long process the success of which depends on availability of resources for investment in equipment and people. The programme in Kenya is being supported by UNIDO, supplementing limited national resources allocated to this important initiative. Kenya appears to be taking control of the issue of standards, and although they are still at the initial steps of implementing the programme, there are lessons that other African technical and policy people can learn.

Initiatives focusing on building capacity and capabilities on standards in local manufactures require coherence/harmony between different approaches. Some global institutions working with African countries, such as the WHO, take a product-by-product approach to standards (WHO pre-qualification), whereas UNIDO and GIZ take a systemic technological approach. This helps to explain different approaches to improving standards in African countries. UNIDO and GIZ prefer to build local technical skills by training local industry. In the next section we look at the Indian standards upgrading to extract lessons that Africa can use.

What lessons can Africa learn from the Indian GMP upgrading road map?

Over the last three decades the Indian pharmaceutical industry has emerged as a major supplier of cheap generic drugs across the world.

The Indian government was credited for infusing life into the Indian pharmaceutical industry through industrial and regulatory policy intervention, and the success of the Indian firms made these interventions a recipe for pharmaceutical industrial development in other emerging countries (see also Chapter 10).

Pharmaceutical production in India is governed by the Drugs and Cosmetic Act of 1940 and the much amended Drug and Cosmetics Rules of 1945. The Act and Rules regulate drugs imported, manufactured, distributed and sold. No pharmaceutical products can be imported, manufactured, stocked, distributed or sold unless they meet the quality standards laid down in the Act. An Indian Pharmacopoeia was published in 1955, and over the years problems in controlling spurious or counterfeit medicines have dominated Indian policy agendas. The Indian government initially aimed to enforce GMP standards in all pharmaceutical manufacturing firms via the Drug Policy of 1986. This laid down requirements for GMP adherence in Schedule M of the Rules, which came into force in 1987. Schedule M was strengthened to require WHO-GMP standards, by amendment in 2001, with the aims of ensuring that firms upgraded and of eradicating counterfeit and substandard drugs. Those pharmaceutical firms that did not comply with these regulations have been refused manufacturing licenses from each State Drug Control Administration office. In the case of manufacturing plants approved before December 2001, non-compliance led to their licenses being revoked, forcing closure of these manufacturing facilities.

The financial cost involved in complying with GMP has proved a significant barrier for small companies in India to upgrade manufacturing facilities. Upgrading of manufacturing plants by small scale firms would result in those firms graduating to become medium-scale firms, thereby losing the tax benefits and other concessions available to small scale enterprises. The Indian government responded to this issue by providing some concessions for the Indian firms, increasing investment limits and turnover thresholds for eligibility as a small-scale firm. On the other hand, several large-scale companies upgraded their plants to access high-income country markets, and their significant financial resources made this transition feasible. The deadline for implementation of GMP was postponed from 31 December 2003 to 31 December 2004, and then postponed again until 30 June 2005. Each State Drug Control Administration office also had the authority to extend the deadline of compliance within its area of jurisdiction.

In spite of these concessions, this mandatory application of GMP had a significant impact on the Indian pharmaceutical firms. According to

official estimates, in 2001, 327 pharmaceutical manufacturing plants closed, had their licenses suspended, or were forced to shift to some other state. A total of 370 plants were not in a position to comply with GMP and have closed since 2005 (Planning Commission, 2002, par. 7.1.192). In addition to an increase in competitive pressure, GMP compliance has been another force that has induced the exit of small firms from the market. However, the introduction of GMP has also contributed to the enhancement of trust in Indian products in the global market. In addition, complying with GMP standards of the US and Europe has increased exports to Western countries and expanded the opportunity for contract manufacturing.

Since 2000, the strong presence of the Indian firms in the markets of advanced countries, and specifically in the US, has brought severe scrutiny from regulatory agencies around the world. More numerous FDA inspections led to an increase in the number of warning letters and import bans for the Indian firms (see also Chapter 6). The FDA has identified a number of Indian pharmaceutical manufacturers who have had problems with data integrity and GMP at their respective facilities. Gaffney (2015) notes that since GMP data are intended to ensure that products meet pre-established specifications, absence of credible data management creates concern that these products cannot be trusted.

The case of Ranbaxy provides a prime example of the FDA attitude towards implementation of GMP in the Indian firms. The FDA has repeatedly issued warning letters and import bans to two of the company's manufacturing plants because of data integrity issues. The warning letters note that the FDA has concerns about non-compliance with US current Good Manufacturing Practices requirements, although 'FDA has no evidence of harm to any patients who have taken drugs made in these two facilities' (Jeffrey et al., 2001; US Food and Drug Administration, 2008). Elaborating on their concerns at one of the manufacturing plants, the FDA warning letter focuses on concern that 'written records of major equipment cleaning and use are inaccurate' (USFDA, 2008) and notes that their investigative team uncovered 14 instances 'where ... records for equipment used in manufacturing operations ... included initials or signatures of employees who reportedly verified cleaning of equipment but were not shown as present by security log records' (USFDA, 2008).

Jeffrey (2001) argues that this experience highlights the way in which international regulatory authorities play a crucial and detailed role in setting production and data management standards at the Indian manufacturing sites, using the set of regulations and rules developed to

protect high-income countries' consumers. The cost of implementing and complying with these regulations is incurred by the Indian manufacturers and government and in most cases passed on to the Indian consumers. Further, these regulatory troubles have caused the Indian firms significant revenue losses and reduced competition in generic markets, contributing to profit margins of multinational pharmaceutical companies. This experience raises issues about the authority of developing country governments in setting standards, and about the appropriateness of international standards to the local context in the developing countries.

Concluding discussion

Pharmaceutical standards and regulations are necessary yet complex institutions which change over time, operate at various vertical and horizontal scales, are subject to different interpretations and applications and have potential to assist the manufacturing of, and access to, safe efficacious medicines. However, they can also act as undesirable market entry barriers. African pharmaceutical industry players accept that standards are important, but they contend that the other regions of the world which are more advanced now 'did not themselves improve their standards overnight'. Rather, it was a gradual and long drawn-out process as countries learned best practice from the first movers. African technical experts argue that Africa should not be pressured to catch up 'overnight'. When African and other developing countries look broadly at pharmaceutical standards, they need to view them as a process, and there is therefore a need to introduce clear road maps for a gradual strengthening of the requirements for standards, driven by local or regional regulatory institutions.

We conclude that in order to improve standards and upgrade technological capabilities, first, standards need to be deconstructed and understood based on risk management principles. Second, institutional or organizational standards that are based on judgement and can be gradually improved should be recognized as mutable in that sense. Third, technically based standards should also be viewed from a risk management perspective. Once this has been done, African technical and policy actors need to take control of the issue of pharmaceutical standards and to design and manage context-sensitive regulatory frameworks and road maps backed by an evidence base that draws from a clear understanding of standards, attendant risk profiles and their role in industry development and access to medicines.

Notes

1. We acknowledge Dr Farah Huzair for proposing the terms 'mutable and immutable' standards at an Innogen Knowledge Exchange workshop on African Local Pharmaceutical and Medicines Supply held in London in 2013
2. The African Union Commission (AUC), Pan African Parliament (PAP), the World Health Organization (WHO), the World Bank (WB), the Bill and Melinda Gates Foundation (BMGF), the UK Department for International Development (DFID), the Clinton Health Access Initiative (CHAI) and the Joint United Nations Programme on HIV/AIDS (UNAIDS)

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Innovative Procurement for Health and Industrial Development

Joanna Chataway, Geoffrey Banda, Gavin Cochrane and Catriona Manville

Introduction

> Procurement is then an integral part of health policy. However, it is of course also a part of industrial policy. This is because the way in which purchasing decisions are structured and regulated impact profoundly on the way in which production happens. Thus, consideration of the pros and cons associated with procurement regimes needs to be in terms, not only of whether immediate health policy priorities are achieved, but also in light of longer term sustainability of supply of innovative health products. Thus, price, value and innovation are closely interwoven. (Srinivas, 2012: 126)

Part II of this book has demonstrated that building synergies between health systems and industrial development is a complex process of reshaping the politics and political economy of the two systems. A key tool for building and sustaining health-industry relationships, as Smita Srinivas observes above and as some Part I chapters also emphasized, is procurement. Yet procurement remains under-researched and over-simplified as a technical, linear, ordering and delivery process (see Chapter 8), rather than an exercise in deepening and strengthening the domestic economy through market and non-market relationships building.

This chapter aims to shift the literature on health sector procurement into a more developmental mould. It is an innovative procurement chapter in the conceptual sense, addressing the question of how health sector procurement can be developmental both by addressing health sector needs and values and by sustaining industrial suppliers. It also puts forward innovative arguments, exploring in some detail how

procurement can constitute a business asset, and using the example of value-based pricing (VBP) in medicines procurement to explore how procurement can better address health sector needs in marketized and fragmented lower-income health systems.

The chapter is divided into two sections. The first section focuses on procurement as an industrial policy in African pharmaceutical markets. It takes a detailed microeconomic look at procurement design from the perspective of local pharmaceutical firms, for whom access to working capital is a major developmental constraint. Using illustrative data from Zimbabwe, the chapter shows that procurement can be either a source of finance or a serious drain on the finances of firms that operate in the context of high bank charges and interest rates, and in highly competitive markets. Careful procurement redesign can have a substantial impact on firms' cash flow and investment prospects.

The second section turns to innovative procurement strategies that stitch industrial production and innovation into the values and needs of health sector users in African countries. It explains and examines the emergent practice of value-based pricing (VBP) as a tool to link medicines prices to health needs. So far applied mainly in high-income countries, VBP nevertheless falls within a category of global and local procurement initiatives that try to foreground need in the design of public procurement. The discussion recognizes that public procurement, because of its scale and the values it embodies, is not simply a process of market purchase. Medicines markets and other related institutions are co-created by public and private sectors in complex and diverse ways. Integral to this pattern of interaction and articulation is the way in which medicines are purchased and the way in which prices are determined. These decisions are political as well as economic, as reflected in the Srinivas quote above.

Public procurement as an industrial policy tool

In the economic development literature, and in the debates on public policies such as defence procurement, there is a long-standing recognition that public procurement can operate as industrial policy. 'Buy local' campaigns and local preferences often formed part of import substitution policies of the type discussed in Part I. The liberalization policies of the 1980s, in both lower-income and higher-income countries, generally removed local procurement preferences and employed international competitive tendering to open up domestic markets to external competition. The development economist Sanjaya Lall, whose

conceptual framework of industrial capabilities is used throughout this book, was a persistent proponent of the continuing need for industrial development policy in these 'globalized' and fast-moving market contexts. In the early 2000s he posed the question: 'What can poor countries do to strengthen their industrial competitiveness in the international economic setting?' (Lall 2003). His argument that in developing countries, industrial capabilities (technological, financial, organizational and dynamic) develop slowly, and are cumulative and 'path dependent' as industries and institutions build on existing skills (Chapter 2), implied the need for local policy interventions such as local content rules for firms' procurement. Lall (2003) identified firms' procurement capabilities, as well as those of governments, as elements of cumulative industrial improvement, and recognized the importance of developing larger groups of firms in one sector so that they generate 'spill-over' benefits (Chapter 2).

Much writing on procurement focuses on its role in providing a market for locally supplied goods and services, and hence sustaining business development (Ogot et al., 2009; Uyarra and Flanagan, 2009; see also Chapter 3). The market impact of public procurement is very large. Among OECD (high-income) countries in 2011, 13% of GDP on average was spent by government on procurement of goods and services (OECD nd). In some African countries, outsourcing has rapidly increased the size of public procurement. In Kenya for example, public procurement as a percentage of GDP rose from about 6% in 2002 to 27% in 2008 (Ogot et al., 2009).

Lall's framework indicates, however, that public procurement as a developmental tool should go beyond providing a market, to support local industrial innovation. Public health procurement can act as a financing and incentive mechanism to improve technological capabilities, a key element of pharmaceutical industry development as discussed throughout this book. Increasingly, public procurement is promoted as an industrial and innovation policy tool (Kattel and Lember, 2010; Uyarra and Flanagan, 2009). Public procurement creates and enhances markets for new and existing technologies by shaping the demand environment. It can promote sustainable consumption and production patterns: for example, the US government in 1993 issued an Executive Order for all federal agencies to procure energy-efficient computers, resulting in market transformation for Energy Star computer equipment (Kjöllerström, 2008). Procurement can target purchase of goods and services that are new to the country, or new to the world. This chapter explores innovative ways to strengthen the role of procurement in

relation to pharmaceutical industry development and the needs of the health sector in Sub-Saharan African countries.

Trade credit and working capital: the view from the firms

To understand how the financial aspects of procurement design can influence industrial development, it helps to start by analysing how pharmaceutical firms in Africa can use trade credit to reduce borrowing and keep down manufacturing costs. Firms can use their input suppliers as an in-kind financing mechanism, via trade credit, in order to reduce their call on their own funds or expensive bank finance. Firms' private sector procurement mechanisms therefore play a critical role in managing working capital financing requirements and cash flows.

By negotiating for generous trade credit terms, firms can fund varying proportions of raw material procurement, production and logistics processes, and sometimes influence the debtors' collection period. Astute use of these options turns the firms' own procurement process into a generator of in-kind finance. Failure to use them causes the firm to haemorrhage cash if it pays suppliers in advance or opts not to stretch its suppliers by paying their invoices early, before reaching the limit of their credit terms.

We describe here how trade credit can aid small to medium enterprises in accessing in-kind finance through contractual relationships with larger and more established firms and organizations with better access to finance. Suppliers endowed with market power and reputation can access formal credit (usually cheaply) from banks and then extend trade credit (an in-kind loan) to buyers with less access to bank or own finance (Nilsen, 2002; Petersen and Rajan, 1997). Because suppliers choose to whom to advance trade credit, trade credit serves as a screening and monitoring device for suppliers (Berlin, 2003). The fact that there are more suppliers, who are better at evaluating credit risk, than there are financial intermediaries makes trade credit an important source of finance in an economy. When suppliers extend credit to buyers, they reduce transactional costs, making business transactions cheaper and easier (Gianetti et al., 2011).

Trade credit is therefore a cheap source of short-term, external, in-kind finance, advanced not as money but goods on credit. If firms understand how to handle finance (if they have good finance capabilities, see Chapter 15), they can use trade credit to reduce cautionary cash holdings thereby alleviating cash flow problems.

Thus for firms in poorly developed markets, trade credit assumes great importance: there is evidence that industries have an elevated dependence on trade credit in countries with poorly developed financial markets (Fisman and Love, 2003). For Zimbabwe, Fafchamps (1997), using evidence from the 1993 Regional Program for Enterprise Development (RPED) panel survey of 200 Zimbabwean companies, found that trade credit indeed played a significant role in financing enterprises. Trade credit as a percentage of outstanding balances constituted 27% for micro enterprises, 26% for small enterprises, 30% for medium enterprises and 30% for large enterprises.

However the economic deterioration of the 2000s decade in Zimbabwe caused a high level of uncertainty, shortage of foreign currency and increased country risk. Consequently, local firms found it difficult to access trade credit from suppliers for APIs and excipients. The dearth of trade credit and reliance on expensive bank finance throttled financial breathing space for the companies.

In those circumstances, firms can find themselves in a perverse situation, whereby local pharmaceutical firms are funding suppliers instead of vice versa. Local companies had low bargaining power because they purchased small quantities of raw materials, and their suppliers were not worried if they lost them as customers. Local firms procured raw materials from merchants and brokers with critical mass to move 15 to 30 tonnes of products, and the brokers then sold smaller quantities at higher margins to local firms. APIs and excipients were paid for in advance because suppliers feared country political risk and foreign currency risk, a legacy from the times when Zimbabwe had serious foreign currency shortages despite the country's subsequent shift to using a basket of foreign currencies. Zimbabwean firms, because they paid in advance, were therefore financing economically stronger suppliers in India and China.

Where international suppliers sold to local firms, they also reduced their perceived risk by demanding a letter of credit (LC). The LC costs 2.5% of value, plus charges for establishing the LC and transaction charges. Local firms sought to reduce these high financing costs by negotiating for in-country bonded warehouses to hold goods for purchase, reducing delays due to shipping and customs clearance and hence the period when the firm would be out of pocket while awaiting the raw materials. Broadly, the trade financing pattern became another example of a perverse subsidy from weaker African economies to stronger trade partners, which one can find reflected also in other markets.

Public procurement terms as a financial asset for businesses

The discussion above demonstrates just how strongly a pattern of trade financing can influence the cash flow and business development of local firms. It follows that the design of the payment and credit systems used in public sector procurement can strongly affect the businesses from which the government purchases goods and services. The payment mechanisms in public procurement constitute implicit business financing mechanisms – or a drain on the business.

Public drug procurement payments can be made in at least in three ways; advance payment, cash on delivery or credit terms. Each of these payment modes affects the manufacturers' cash flows, cost of finance and eventually the cost of manufacturing pharmaceuticals. The payment terms can be a source of finance for the firm to use in the production process, or they can cause the producer to seek external expensive finance whilst awaiting payment for goods produced and delivered for periods ranging up to six months.

Advance payment provides direct business funding, as payment is made in advance of goods and services delivery. Advance payment reduces the need for manufacturing firms to borrow expensive bank finance when it does not have sufficient cash holdings. With advance payment, the firm uses these funds to purchase raw material, fund the production process and pay labour. While advance payment, in accounting terms, becomes a short-term liability on the balance sheet of the firm, nevertheless the funds obtained for the pharmaceutical products to be supplied constitute an asset (cash holding) that the firm uses for production and logistics.

With the cash-on-delivery payment method, the buyer pays on receipt of goods and services. The manufacturing firm therefore funds raw material acquisition, production and logistics with either own or borrowed (expensive) funds. Compared to the advance payment method, cash on delivery therefore imposes varying degrees of financing costs on the firm. If the firm uses its own funds, the financing costs are lower than bank borrowing, though accountants will argue that using internally generated funds has important opportunity costs for the business.

The third payment method involves credit terms. The manufacturing firm delivers goods to the procurement agency, which pays after a certain pre-agreed period of time from the date they receive the invoice. The period can generally range from 30 to 90 days and in some instances as much as 180 days. This is the most strenuous payment method of the three described for the manufacturing firm's cash flows. The firm must fund raw materials acquisition, production and logistics processes

through the period up to payment. The firm must also have skills in chasing on-time payment by the buyer. This chasing process is especially difficult in many instances when the government or state agencies are the buyer, and they need to wait for disbursement of funds from central treasury (see, e.g. Chapter 3). Onerous credit terms of this kind have constrained many African pharmaceutical manufacturing firms to resort to very expensive bank financing prior to receiving payment.

In effect, many local pharmaceutical firms have no option but to provide the government with credit terms: they are effectively helping to finance the local health system. This generates recurrent cash flow problems as they try to fund successive operating cycles. The process of waiting for payment, especially on an order which is large relative to the firm's capacity, can undermine the firm's ability to procure raw materials and pay labour and associated production costs for the next production cycle, as well as constraining effective sales and distribution.

In these constrained situations, there are ways in which a confirmed order or an invoice can be used by a firm to fund production cycles. Two possibilities are a supply chain structured-credit finance approach, and invoice discounting or factoring.

In the first, supply chain structured-credit approach, the firm can use the strength of the procurement agency's own high credit standing. Once the firm has a confirmed order, it can go to a bank to approve a credit facility with conditions. One of the conditions could be the firm assigns the amount payable after fulfilment of the order to the bank. By assigning the firm's (creditworthy) debtors to the bank, it gives the bank control over the funds to be paid. Because funds are disbursed before products have been produced, the firm needs to procure raw material and produce and deliver products before the buyer pays. Consequently, this type of financing carries production, performance and payment risk, hence the need for the firm to have an acceptable production reputation and for the buyer to have good payment reputation. What is key is that the firm can access funds based on a confirmed order from a reputable buyer: an efficient public procurement body that pays reliably can fulfil this role.

The second approach of invoice discounting and factoring requires a much broader and deeper financial institution architecture in the country, including banks and factoring and discounting institutions. This financing method involves a financial institution paying a proportion (up to 85%) of invoice value to a firm in advance, against invoices billed to the firm's buyers. Factoring and invoice discounting are prepayment methods against a sales ledger for a firm – in other words, it offers advance or early payment to the firm that sold its goods. Instead of the

firm waiting for payment by the buyer after, say, 180 days, the firm is able to access working capital finance to fund its production cycles. In this instance, instead of getting advance payment from the customer, the firm gets the advance payment (a proportion) from the financial institution.

Essentially invoice discounting and factoring work in the same way, the difference residing in who has credit control over collection of the debt (amount payable to the supplier). With discounting, the firm has control on debt collection, while in factoring, the firm hands over the collection of the debt to the financial institution, writing formally to its customers to pay the bank directly; the bank then carries the responsibility of collecting the debt.

It follows that if the public procurement agency for the health sector has a good track record for paying on time, it opens up an avenue for firms to access funds based on invoices. This financing approach is attractive because production risk is no longer an issue as the products have already been manufactured. The greatest risk is payment risk by the procurement agency, since many agencies procuring medicines using African government funds may find it hard to pay consistently on time, since their own funding may be erratic (see Chapter 8).

Procurement as an asset: a Zimbabwean example

Where there is political will and substantial financing, public – including donor-backed –procurement can become a substantial asset for local manufacturing firms and the health systems they supply. An example is the support generated for manufacturing anti-retroviral (ARV) drugs in Zimbabwe. The Zimbabwean government initially created and assured the market for locally produced ARVs by providing a funding mechanism, in a context where there were strong local manufacturing capabilities. As a result, Zimbabwe became one of the first African countries to manufacture ARVs locally, in 2003. We explore how this came to pass.

During the economic challenges of the late 1980s and 1990s, Zimbabwe faced a huge social and health challenge emanating from the HIV/AIDS pandemic. HIV/AIDS was placing a huge strain on an overburdened and underfunded health system. In response, the government converted an existing drought levy into the AIDS levy to finance the HIV/AIDS programme. The government set up the National Aids Council and the National Aids Trust to collect and administers the AIDS levy, set at 3% of salaries for formally employed people. Fifty per cent of the AIDS levy is reserved for medicines procurement, with the balance allocated to prevention, awareness and administration costs.

The government issued a compulsory license to manufacture ARVs and promised to purchase 75% of the locally manufactured medicines (Osewe et al., 2008). It is important to recognize that the government could only issue a compulsory license because Zimbabwe had built the infrastructure and capabilities to locally manufacture pharmaceutical drugs from the 1950s (Chapter 1). Transferring the technology in order to manufacture ARVs locally was thus possible because of this industrial background.

However, in spite of government's intentions, the hyperinflationary environment of the 2000s constrained public health financing capacity, culminating in the collapse of the public health system (2003 to 2009). The result was a shift to high donor dependence for financing the public health system and medicines procurement. This shift incapacitated public procurement as an industrial policy tool (NECF, 2010), and was the greatest cause of decline in local industry capacity utilization. Reliance on donor funding that fragments public procurement policies continues to pose a demand-side constraint for local pharmaceutical manufacturing.

However, there are exceptions: one donor-funded programme in Zimbabwe provides an unusual example of support from donors for local pharmaceutical production. Ordinarily, in many African health settings, donor-funded health programmes tend to import medicines from India or China independently of public procurement mechanisms. For example, in Zimbabwe the principal purchaser of anti-retroviral drugs for The Global Fund is the United Nations Development Programme (UNDP), which procures the drugs through their pooled procurement base in Copenhagen.[1] This removes public procurement as an industrial policy tool from the available policy arsenal for stimulating and supporting innovation and industrial development in the African context. In such situations, the market becomes unreachable for local manufacturers.

However in this case, purposive support for local manufacturing was provided. The Extended Support Programme funded by the European Union and DFID (the UK Department For International Development) supported local manufacturers CAPS Pharmaceuticals and Varichem in Zimbabwe to manufacture and supply medicines to the local health system during the era of economic collapse (Table 13.1). This example shows that donor-funded programmes can support local industry and operate as an effective industrial policy tool. Table 13.1 shows that CAPS and Varichem were contracted to supply more than US$4 million worth of drugs to the programme. The contract value shows the values

Table 13.1 Donor support for local industry through contracting for local health supplies: Zimbabwe

Contracts for drug supply by some pharmaceutical manufacturing firms and importers

Supplier	Contract Value (Euro)	Value Delivered (Euro)	% Completion of Supply
Varichem Lot 2	1,788,800	1,522,404	85.11
Varichem Lot 4	198,500	198,500	100
CAPS Lot 1	2,289,784	961,139	41.98
PCD Lot 2	433,967	433,967	100
PCD Lot 3	570,235	570,235	100
PCD Lot 4	198,500	198,500	100
GHC	1,585,464	1,585,379	99.99
Mission Pharma Lot 1	986,615	981,044	99.44
Mission Pharma Lot 2	63,000	63,000	100
SJV	253,280	253,280	100
Total	**8,368,145**	**6,767,488**	**80.87**

Source: EU, 2010.

of medicines that were supposed to be delivered, and value delivered shows what the companies had actually delivered by the time the report was compiled (EU, 2010). Table 13.1 also shows that locally based pharmaceutical wholesalers, including PCD, GHC, Mission Pharma and SJV, were allocated quotas that they filled through imports.

A key issue raised by this example is the political scope for governments to incentivize or compel large donors to purchase locally manufactured pharmaceutical products. Such a move can increase governments' space for policy manoeuvre. The South African government, for example, insists on local suppliers in many circumstances: when foreign companies win tenders, they must go into an agency arrangement with a local South African firm, as exemplified by a case where a Zimbabwean firm won a tender to supply ARVs to the South African public health system and had to partner with a South African firm. Other African governments have been less energetic or effective in imposing local partner requirements on overseas suppliers.

Public industrial procurement to serve health needs and values

The previous section has centred on the scope for aligning demand for health commodities with industrial development needs. This section

reverses the view, to ask: To what extent can medicines procurement be shaped to ensure that local industrial development increasingly serves the health needs of the populations dependent on the local health system? This is a question raised and addressed for the Brazilian health-industrial complex and its policy development in Chapter 9. Here, we examine schemes that link reimbursement and assessment of a product's value to the impact that products have in real-world contexts. These efforts can be seen as reflecting a desire to link the introduction of new products to competent health care, which allow for maximum access and benefit. The objective is to bring local industrial production and innovation closer to the health needs it should serve

Our focus is on a particular innovative procurement mechanism: value-based pricing of medicines. While this is to date a mechanism largely experimented with in high-income countries, we think it is important because it shifts the attention of procurement policy from a market (often monopoly) price for an already developed drug to an assessment of how a drug will actually work in particular country contexts and for identified needs. Its attractiveness is in indicating ways forward in adapting procurement to a focus on population health benefit and patient needs.

The broader lessons are particularly pertinent for developing country contexts, where fragmented and marketized health systems may generate wide gaps between population needs and market demand. Public and donor procurement mechanism then need to specify as well as address population health needs. An early and widespread example of such an innovative procurement mechanism was the essential medicines lists, developed by the WHO and by health activists, that specify priorities for procurement of essential medicines, by generic names, to support access to drugs that are deemed essential for particular populations (Laing et al., 2003). The parallel to the discussion of VBP here is that the essential medicines lists also aimed to shift the design of public procurement towards better serving needs.

Public procurement and industrial innovation for unmet need

The use of VBP has focussed to date on the role it can play in relation to innovator drugs targeted for currently unmet or poorly met health needs. The dominant framework of thought on incentives for industrial innovation identifies an imbalance between investment risk in innovation and reward for the innovation. This 'market failure' is then put forward as the rationale for public sector investment in basic science: there is insufficient incentive for the private sector to invest in basic and

long-term research, so the public sector should underpin drug discovery with support for early-stage research.

However, this conceptual apparatus does little to explain the actual way in which the public and private sectors invest in drug discovery, development and procurement. At all stages, public and private sectors inform each other in influencing the rate and direction of innovation. As argued in the introduction, markets and other institutions are co-created by public and private sectors. The discussion of VBP locates it as one example of this changing pattern of political and economic interaction and articulation, in this case in the way in which drugs are purchased and prices are determined.

One observation from recent patterns of public and private interaction is that market and institutional failures clearly occur not only at the research stage but also at the other end of value chain – at the market access end. This is especially the case in developing country contexts, and a growing international focus on policy, charitable and public sector initiatives has emerged over the past two decades using procurement to address the problems. The institutional vehicles include The Global Alliance for Vaccines and Immunization (GAVI), set up in 2000, which brings together public and private actors to address the challenge of equal access for new and underused vaccines programmes in the world's poorest countries. As of 2013, GAVI stakeholders have committed US$8.2 billion to achieving their mission and have supported the immunization of an estimated 440 million children (GAVI, 2013).

The Global Fund and access initiatives that are disease specific include other examples of efforts to raise the financial endowment needed to generate innovation, product uptake and access to markets for producers, as well as access to medicines for the patients. Their procurement initiatives are designed to support the skills, finance and technological resource endowment required for innovation. In Europe, there has also been renewed policy thinking about how to construct public and private interaction so that appropriate products get to patients (Chataway et al., 2012). Initiatives such as the European Commission's Innovative Medicines Initiatives support basic and applied research (Morgan Jones et al., 2013).

Other high-income country initiatives such as the Innovate UK stem cell programme support policy thinking and address regulatory, business development, funding and access to market issues. At the same time, new approaches to health technology assessment constitute what has been colloquially termed 'the fourth hurdle'. Going beyond efficacy, effectiveness and product approval, they cover value assessments and relate

to pricing and procurement. Procurement and the technology assessment that goes along with it should be seen as a form of regulation.

Previous work has suggested that well-targeted systems of regulation and standard setting result in better outcomes than broad-brush approaches in terms of overall outcomes, including innovation (Chataway et al., 2006). For instance, broad regulatory judgment across Europe that banned all products that left chemical residue in water had the unintended consequence of encouraging use of products that were environmentally damaging in a number of other respects than the products that had been banned. The message this regulation sent out to innovators who had worked on creating more environmentally friendly products was negative. It may well be the case similarly that regulation that bans all use of medicines that have undesirable consequences for a very limited number of patients can result in treatments that are less beneficial for the majority. New regulatory science as conceived of by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) hopes to target regulation ever more carefully to those who are at risk.

Value-based pricing

This hope that targeted policy and intervention will deliver better results also underpins value-based pricing. The central idea of VBP is that the price of a drug may differ according to the impact that it has on different groups of patients, and maybe also across different health system contexts (Claxton et al., 2008). The desire to become more targeted and specific is common to both traditional rule-based regulation and innovative procurement-based regulation.

Lying behind VBP is a concept of health benefits and costs. Pricing of new innovator drugs is a question not of how much they cost, but of how much the firm can take out of a health system through the price it manages to charge. Where there is a highly competitive market for a medicine, competitive tendering can drive down prices. Where there is a monopoly supplier, the price is a matter for negotiation if procurement agencies have the competence and methodologies. A recent MSF report reported from contacts with nine pharmaceutical companies that value-based and differential pricing strategies were used predominantly in non-competitive markets for vaccines (e.g. for new products) where manufacturers do not have to compete on price (MSF, 2015).

Since resources in all health systems are limited, health economists use tools for technology assessment to feed into assessments of whether a certain therapy should be reimbursed. The concept of the incremental

cost effectiveness ratio (ICER) has become one driver of reimbursement for new drugs. Along with measures of Quality Adjusted Life Years (QALYs), ICER calculations are used to measure health benefit and cost to health care provider, and these metrics are used to compare the attractiveness of different therapies. VBP provides a different approach to the logic of reimbursement. The UK is one of the countries that has been debating the introduction of a new way of determining the price for new drugs. The new UK regime has been partly driven by fiscal austerity in the country, in which funds for the purchase of new drugs may well depend on savings in other aspects of health spending. VBP seems to offer a broader approach to pricing decisions, which looks at the impact of drugs on overall health and social care systems.

The UK Department of Health has traditionally used a pharmaceutical price regulation scheme to control expenditure on branded drugs.[2] Recently, however, it has been considering a move to a more outcomes- or value-based approach (Persson et al., 2010). Like the calculations of quality-adjusted life years (QALYs) gained from using the new drug, VBP would also assess the benefits of a drug to individuals. The difference is that VBP signals a move to determining the price to be paid for the drug on the basis of assessment of a drug's impact in terms of health benefits *and* its contributions to the overall health system. The value-based price is in theory the price that ensures that health benefits for patients and the wider society exceed the health benefits displaced elsewhere in the health system and in the society due to the medicines' additional costs (Camps-Walsh et al., 2009; Claxton et al., 2008). The move is also to a more targeted and perhaps more adaptive system, with ongoing assessments of a drug's value potentially influencing its price. Again in theory, the calculation would take into account the importance of incentives for innovation.

The move has a number of implications, and Verhoef and Morris (2015) provide a summary of what value criteria other than QALYs (or similar measure of patient-level health gains) have been advanced in the literature as possible components of VBP. These include:

- Wider patient- or disease-related value criteria such as severity of disease (e.g. whether it is an acute, chronic, rare or terminal disease); unmet need; size of relevant population; age groups particularly suffering an impact of the disease (e.g. children); socially disadvantaged patients; number of other treatment options.
- Health care-related value criteria: being treated at a convenient time and location and after only a short wait; being treated in a way that

patients consider less unpleasant (e.g. taking a medicine once a week as opposed to three times a day); and the degree of risk of the treatment.
- Wider societal value criteria such as ability of patients (and carers) to resume work or to work more productively; cost savings to other publicly funded services (e.g. social care), patients or carers; and how innovative the medicine is.

Some versions of VBP schemes might also involve differential pricing for different patient cohorts. For example, a group of patients with one genetic makeup may benefit more than another group, and therefore the price paid for the drug being taken by the group that benefits more would be higher.

Value attributes will need to be collected, measured, aggregated and converted to evaluate a 'value metric' (Deloitte, 2012).[3] The data that will feed into this assessment will need to go beyond purely clinical trial data. Real-world data – that is, data relevant to the drug in use, not just in trials – would apply both before the market launch (e.g. up-to-date cost of illness data) and post-launch: comparative real-world data, information on side effects and changes in effectiveness over time (Greiner, 2011). The sources of such data could transcend patients, clinicians, hospitals and social networks. The quality of the data and its format, governance and ethical considerations are likely to influence the feasibility and extent to which VBP can reflect real-world values. There may well be a need for the development of new methods which can assess value in different contexts and under different conditions, and which can incorporate trade-offs.

A move towards VBP is certainly not without its complexities and dangers, and it is important to note that only a limited number of countries have attempted to implement VBP schemes. However, it is also the case that those countries do appear to be experiencing benefits as a result of the schemes they have implemented. Sweden is the most widely cited example of a country that has implemented a workable and successful scheme. Evidence from Sweden summarized in Persson (2012) suggests that a VBP scheme may be well placed to encourage the adoption of innovative medicines, especially those that address unmet needs. This is particularly important in the case of orphan drugs designed to treat rare diseases and which due to their high cost-per-QALY often fail to obtain reimbursement. The Swedish Dental and Pharmaceutical Benefits Agency (TLV), from June 2003 to April 2010, received 30 requests for orphan drugs reimbursements and awarded 29 (Cochrane et al., 2015).

Nevertheless, there is limited evidence about how the approach can work in practice, and the evidence available comes from international examples applying only a few elements of the VBP approach. The situation is made additionally complex because VBP metrics are often used on conjunction with other schemes. Sweden combines VBP with other approaches such as coverage with evidence development (CED) schemes (Cochrane et al., 2015), and this in turn makes gathering evidence on the effectiveness of VBP approaches challenging (Persson, 2012).

Additionally, it is difficult to judge what impact funder silos, which mean that costs and benefits from health and social care, for example, are calculated without reference to each other, will have on the way that treatments are rewarded. How will methodologies be developed to assess the full costs and benefits in the health, social care and domestic settings? Can multiple budgets be brought together and analysed coherently? These and other unresolved issues seem to have led to delays in the introduction of VBP-based schemes, although thinking about how VBP might be introduced on a large scale is beginning to influence approaches to determining price.

So why focus on VBP? Earlier we argued that the classic image of publicly supported fundamental science and private support for more applied work is not useful. Innovation emerges from a more diverse and complicated patterns of interactions between private and public sectors that work across the R&D and product development processes to create new medicines and make them accessible to patients. The public sector has to intervene in multiple ways to ensure that incentives offered for drug development are balanced with broad public interest agendas in ensuring access to medicines in response to need.

Value-based pricing is thus not about the drug; it is about the impact of the drug in the context of the health system and unmet health needs. In this respect, VBP could act as an incentive for innovation that is more focussed on delivery of and access to products that are designed to meet the most pressing needs in particular contexts. Perhaps VBP could be thought alongside other mechanisms to try and address local health needs in developing countries. For example, it could be used in conjunction with product development partnerships (PDP) or market guarantees focussed on particular health challenges.

A shift to pricing mechanisms for procurement that use local health needs assessment is challenging for developing countries. Nguyen et al. (2014) emphasize the difficulties more broadly with pharmaco-economic evaluation in developing countries, citing a lack of capacity due to a shortage of qualified researchers and health care data. Fragmented

health systems generate poor data on health needs. However, African and other low- and middle-income public procurement bodies face the challenge of procuring innovator medicines as well as generics, and need to develop assessment skills for price negotiations. More generally, a procurement process that seeks to identify population health needs and then encourage local supply development has to build up tools over time to assess the benefits of local innovations.

Conclusion: procurement as development policy and process

Public procurement is an important development tool, and in medicines it needs to be designed to interlock industrial innovation and development with the huge scale of African unmet health need. Given the scale of medicines procurement, and its life-or-death importance, its institutional design and operation therefore require much more policy and research attention. Medicines procurement is at the same time highly technical – requiring capabilities identified in this chapter in financing and health benefit assessment – and also highly political. It involves sets of rules, but it is also a complex set of social and institutional relationships. When it goes wrong, both health and industry suffers.

We have suggested two innovative aspects of procurement that will occupy much more attention of African policy makers. The first is the procurement payment systems and the ways in which they can be designed to act as assets and incentives for local industrial development. The other is the assessment processes that can underpin pricing systems that go beyond competitive tendering to generate negotiated prices for innovative suppliers. Finally, we have argued that value-based pricing is just one example of potential innovative procurement mechanisms that can be designed to have at their heart the objective of both incentivizing industrial suppliers and directing their efforts to address unmet health need. Public procurement may be underfunded by national budgets, but collaboration with donors and private firms can, if purposively designed, promote local production, innovation and access to medicines.

Notes

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1. The Global Fund to Fight AIDS, Tuberculosis and Malaria, http://www.theglobalfund.org/en/ (accessed 25 April 2015).

2. The NHS spends about £11 billion annually on drugs of which £8 billion is on branded drugs. This represents about 13% and 10% of available resources, respectively (Claxton et al., 2008).
3. Figure 6 in this report has some case vignettes of VBP agreements.

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Industry Associations and the Changing Politics of Making Medicines in South Africa

Theo Papaioannou, Andrew Watkins, Julius Mugwagwa and Dinar Kale

Introduction

The making and delivery of new medicines is not only a process of science and technology, of production and marketing, but also a process that is inherently political. As such, the relational and political interactions between industry and government are key to shaping regulatory environments that either promote or constrain an industry's ability to collectively learn, innovate and grow (Malerba, 2002). Often critical to the governing of these relations over time are intermediary actors such as industry associations and various advocacy groups that through processes of conflict, negotiation and collaboration promote knowledge exchange and institutional capacity building. In developing and emerging countries, such intermediaries are likely to play a particularly prominent role in filling institutional knowledge gaps towards shaping regulation and subsequent industry development (Kshetri and Dholakia, 2009). Moreover, these interactions between industry and government can be particularly complex and often contentious when government views an industry as potentially contributing to the public good, as in the case of the pharmaceutical industry and its role in the provision of health care. In such cases, it can be suggested that the strategies employed by industry associations over time will need to address the needs of the government and the civil society it negotiates with in order to effectively advance the interests of the industry it represents.

This chapter builds on these notions by analysing the changing role of biopharmaceutical industry associations and related umbrella organizations in South Africa since the 1960s when the sector's first industry

association was formed. More specifically, we examine the ways in which the changing political context and institutional interplay have shaped a South African industry-government relational trajectory that is historically uneven and reactively contentious. In this case, respective pharmaceutical associations have shifted gradually away from pure, narrowly aimed lobbying tactics to greater cooperation with government and civil society on a host of policy-related issues, from health innovation to national goals of development.

Our analysis considers developments during three main periods through which the South African biopharmaceutical industry has evolved: (1) a period of pre-liberalization; (2) a period of expanding pluralism; and (3) a period characterized by increasing partnership. While the activities of industry associations reside primarily in the second and third periods, a discussion of the first period is deemed essential in understanding the unfolding of industry-government relations in subsequent and more recent periods. Findings indicate that two decades of both increasing pluralism and globalization have created tensions amidst regulatory uncertainties between government and the pharmaceutical industry regarding access to medicines on the one hand and strong intellectual property rights (IPRs) on the other. We suggest that such uncertainties can be reduced through improving interaction between biopharmaceutical industry associations, government and civil society organizations (CSOs). This can result in more legitimate and cumulative platforms for partnering on a number of regulatory issues and broader, more holistic developmental aims.

We begin this chapter by positioning industry associations as intermediaries within a broader policy subsystem and clarifying their importance in the developing and emerging country context. We then consider the activities of industry associations within wider government-industry growth and development coalitions, presenting both the challenges and opportunities towards potentially collaborative yet inherently political relations. We follow this with a brief overview of the South African case and the approach and methodology employed in our analysis. Next, we consider the importance of historically embedded relational dynamics between government and the pharmaceutical industry in South Africa that are punctuated by periods of regulatory uncertainty, mostly involving intellectual property regimes that either reinforce or alter existing relational trajectories. We underpin our analysis with evidence from case studies on four industry associations engaged in the South African pharmaceutical industry.[1] These case studies include interviews with senior managers, biopharmaceutical and other industry association

presidents and government policy makers in relevant departments. These findings, along with data collected through various secondary sources, lend insights into the current political strategies of biopharmaceutical industry associations and the possibilities of more development-oriented government-industry coalitions going forward.

Industry associations and the policy subsystem

We define industry associations as industry specific member-based organizations that actively lobby and negotiate with government on their members' behalf to shape government policy and regulation. Included in this are business umbrella groups such as chambers of commerce who represent the interests of a number of industries and sectors, and are engaged in broad industry coalition building. These organizations are part of what Sabatier (1991) describes as the 'policy subsystem' comprised of intermediary bodies regularly involved – through a variety of aggregation processes – in the shaping of policy within their specific domain of interest (Jenkins-Smith and Sabatier, 1994). For developing and emerging countries, this subsystem is bound to be particularly important where given institutional capacities for innovation and industry growth will often be lacking (Frankel, 2006), and where their potential development will be the result of politically contested relations between government, industry and civil society. Furthermore, these are likely to involve considerable negotiation between local and global interests (e.g. international bodies and multinational companies [MNCs]). In this context, industry associations will likely play a leading role in bridging institutional knowledge gaps between government and industry, and between the local and the global (Kshetri and Dholakia, 2009).

To advocate their members' interests successfully, industry associations will generally need to engage in and perform the following activities and functions. First, industry associations will employ far-reaching knowledge and information gathering and dissemination activities that target government, the broader industry community and the public. Second, industry associations will develop and maintain working relations with key individuals and ministries in government, often using 'elite' members and officials to lead outreach and lobbying efforts (Kshetri and Dholakia, 2009). Third, industry associations must be capable of building widespread industry coalitions for engaging with government. Otherwise, industry fragmentation can result in an ineffective industry voice; this can lead to government-industry tensions during times of regulatory uncertainty and less-than-optimal policy outcomes. Finally,

industry associations will need to function as 'veto players' which influence politics of development and therefore governing structures of innovation capabilities (Tsebelis, 2002). In the context of developing countries, it is increasingly acknowledged that the political creation of successful institutions of innovation happens under significant pressure from industry associations (Doner and Sheneider, 2000).

Despite their potential contribution to development, negative connotations are often ascribed to industry associations and their activities, as they have been viewed as controversial actors of innovation and development. For instance, as early as the 18th century, Adam Smith, in his *The Wealth of Nations*, accused industry associations of playing a negative role in the economy, conspiring against the public or raising the prices of goods. More recently, industry associations have been viewed as special interest groups and/or elitist organizations that pursue narrow rents for a limited number of members at the expense of the wider sector and economy, discouraging competition and thus curtailing collective innovation within an industry (see Olson, 1982; Schmitter and Streeck, 1999). This aligns with ideas concerning corporatism where national economic policy is formed through closely coordinated collaboration between government, industry and labour, either imposed by the government (state corporatism) or formed voluntarily (neo-corporatism) (see Schmitter, 1974; Cawson, 1986). Examples of these might be apartheid-era South Africa and contemporary Sweden, respectively (Thomas, 2004). Schmitter (1974) was concerned with what he coined 'societal corporatism', where a small number of interest organizations are able to monopolize the policy subsystem, competitively eliminating other interest groups and essentially forcing the government to enter into collaborative relations with industry due to political necessity (Maree, 1993). In some cases, some form of societal corporatism may be beneficial, allowing for more rapid development of national capacities during times of necessity or crisis. The obvious downside of societal corporatism is that the state can become beholden to a few key interest groups, for example a small group of domestic conglomerates or a select number of foreign companies. In this way it is thought that industry associations, in certain political contexts, can even threaten democracy (Cawson, 1982).

State-industry relations and coalitions towards development

While industry associations may influence the shaping of government-industry relations, the strategies they employ and the subsequent extent

to which government and industry work together may be determined more by long-standing and embedded relational dynamics between the two. Relations between government and industry are often referred to as coalitions, in that some degree of co-dependence and thus cooperation between government and industry is not only inevitable but necessary. In the context of developing countries, relations between government and industry may be characterized as 'growth coalitions', ranging from 'weak growth coalitions' where there is at least a minimal recognition that 'business needs the support of government to make profits; governments need to share in these profits to finance government and politics' (Moore and Schmitz, 2008: 1), to 'strong growth coalitions' where government and industry engage in active cooperation towards the goal of policies that both parties expect to foster investment and increase in productivity (Brautigam et al., 2002). According to Schneider and Maxfield (1997), strong growth coalitions require government and industry to share information and to have a high degree of 'reciprocity, trust, and credibility' towards one another. However, this does not change the fact that growth coalitions presuppose bargaining or compromises between industrial and political elites and CSOs. Khan (1995, 2000) refers to such coalitions as forms of political settlements – the balance-of-power among contending elites, CSOs and social groups. Political settlements are based on a common understanding of how narrow elitist interests can be served through policies of innovation and development.

Since the 1980s, a main focus of political-industrial settlements or government-industry relations for many developing countries, including South Africa, has been the implementation of neo-liberal economic policies. Cornerstones of this policy approach include currency stabilization, denationalization of industry, trade liberalization through the lowering of trade barriers, providing incentives for exporters and reducing favourable treatment of domestic firms, as well as the cutting of deficits for decreasing inflation and lowering interest rates – all aimed at spurring domestic innovation and growth in conjunction with increased foreign direct investment. Results of such neo-liberal-focussed growth coalitions have been mixed, with many developing countries experiencing sharp yet isolated increases in growth and wealth production amidst continued widespread poverty. For developing countries, therefore, it has been argued that government-industry growth coalitions need to evolve to a more development-oriented model that focuses on poverty alleviation over an extended period of time (Brautigam, 1997, 2009; Handley, 2008). Seekings and Nattrass (2011: 339) argue, however, that

development coalitions necessitate 'much deeper deliberation and negotiation than a growth coalition: the objective is not only to agree on the mix of public sticks and carrots that serve to promote economic growth, but to agree on a mix that promotes a particular pattern of growth', one that is focussed on the needs and welfare of the poor. For industry and the associations that negotiate with government on industry's behalf, such a move would require a considerable shift away from pure lobbying to greater partnering with government.

The global pharmaceutical industry and the case of South Africa

The global biopharmaceutical industry is comprised of a relatively small number of large research-oriented MNCs based mainly in the developed North and a large number of both small and large companies that manufacture generic medicines both in the developed North but most prominently and increasingly so in the developing South (see Chapter 6). Most generics manufacturers operate as independent companies while others are subsidiaries of large MNCs. The research-based MNCs make generally large profits through the global sale of patented blockbuster drugs which are more expensive than generics and are at times priced out of the reach of poor patients. The research-based MNCs insist that the high prices for the medicines they sell and the profits they garner are necessary for covering the costs of marketing and continued R&D activities. But the inability of many to pay these prices, including the governments of developing countries, and the increasing expiration of many patented medicines have facilitated the tremendous growth of the generics industry which has substantially lowered the price for a number of essential medicines, including anti-malarial, and anti-retroviral drugs, among many others, some experiencing a 50–90% reduction in price, thus considerably increasing access to these medicines. The growth of the generic medicines industry and its impact on research-based MNCs have created considerable fragmentation and conflict within the pharmaceutical industry and between the pharmaceutical industry and the governments of emerging countries such as South Africa.

South Africa's economic growth for the last few years has averaged 2–3% and it slowed down to 2.0% in 2014. However, as the second-largest African economy after Nigeria the country exerts strong economic and political influence on the African continent. The country made the transition from an apartheid state to a constitutional democratic state in 1994. Since then, South Africa has experienced considerable economic

growth, but also increased inequality and extreme poverty in certain sections of the population. In the area of biopharmaceuticals, the country has emerged as the industry forerunner in Africa with a significant presence of both domestic manufacturers and MNCs, although the domestic manufacturing industry is relatively small, with up to 65% of the country's pharmaceuticals still being imported (IPASA, 2013). Furthermore, its private market, worth US$2.8 billion in 2012, is relatively small and constitutes less than 1% of the market globally. In 2011, two leading pharmaceutical companies in South Africa were domestically based MNCs, Aspen Pharmacare and Adcock Ingram; domestic companies import up to 90% of active pharmaceutical ingredients from other countries, including India and China. Meanwhile, historically, and presently, the country has had a number of active biopharmaceutical industry associations, making it an important case study for investigating the realities of pharmaceutical production in Africa and the role of industry associations in it.

With respect to industry associations, companies in this sector are members of different associations depending on the segment of the market that they occupy. Most foreign MNCs are members of the newly formed Innovative Pharmaceutical Association South Africa (IPASA), which emerged from a merger between two former associations, Innovative Medicines South Africa (IMSA), for research-based/innovator MNCs; and Pharmaceutical Industry Association of South Africa (PIASA), whose membership included both innovator and generics companies. The new association, IPASA currently represents 24 innovative pharma companies dedicated to producing or importing innovative medicines in South Africa. According to IPASA, only companies that conduct their own R&D qualify for membership. This means that domestic companies with no intellectual property (IP) are excluded from the new association. Only IP holders, for example MNCs with innovator products, can become members of IPASA. In addition to IPASA, there is also the National Association of Pharmaceutical Manufacturers (NAPM), Pharmaceuticals Made in South Africa (PHARMISA), Self-Medication Manufacturers Association of South Africa (SMASA) and National Association of Pharmaceutical Wholesalers (NAPW), among others. They also all belong to the Pharmaceutical Task Group (PTG), a broad coalition involving IPASA, NAPM, PHARMISA and SMASA. The PTG deals with the government on issues of mutual concern such as pricing, regulation and national health insurance. For example, the PTG has retained an advocate to represent the pharmaceutical industry in the Competition Commission enquiry into high health care prices. That

being said, many of these associations and member companies are also members of the leading chambers of commerce, CHAMSA and SACCI, and connect with one another through these platforms. This current status of industry has evolved through two main periods: pre-liberalization and the post-apartheid.

Pre-liberalization era

While disagreements over the past two decades on particular regulatory issues have at times stymied relations between the South African pharmaceutical industry and the South African government, tensions between the two are very much rooted in a long history of tense and generally non-negotiable relations between the South African government and the South African business elites, which have carried over into more recent periods from the apartheid era. As Seekings and Nattrass (2011: 343–44) explain,

> Indeed, relations between state and business in South Africa throughout the 20th century were framed by the coexistence of a strong state and powerful corporate capital. The state enjoyed considerable political autonomy from capital, but remained dependent on capital for continued economic growth. The outcome was often tense relationships, as the state sought to push and bully capital into subordinate co-operation, whilst avoiding genuine deliberation, and being careful not to undermine white prosperity.

As such, during the apartheid era, the South African government was intent on maintaining and enriching the white minority through ever increasing control and exploitation of the black majority. This necessitated a command-oriented state, the brutal subjugation of blacks and the complicity of white-owned industry which was dominated by a small number of large state-supported conglomerates all linked in some manner to the South African gold-mining industry. Offering considerable trade protection (much of this induced through international boycott) and ensuring low-wage black labour, the South African government expected industry to operate within certain constraints and to be 'subservient, as long as it was dependent on state patronage' (Seekings and Nattrass, 2011: 344); this resulted in a state-industry relationship that was generally reactive yet ultimately accommodating in terms of industry response, and largely devoid of negotiated compromise.

With an economy centred on mining and energy extraction, and stagnated by the apartheid system and resulting sanctions and boycotts, the

South African government lacked the ability and capacity to either invest in a broad-based science and technology infrastructure (e.g. weak university R&D) or facilitate the growth of technology-based industries (the exception being defence). A strong domestic pharmaceutical industry was never really established in South Africa during this period. The need for medicines, however, meant that large research-based pharmaceutical MNCs continued to sell and distribute medicines in South Africa, with some operating manufacturing facilities in the country. That being said, two pharmaceutical companies, Sterling Winthrop and Merck, divested their interests in South Africa and left the country due to the boycott. A few domestic generics-based pharmaceutical companies such as Adcock Ingram were able to successfully operate under the constraints of apartheid, but their growth and proliferation would not really occur until after apartheid's end. During this period, two main biopharmaceutical industry associations were established. The first was the South African Pharmaceutical Manufacturers Association (PMA), established in 1967, and the second was the National Association of Pharmaceutical Manufactures (NAPM), established in 1977. The membership of the PMA was a mix of domestic and foreign-owned pharmaceutical companies, but the MNCs were more dominant given their market strength; members of NAPM, by contrast, were almost solely domestic manufacturers of generics. Both associations used to work closely with government and/or play advisory roles in policy areas such as health and drug manufacturing. This was consistent with the corporatist state-industry relations of the apartheid era.

Post-apartheid South Africa

South Africa's transition to democracy in 1994 led to weakening of the corporatist hold of the state and strengthening of the civil society (Lehman, 2008). This does not imply that a pluralist approach to state-industry relationships prevailed. Rather, pluralism and corporatism seem to coexist in post-apartheid South Africa. The relationships between industry associations and state appear to be co-operative; governments tend to view the business elites as a key player in pro-market liberal reforms. Indeed, as Seeking and Nattrass (2011: 339) point out, 'Capitalism not only survived the transition from apartheid to democracy, but high profit rates suggest that capitalism continues to flourish in the post-apartheid environment'. This is precisely the reason why South Africa, despite its exceptional economic performance, experiences increased inequality and extreme poverty in certain sections of population, namely the black majority. The co-operative state-industry

relations in the post-apartheid era failed to form a strong 'growth coalition' that could also deliver development. Therefore, within the governing party – the African National Congress (ANC) – the new political elite(s) developed distrust against the business elite(s). The ANC adopted pro-market policies with respect to the global economy without necessarily having a pro-business or pro-industry attitude. According to Seeking and Nattrass (2011: 344), 'In the early 1990s, two views of businesses coexisted within the ANC. On the one hand, business was seen to have been one of the pillars of apartheid, exploitative of workers and abusive of consumers. On the other, there was a growing appreciation of the overall weakness of South African capitalism, in particular its inefficiencies stemming from chronic protection against foreign competition and over-concentration'. The first view clearly supported regulation of employment relations and protection of black businesses. The second view supported trade liberalization and industrial policy. As Seeking and Nattrass (2011) observe, both views entailed a commandist approach to business and industry without so much negotiation.

In this post-apartheid mix of corporatism and pluralism, large pharmaceutical companies began to re-establish themselves in South Africa, insisting on strong protection of patented drugs through TRIPS. On the other hand, CSOs such as non-governmental organizations (NGOs) and advocacy groups began to formally participate in the policy-making process (Lehman, 2008). In 1994 there were more than 50,000 NGOs in South Africa, most of them pursuing development objectives (Fioramonti, 2005). In the post-apartheid era, the state inherited a strong regulatory capacity (ibid) and relied on it to protect public health from the spread of diseases such as HIV/AIDS through the poorest sections of population. According to Seekings and Nattrass (2011: 353), 'Its interventions in the private sector were programmatic rather than targeted in that the state legislated frameworks for change…and then endeavoured – with mixed success – to ensure that private sector complied with the statutory requirement'.

One well-known intervention was the government's 1997 Medicines and Related Substances Control Act that would allow South Africa to import and manufacture cheaper generic HIV drugs. This Act prompted 39 big pharmaceutical companies (mainly MNCs) to file through PMA a patent right lawsuit against the South African government – the so-called Big Pharma v Nelson Mandela case. In response, CSOs and activists accused PMA of violations of the human right to health by making essential medicines unaffordable and called the international

community to protect developing countries against big pharmaceutical companies (Wolff, 2012). Although in 2001 PMA agreed to drop the lawsuit as a result of the growing opposition, it was too late. The PMA suffered an international public relations disaster with three MNCs, GlaxoSmithKline, Merck and Bristol-Meyers Squibb, breaking ranks with 36 other companies and pushing hard for a settlement that would stave off increasing damage (*The Guardian*, 2001). Eventually, these 36 companies agreed to go along with the lawsuit withdrawal, but PMA dissolved, splitting into two new associations: the Pharmaceutical Industry Association of South Africa (PIASA) and the Innovative Medicines South Africa (IMSA).

PIASA was established as an association of companies involved in the manufacturing and marketing of medicines in South Africa. Its members were research-based MNCs and local manufacturers of pharmaceuticals. PIASA had about 90 members, consisting of both large and small companies. Other organizations, such as the South Africa Medical Device Industry Association (SAMED), were members of PIASA, testifying to the diversity of the association. The objective of PIASA was to shape strategic regulatory issues relating to clinical trials, registration of medicines and IPRs. In addition to this, the association tried to tackle regulatory hurdles that discourage investment in South Africa's biopharmaceutical sector. PIASA was also engaged in activities to influence the quality and cost of medicines, access to treatment, health insurance, drug laws and pharmaco-economic evaluation. Among such activities advocacy, networking and innovation diffusion appear to be the most crucial ones. PIASA interacted with government but also with other associations, including IMSA in the health policy and regulation arenas. For instance, it had substantial involvement in the formulation of the South African Health Charter and Private Health Care Reform programmes. This close interaction of PIASA with government was often seen as uneven, given the conflict of public and private interests. Another important activity of PIASA was diffusion of knowledge through hiring consultants and providing members with expert advice on pertinent issues in the health innovation and regulation terrains. Such issues included standards for manufacturing facilities, drug registration fees and regulatory harmonization. This range of activities in the institutional context of South Africa indicates that PIASA played a crucial role in influencing the country's innovation system.

By contrast, IMSA was established as an industry association for research-based companies, even though some of its members also used to produce generics. This is not surprising; generics are crucial for the

public health service in the country. Among IMSA's members there were 12 MNCs who captured about 53% of the MNC market share in South Africa. Generally speaking, this biopharmaceutical association engaged in R&D policy, innovation regulation and lobbying. IMSA did not always perform such activities alone but in collaboration with other associations. Thus, for instance, in the PTG initiative IMSA played an active role in national health insurance issues, working jointly with PIASA and other public actors of South Africa. Another key focus of IMSA was on IPRs, especially access to drugs and marketing. The association worked with and through its members to exert influence on these issues. IMSA's key contacts in government were the Department of Health, the Department of Science and Technology and the Department of Trade and Industry. It also made policy contributions to parliament's portfolio committee on health. However, IMSA also functioned as a government tool for industrial policy implementation. That is to say, it worked closely with government for the implementation of broader national policies by their members, for example requirements under the Black Economic Empowerment (BEE) programme.

The split of PMA into PIASA and IMSA was not the most negative consequence of the 'Big Pharma v Nelson Mandela' case. After all, in April 2013 these associations came together again, forming the Innovative Pharmaceutical Association South Africa (IPASA). It might be argued that the most negative consequence of the 'Big Pharma v Nelson Mandela' case was the damage to trust between government and biopharmaceutical associations. As one interview respondent pointed out,

> [P]re-1994 I think the industry was more in an advisory role, although perhaps not with lobbying focus, access to government ministries was quite possible. What changed it completely for the industry was the court case of 1998 to 2004 which was all about weakening intellectual property and so created a sense that we [the industry] were against the government. So from that time onward, whenever you went into the halls of government, they [the government] would see you as 'you are that industry that took us to court'; so that created such animosity between the Department of Health, the relationship has never really been constructive. (Interview extract: 23)

This statement confirms that, in South Africa, state-business relations (SBR) in the area of biopharmaceuticals remain fragile and therefore lack essential characteristics of effectiveness. According to Cali and Sen (2011: 1543), such characteristics include:

> (i) transparency: whether there is a flow of accurate and reliable information, both ways, between business and government, and from representatives of business to their own members; (ii) reciprocity: whether there is capacity and autonomy of state actions to secure improved performance in return for subsidies; (iii) credibility: whether the state command credibility of the private sector, and whether capitalists are able to believe what state actors say; and (iv) whether there is mutual trust between the state and the business sector.

Clearly, South African SBR in the area of biopharmaceuticals are neither transparent and reciprocal nor credible and mutually trusting. Rather, due to the long-term impact of the 'Big Pharma v Nelson Mandela' case, these relations are based on mutual suspicion and distrust.

Analysis and discussion: resetting the state-industry relationships

Since its formation in 2013, IPASA has been engaged in a highly uneven relationship with government over the latter's policy plan to change the patent rules for medicines. That plan incorporates patent flexibilities after the Doha Declaration (WTO, 2001) and recommends elimination of weak patents, promoting the production of generics (DTI, 2013). In response, IPASA embarked on a campaign against the full implementation of the government plan, lobbying the government and other national and international actors for a stronger IPR regime. Its main objection is that by using TRIPS flexibilities and by promoting generics, the South African government's plan on IP policy will reduce innovation and fail to attract investment, particularly FDI, into knowledge-based firms such as those in biopharmaceuticals (IPASA, 2013). The South African government insists that the issue is not about weakening the TRIPS regime and the country's biopharmaceutical innovation system, but about implementing TRIPS with all the necessary flexibilities for the sake of public good (*The Economist*, 2014). The tension between government and IPASA (the majority of research-based pharma MNCs) heightened substantially when it was made known that IPASA was participating (perhaps leading) a campaign in collaboration with a Washington, DC-based public relations firm that aimed to promote the supposed adverse consequences of a weak IPR regime as proposed by the government, to target the South African public, business community and academic institutions. This bypassing of the government by IPASA in its attempts to thwart

government policy, and doing so during an election year, fuelled already high levels of distrust between the South African government and the research-based, primarily foreign-owned pharmaceutical companies.

The above episode is an apparent setback to relations that, while recently punctuated with conflict, have been defined more by increasing collaboration both within industry on key regulatory issues, particularly taxation and medicine registration procedures, and with government on broader health care policy. For example, a number of these biopharmaceutical industry associations have been involved more recently in wider policy discussions with government regarding science and technology workforce development, industry-university collaboration and the role of research-based pharmaceutical companies in the development and implementation of a South African National Health Insurance scheme. Resetting relations will require reengaging government on such issues, but huge differences on IPR will need to be addressed, if not wholly overcome. Even though stronger IPR laws are supported by much of South Africa's business community (e.g. SACCI supports a stronger IPR regime), the research-based pharmaceutical industry, due to its status as an important yet 'reluctant' and untrustworthy medicines provider, will need to go further. It needs to shed the perception that its interests in South Africa do not go beyond clinical trials and the profit-driven motive of protecting of its patented medicines and future therapies for sale not only in South Africa but the entire African continent.

For its part, the South African government needs to decide what type of role it sees the pharmaceutical industry playing in a relatively poor yet modern South Africa. On one hand, the South African government's approach to access to affordable medicines has indeed increased access, but has also resulted in a growing reliance on foreign generics (e.g. from India) rather than the development of a domestic generics industry. On the other hand, it has recently put forward public-private partnership (PPP) initiatives towards developing indigenous high-tech industries such as biotech, yet has not sufficiently articulated, at least in public, the role of IPR or the pharmaceutical industry in this new policy vision. This seeming contradiction is played out between government ministries, particularly long-standing divisions between the Department of Health, which supports weak IPR laws for ensuring access to affordable medicines, and Science and Technology (DST), which favours stronger IPR laws as a means of fostering innovation more generally and realizing the positive externalities that a robust research-based pharmaceutical

industry might provide South Africa. However, DoH and the Department of Trade and Industry (DTI) are aligned in the area of access to health. Such intra-government divisions, while justified, do complicate negotiations with industry and likely reinforce industry fragmentation between research-based MNCs and generics manufacturers. Current fragmentation on both sides of the negotiating table are contributing to tense relations between the South African government and the pharmaceutical industry and probably resulting in policy inertia and far less-than-optimal regulation.

Conclusion

In this chapter, we have considered the neglected role of industry associations in Africa as key intermediaries in innovation that, through evolutionary processes of conflict, negotiation and knowledge diffusion, facilitate institutional capacity building while shaping regulation and subsequent industry development. To do so, we have analysed the shifting strategies over time of biopharmaceutical industry associations and related organizations in South Africa. We have considered the importance of historically embedded relational dynamics between government and the pharmaceutical industry in South Africa involving critical junctures of regulatory uncertainty, mostly involving highly contested intellectual property regimes. Tracing developments during three main periods within different national context, our findings support previous research that suggests industry associations are more effective in lobbying and negotiating with government when industry is relatively cohesive and able to speak with one voice. This chapter, however, also suggests that in the case of the pharmaceutical industry, the extent to which industry associations can effectively engage with government is determined, in large part, by the willingness of government over time to neither demand nor capitulate, but to compromise with industry in ways that meet its own requirement for accessible medicines while recognizing the positive externalities of a robust domestic pharmaceutical industry. When such willingness is limited, either long-standing or temporarily, biopharmaceutical industry associations in South Africa are increasingly asserting themselves as 'partners' with government in attempts to correct these long-held tensions with the aim towards negotiating better policy outcomes.

In the case of South Africa, decades of tension between government and industry in general, which carried over from the apartheid era, have

exacerbated long-standing pharmaceutical industry fragmentation on key policy issues such as IPR, particularly those between MNCs and domestic generics companies. In turn, this has inhibited constructive policy dialogue and reinforced industry-government distrust, particularly regarding the pervasive assumption that the growth of an innovation-led biopharmaceutical industry in South Africa is incompatible with widespread access to effective and affordable medicines. Subsequent policy divisions between the DOH and DST both mirror the overall divisions and mistrust between industry and government and may contribute to regulatory inefficiencies. This has placed South Africa's biopharmaceutical industry associations, particularly those representing MNCs, often in direct and open conflict with government.

Finally, the historical trajectory and the shift to greater partnering strategies captured here provide insight into the conditions and processes through which 'growth coalitions' in developing countries such as South Africa either remain weak and ineffective in terms of developing a domestic industry or grow strong in that they effectively promote both the growth of domestic industry and the subsequent realization of positive externalities and spill-overs. In doing so, the challenges of moving government-industry relations to a more effective 'development coalition' model that is focussed on growth and poverty alleviation are laid bare. In the case of South Africa, the government and the pharmaceutical industry seem to be locked, based on decades of tension and mistrust, in a rather weak 'growth coalition' that, while promoting the interest of a few key industry players and keeping prices of medicines low, has kept the domestic South African pharmaceutical industry relatively small, dependent on foreign generic suppliers, with few positive externalities or spill-overs gained. For moving towards a stronger growth coalition, the biopharmaceutical industry associations of South African will need to build trust with government and to reconcile industry divisions among themselves.

Notes

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1. In total, 19 interviews were conducted, involving 4 industry associations: Innovative Pharmaceutical Industry Association (IPASA), National Association of Pharmaceutical Manufacturers (NAPM), South African Chambers of Commerce (SACCI) and South African Medical Device Industry Association (SAMED).

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15

Finance and Incentives to Support the Development of National Pharmaceutical Industries

Alastair West and Geoffrey Banda

Introduction

There is a now a growing international consensus that development of the pharmaceutical industry in Africa can contribute to both economic development and improved public health. This final chapter begins by identifying the striking convergence of thought and initiative that has recently been generated across continental African representative bodies, international agencies and national governments. We outline this emergent consensus and then examine challenges it faces by focusing on the core interconnected policy issues of financing and incentives for industrial development in pharmaceuticals. A sustainable and expanding pharmaceutical industry must reach essential quality standards and also constantly upgrade, moving up the technology ladder while improving cost efficiency. This requires a cocktail of incentives in which finance is key (Chataway et al., 2009). These incentives, in turn, rely on the building up of appropriate financial capabilities within firms and financial institutions as well as within governments. This chapter innovatively traces the interconnections between micro-level financial capabilities and national government policy competences in the design and effective implementation of financial incentives and associated policies to facilitate industrial development in pharmaceuticals in Africa.

The emerging commitment: transforming pharmaceutical manufacturing in Africa

At the African continental level, the African Union Commission (AUC) identified the imperative of pharmaceutical industry development in

their *Pharmaceutical Manufacturing Plan for Africa* (PMPA) (AU, 2007), endorsed at the African Union Heads of State and Government Summit in 2007. Progress on realizing the ambition espoused in this document was initially slow to materialize, prompting the Conference of African Ministers of Health (CAMH) to call at their fifth meeting in 2011 for a 'Business Plan' for the accelerated implementation of the PMPA. A partnership was formed later that year between the AUC and the United Nations Industrial Development Organization (UNIDO) to develop the business plan, and in May 2012 the resulting document (AU, 2012a) was approved by a special session of the CAMH in Geneva. In July 2012 the Business Plan was endorsed by AU Heads of State and Government at their summit in Addis Ababa.

Regionally and institutionally, collaborative work on local pharmaceutical development has snowballed. The African Ministers of Industry have also now recognized the pharmaceutical industry as a priority, in the Accelerated Industrial Development of Africa (AIDA) framework endorsed at their 19th meeting in Algiers in 2011. African Regional Economic Communities have also developed plans. The East African Community Regional Pharmaceutical Manufacturing Plan of Action 2012–16 was launched in 2011 (EACRPMPA, 2011). The West African Health Organization (WAHO) has been developing the Economic Community of West African States (ECOWAS) *Regional Pharmaceutical Plan* (ERPP) and its implementation. The ERPP explicitly aligns with the principles and objectives of the Business Plan for the PMPA, and WAHO has rapidly developed a comprehensive approach, despite wrestling with the unprecedented crisis of the Ebola outbreak in the region.

The public health commitment

International organizations concerned with public health are also now indicating growing support for this agenda. The Joint United Nations Programme on HIV/AIDS (UNAIDS) under the leadership of Michel Sidibé has long been an advocate of the importance of strengthening local production, in particular to address the sustainability of HIV/AIDS treatment, as well as access to medicines for tuberculosis and malaria. It is a central component of Pillar Two of the African Union's *Shared Responsibility and Global Solidarity Roadmap for HIV, TB and Malaria Response in Africa*, developed with support from UNAIDS (AU, 2012b).

In 2008 the World Health Assembly adopted the *Global Plan of Action and Strategy on Public Health*, a broad document that identifies the role that local production of essential medicines could play in improving public health. As part of its implementation, the World Health Organization

(WHO) has run an EU Commission-funded project to assess this role. Phase 1 of the study concludes that the development of the local pharmaceutical industry does not inevitably lead to improved public health, and hence that promoting the public health impact should be central to efforts to strengthen the industry. These initiatives have helped to ensure that public health considerations are central to the Business Plans that are being developed. They plot a practical path whereby the industry can contribute to both public health and economic development agendas that were previously considered by some to be mutually exclusive (Kaplan and Laing, 2005).

The strong current consensus amongst the international community, that the development of the pharmaceutical sector in Africa is an imperative, was notably underlined by the Joint WHO Bulletin Editorial by Mr Sidibé, Mr Li (Director General of UNIDO) and Dr Chan (Director General of WHO) (Sidibé et al., 2014). The authors strongly supported the development of the industry in Africa through the implementation of the PMPA Business Plan.

The challenge of implementation

Practical bilateral and multilateral support for the industry is growing. The German government has a long track record of supporting the pharmaceutical industry in Africa. Since 2006 it has funded a UNIDO project on strengthening the local production of essential medicines in developing and least-developed countries, a project initiated by the previous UNIDO Director General Dr Kandeh Yumkella. Bilaterally through its aid agency Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ), Germany has supported the EAC pharmaceutical plan and many other initiatives such the bioequivalence centre in Addis Ababa (see Chapter 5) and initial feasibility studies for a similar centre in Ghana.

Other international support includes the United States Pharmacopeial Convention (USP) which, with funding from the United States Agency for International Development (USAID), has been running a programme on Promoting the Quality of Medicines (PQM), including capacity building for manufacturers and regulators. In 2013 it opened the Centre for Advanced Pharmaceutical Training (CePAT) in Ghana, to train regulators and the industry in quality assurance and quality control. The St. Lukes Foundation in Tanzania has similarly been training industry professionals on international standards of production through its Industrial Pharmacy Advanced Training Programme, taught by US academics from Purdue and Howard universities, supported by UNIDO.

The need to exploit opportunities under the exemptions and flexibilities offered by the Trade Related Aspects of Intellectual Property Rights (TRIPS) agreement[1] has led the United Nations Development Programme (UNDP), the United Nations Conference on Trade and Development (UNCTAD) and the African Regional Intellectual Property Organization (ARIPO), amongst others, to establish relevant programmes.

The PMPA *Business Plan* identifies the problem of a piecemeal approach that has not delivered rapid development of the industry, and proposes that coordination across different initiatives is required. The international organizations need to invest in supporting emerging national and regional processes to enable development of the industry. Coordinated technical assistance is required to support relatively weak skills availability in the short term and to engage in capacity development across public and private sectors for the long-term sustainability of the industry. National governments too need to invest to support their industries: this point was underscored during a high-level side event at the Ministers of Finance and Economic Planning meeting co-hosted by the African Union Commission and the United Nations Economic Commission for Africa (UNECA) in Abuja in March 2014.

Ghana is an example of a country where a coordinated agenda is progressing. In October 2013 early implementation of the AUC's PMPA *Business Plan* began in Ghana, following an invitation from President Mahama to the Chairperson of the AUC, Dr Nkosazana Dlamini Zuma. A technical assistance work plan was agreed by the national stakeholders and a consortium of partners including UNIDO, WHO, UNAIDS, UNDP, UNFPA, the New Partnership for Africa's Development (NEPAD), the African Network for Drug and Diagnostic Innovation (ANDI) and the Federation of African Pharmaceutical Manufacturer's Associations (FAPMA). The work plan recognizes both the critical need to build capacity within public sector institutions and the private sector and the need within the industry for time and support to invest in upgrading.

The need for complex cross-institution coordination to implement the work plan is illustrated by the collaboration with the Ghanaian Food and Drug Authority (FDA) to develop and implement a good manufacturing practices (GMP) road map; the development of training modules for industry on developing capital investment plans and managing capital project life cycles; the creation of a business linkages platform to enable companies to access the know-how that they require in the short term whilst internal technical capacity is developed; and a market data initiative to provide market transparency to inform policy makers, industry and investors in their decision making. Technical assistance has also

been provided to assist government in assessing investment proposals made by pharmaceutical companies under the Export Development and Agriculture Investment Fund (EDAIF) stimulus package, described below.

Upgrading, market consolidation and the challenge of finance

Central to all this work is the recognition that the pharmaceutical sector in Africa needs to upgrade standards in order to be able to provide safe, efficacious, quality-assured essential medicines. Achieving this objective is a highly complex undertaking requiring coordinated action of many parties at national, regional, continental and international levels (Chapter 12). Africa-based companies are able to compete at international standards, contrary to some earlier expressed views (see Chapter 6; Chaudhuri and West, 2014). The most technically advanced companies such as Universal in Kenya (WHO-prequalified for its Lamivudine Zidovudine FDC), Quality Chemicals International Limited in Uganda (with additional site licence for Cipla's pre-qualified products) and four companies in Nigeria that have recently received WHO-GMP certification (including May and Baker and Evans Pharmaceuticals) have attained high international standards.

However, the industry's contribution to economic development and improved public health requires a broader swathe of companies to upgrade to international quality standards, not just for products to treat the major pandemics but for all medicines that have a critical role to play in treating communicable and non-communicable diseases. As earlier chapters have shown, companies across Africa are striving to upgrade their facilities and their manufacturing processes and procedures. However, whilst there have been no published systematic studies on the range of quality standards to which manufacturers on the continent adhere, it is clear that many companies licensed to manufacture pharmaceuticals in Africa currently operate in premises and/or have quality management systems that fall below what should be acceptable.

The concept of the GMP 'road map' establishes rising quality targets over a defined period of time. During transition to meet these milestones, those companies that are operating below them should be restricted to manufacturing products where the risk to health is minimized. Such a stepwise approach creates a transition process for the industry whilst protecting public health. So long as the requirements are enforced by credible sanctions, the framework can discourage unproductive use of

subsidies by manufacturers not in practice investing in upgrading. It also provides some market protection for leading companies that have made significant investment, since they can sell a broader range of products during the transition phase.

The PMPA Business Plan focuses initially on generic small-molecule non-sterile production of final formulations in Africa. Even with this subset of essential medicines, the complexity of the system within which manufacturing takes place is significant (see Chapter 2). The industry has multiple stakeholders, operates in widely varying contexts across countries and regions, and includes manufacturers at significantly different levels of industrial development.

Nevertheless, some general requirements for industry development can be identified, and of these the central requirement is finance. Companies need to access capital to invest in retrofitting facilities or building new plants to meet international standards. The magnitude of investment required will depend on many variables including the specific pharmaceutical forms that a manufacturer wishes to produce, the scale of the plant and the starting point of the organization, but most companies will require at least US$10 million (see also Chapter 5 for the financial requirements for a start-up). The efficient use of this investment requires that companies in this knowledge-intensive industry can access the capabilities to design and build GMP-compliant plants and develop or acquire the capabilities to run them. Companies need assistance to access know-how, time to develop plans and implement them, and more time to develop the capabilities first to operate efficiently and then to adapt and innovate.

Upgrading is done by companies, not governments. But policy makers and international development organizations need to understand the challenges faced by manufacturers, and to work with them and with national and regional entities to enable effective upgrading whilst avoiding wasteful use of scarce resources. The AUC has recognized this need for close collaboration, convening a consortium of continental and international partners, including the Federation of African Pharmaceutical Manufacturers Associations (FAPMA), to implement the PMPA Business Plan. The consortium will work with African trade associations, regions and sovereign states on strategies for upgrading the industry.

Regulatory market shaping

In order to invest sustainably, pharmaceutical companies also need access to a large and effectively regulated market in which returns can be

made. Further strengthening of regulatory authorities is needed to ensure that legitimate manufacturers do not face competition from spurious, substandard and counterfeit products. Pharmaceutical manufacturers also need to utilize capacity efficiently in order to be competitive, and market scale is an important contributor to achieving cost efficiency. Since many African countries' populations are relatively small, current efforts to defragment African regional markets, and confidence in their likely success, are vital prerequisites to mobilizing investment for many pharmaceutical manufacturers. While for a few firms international donor-funded markets may offer larger-scale market opportunities, the sustainability of an exclusive focus on these markets in the long term is questionable.

Important progress has been made in the direction of regional market consolidation, through the African Medicines Regulatory Harmonization initiative (AMRH), particularly in the EAC and ECOWAS Regional Economic Communities. The documentation for regulatory approval across member states will at least be standardized, removing significant transaction costs from manufacturers, and boding well for increasingly harmonized regulatory requirements in the future (see Chapter 12).

Finally, as earlier chapters have documented, local manufacturers are frequently at an inherent disadvantage in competition with imported medicines, and corrections to the tax and tariff frameworks are required at regional level. The ECOWAS Regional Pharmaceutical Plan (ERPP) advocates for zero tariffs on raw materials, machinery and equipment for pharmaceutical manufacturing within the Regional Economic Community and exemption of inputs from VAT. It also recognizes the need for an appropriate regional framework to support the stepwise approach to upgrading.

Such initiatives can help investors to assess potential returns. However, the quantification of the market opportunities remains elusive, given the paucity of market data for most African countries and regions. This market opacity increases the perceived risk for investors, leading in turn to higher interest payments through an increased risk coupon required for debt providers, or to a higher internal rate of return required by equity investors. The cost of investment capital for African pharmaceutical investors remains a barrier for many companies in countries where interest rates on bank loans may exceed 25%. The next two sections tackle the funding challenge in more detail, first from the point of view of the manufacturers and private financing institutions, and then from the point of view of governments seeking to enable investment for industrial growth.

Building financial capabilities in manufacturers and financial institutions

The African local pharmaceutical industry is playing technological catch-up based on building technological capabilities (Chapter 2). These technological capabilities are sometimes summarized as know-what, know-how, know-why and know-who (Ernst and Lundvall, 1997). They include the skills needed for investment, production and creating market and non-market linkages (Lall, 1992): using technology effectively for expansion; handling key production systems from quality control and operation and maintenance to adaptation and improvement; and dealing effectively with suppliers and customers. While it is accepted that finance plays a strategic role in funding working capital requirements and capital investment, it is however less well documented that many Africa-based firms lack essential capabilities in raising and managing finance effectively (Banda, 2013).

The essential finance capabilities include the ability to understand a project life cycle and phase finance and to structure the most relevant type of financial product. It also encompasses lending technology, pricing and an overall financial approach that does not choke the financial health of the borrowing firm, but rather enhances its productive capacity. Financial capability involves knowing where to get the most appropriately structured financial products, from whom, and when to use them. These firm-level financial capabilities are particularly important for developing-country contexts, where financial systems are not well developed and growth of capital-intensive enterprises depends on capital investment financing (long-term foreign loans), in most cases from offshore sources.

In this section we explore finance capability in the firm and financial institution. This discussion is grounded in empirical work carried out on Zimbabwean pharmaceutical companies and financial institutions, and additional interviews with pharmaceutical sector players in Uganda, Kenya, Tanzania and Ethiopia up to 2013. We analyse how firms use finance expertise and competencies, to identify and manage short-, medium- and long-term funding cycles. We focus on financial institutions at a micro-level and attempt to tease out the technical knowledge and capabilities needed to competently assess, classify, monitor and manage risks. The classes of risk may include credit, management, performance, regulatory, foreign exchange, payment and market risk which in various combinations manifest during a project lifecycle.

The financing context for pharmaceutical firms in Africa

Economic, social and financial history shows sources of finance for setting up enterprises globally have been predominantly internal or own finance, made up of savings, wealth and loans from family and friends (Lazonick and O'Sullivan, 1997a, 1997b), in the industrialization era. Enterprise growth was funded internally by retained earnings, and externally banks were the most prevalent source of finance historically (Lazonick and O'Sullivan, 1997a, 1997b), specifically for the period from 1970 to 1989 (Corbett and Jenkinson, 1996). Other sources of external finance were venture capitalists and capital markets. The key determinants of financing source were the enterprise's management experience, skills and credit reputation.

Growing companies with experienced management, poor to good future prospects, medium to high risk and established credit reputations are likely to use banks as sources of external funds (Corbett and Jenkinson, 1996). African enterprise financing studies similarly find that of all external funding sources, bank finance has been the most prevalent (Fafchamps et al., 1995.)

For established companies, with established credit records, low credit risk and run by experienced management, capital markets are the most likely source of external finance. However, capital markets did not play a major role in raising capital for industrialization, except to a certain extent in the US (Lazonick and O'Sullivan, 1997a, 1997b). Capital markets were used particularly to transfer ownership of corporate entities from family-run or close-knit ownership structures to publicly quoted companies, rather than to raise finance for industrialization.

Capital markets, however, are of little significance in Sub-Saharan African markets because of their small scale and low capitalization, with the possible exceptions of South Africa, Nigeria and Kenya. Venture capital and capital markets are more the exception than the norm in Africa. A more important source of external finance is foreign direct investment (FDI), which can embody technology flows (Portelli and Narula, 2004). FDI allows the developing country to import technology without payment, since the investor brings in knowledge and skills required to operate the technology. Ensuring effective technology transfer is a challenge. However, data on financing manufacturing industry in seven countries in Sub-Saharan Africa indicate that FDI and external/offshore financing were the main sources of capital, reinforcing Ndlela's (2007) and Riddell's (1990) accounts of FDI as being critical for the emergence of the manufacturing industry in countries such as Zimbabwe.

How then do firms select internal or external avenues for financing investment? Internal funds include retained earnings, depreciation or fresh equity injection from existing shareholders. External funds include bank debt, hybrid bonds or issuing of new equity to new shareholders. When internal funds are limited, management seeks external funds. A 'pecking order' theory (Myers, 1984) argues that in the face of limited information, firms will prefer to use own financial resources such as retained earnings or profits; only if self-financing is insufficient will management use external debt instruments: first bank debt, then hybrid bonds, and the last option will be new equity. The order of preference is determined by the objective of retaining management control. Hybrid securities such as convertible bonds dilute management control less, and carry fewer external accountability (discipline and reporting) requirements compared to stock exchange equity. Equity is a last resort because of onerous reporting standards and controls when dealing with broad shareholding structures and professional managers as agents of shareholders (Myers and Majluf, 1984).

Finance capability gaps in pharmaceutical firms

Faced with these financing constraints and choices, a firm with limited internal funds needs to develop capabilities to scan for potential funders and financial products nationally, regionally and internationally. The firm needs to articulate its organizational, dynamic and technological capabilities in a robust well-argued project finance document with supporting data. In building the project finance document and data, the firm needs to use its external networks to assess economic, industry and business environments and attendant risks, as well as stress-testing project data. The finance department as the key operating contact point with external financiers articulates the firm's competencies and capabilities in procurement (trade credit included), research and development, production and engineering, as well as sales and marketing capabilities. Table 15.1 Column 1 summarizes the financial capabilities the firms require.

The firm then needs to negotiate with financial institutions on appropriate finance products by competently structuring the debt or equity relevant to business needs. If this is not managed properly, financial institutions can push their preferred high-yielding products. The firm may then be burdened with finance products characterized by high charges, onerous covenants, triggers and security (collateral) requirements. Firms thus have a great deal to gain from finance capability to identify and structure appropriate borrowing products and negotiate on pricing.

Table 15.1 Finance capabilities at the firm and financial institution levels

Pharmaceutical firms' required competencies	**Funder's (financial institutions') required competencies**
Identify the businesses' financial needs: Working capital and capital investment requirements	Understand the industry, business, economic, political, and regulatory environment.
Ascertain the best available financing structure; a mix of short, medium and long term finance through debt, equity or hybrid instruments to structure the funding model for the firm	Sector-specific knowledge to competently identify, analyse and manage risks in business, industry, management, markets and regulation. Some funders have a central set of industry and sector specific skills that assists all business units.
Structuring the funding model requires development of knowledge of lending technologies and funding instruments on the market and outside national borders	Alignment of internal capabilities in prospecting, screening, analysis, structuring financial products/ funding schemes, document perfection, disbursement of funds, monitoring and control and eventual repayment of principal and interest.
Crafting a competent project finance proposal that identifies project risks and how they are managed through the management, organisational and technological capabilities of the firm.	Whilst managing projects identify opportunities and the exhibit flexibility to change within and after the life of the funded project.
Competency to apply financial resources to originally identified funding needs, and through financial management capability run successive asset conversion cycles to generate profit and maintain commercial viability.	Through learning-by-doing transfer skills and capabilities developed to other industrial sectors and within departments in the institution.
Competence to repay interest and principal on time, and meet challenges in restructuring debt after negotiation with the funders.	

Source: Compiled by author from fieldwork in Zimbabwe, 2010–13.

Our interview data show, however, that these finance capabilities are lacking in many firms. One respondent in Zimbabwe remarked that the firms 'were afraid to approach international banks because they are not able to produce a robust project proposal and are afraid of being asked questions'. Crafting a project proposal requires knowledge of the firms'

capabilities, what the money is needed for, and how revenue will be generated to repay debt. Based on the dynamics of the proposed project business cycles, the firm needs to be able to know which financing tool would be most advantageous to it instead of waiting for the bank to always propose the mode of financing.

Building finance capabilities in banks

Finance capability in financial institutions refers to their ability to source projects to invest in (investment capability); analyse the risks; structure the finance instrument, price the debt instrument and loan duration; followed by monitoring and control and eventually repayment of the debt by the borrower. Various players within the financial institution interact in the process of financing a project. The internal staff identify and analyse risks that include but are not limited to business, industry, management, country, political and foreign currency risks. The risk management process is closely tied to loan structuring, documentation, disbursement and monitoring and control procedures.

These processes depend on in-depth knowledge of the sector being assessed (Table 15.1). In practice, information is opaque and hard to assess. Our research evidence from Zimbabwe and secondary data evidence from East and West Africa suggests lack of in-depth and relevant pharmaceutical sector knowledge by financial institutions. A repeated claim by pharmaceutical executives is that financial institutions do not understand the business of African pharmaceutical drug manufacture. Evidence from Zimbabwe suggests that financiers also need to develop an in-depth knowledge of the economy, industry and health sector for preliminary analysis of projects. They need to greatly improve their networking within the financial sector and the national economy to acquire relevant information for prospecting and analysing projects.

Table 15.2 maps, using Lall's (1992) concept of firm-level technologies, the capabilities needed by these financial institutions. The table maps prospecting, risk analysis, facility structuring and documentation, loan approval, loan disbursement, monitoring and control and ultimately loan repayment. Under prospecting capabilities, relationship managers use investment and networking capabilities to scout different industrial sectors for potential deals. They need intimate knowledge of the economy, industry, various business sectors, credit policy and underwriting standards. Interview respondents pointed to the use of both codified and tacit knowledge at this early stage. They emphasized the importance of experienced 'old-timers' for connections and

Table 15.2 Finance capabilities required by financial institutions, mapped using Lall's (1992) firm-level technological capability framework

Commercial Bank Activity	Processes Carried Out	Equivalent Technological Capability
Deal Prospecting	Based on local knowledge and economic set-up, the market development and sales team prospect for lending candidates that fall within credit policy and underwriting standards. They use networked capabilities for introductions and access to potential borrowers.	The bank uses **linkage capabilities** and **investment capabilities** in accessing borrowers and internal project finance appraisal systems.
Credit Risk Function	Using the following lending technologies: financial statement lending, leasing/asset backed, small business credit scoring or relationship lending in various combinations risk experts analyse for various forms of risks.	The banks use **investment capabilities** to ascertain their appetite for lending to the borrower. **Linkage capabilities** are used to collect information that informs risk analysis and management.
Approval Process	Internal credit processes are followed to independently assess the project documents produced within the institution. The approvers use their knowledge and networks to make informed decisions in the approval process.	**Investment capability** and **linkage capabilities** are used to assess the project for funding.
Accessing Funds by The Borrower	Internal loan administration departments ensure compliance with internal processes, all conditions precedent, and regulatory requirements.	This is mainly **process engineering capability.**
Ensuring Repayment of Borrowed Funds	Based on conditions laid out in the loan agreement, internal experts in sales, credit and credit administration control and monitor the project loan. They use proprietary data and processes as well as external sources of information such as trade and press reports for adverse or positive information. This can also serve as a source of further deal prospecting.	The main capabilities used are **investment, linkage, product and process engineering capabilities**.

Source: Compiled by author from experience and fieldwork between 2011 and 2013.

networks evidencing the need for linkage capabilities. Risk analysis, loan structuring and approval use codified and tacit knowledge for decision making by way of agreed financial ratios and internal metrics. Chief Risk Officers also acknowledged the inherent use of 'gut feel', implying relevance of tacit knowledge.

Capabilities that need to be built thus include loan disbursement, monitoring and control and finally repayment of the loan (Table 15.2). The process involves agreement of terms and conditions between the borrower and financier through a loan agreement document (commonly called the loan facility). On fulfilment of the conditions precedent, the loan administration department processes the security for the loan facility and disburses the funds. Monitoring and control is based on the conditions set out in the loan facility. The capabilities at this stage include those of product and process engineering and also linkage capabilities. Our evidence from empirical work in Zimbabwe and interviews with pharmaceutical executives from East Africa shows a clear perception of financial institutions' deficit of in-depth knowledge of pharmaceutical manufacturing business dynamics and attendant risks and opportunities. These challenges were acknowledged by financial institution executives who agreed that they did not understand the pharmaceutical industry. This information asymmetry and opacity leads to classification of the African pharmaceutical manufacturing sector as high-risk, negatively influencing loan pricing.

The financiers and pharmaceutical executives interviewed proposed to tackle these failings through training and exposure to the pharmaceutical industry. Finance capability cannot be taken for granted and requires purposive and strategic investment to build these competences. An illustration of what can be done is drawn from an innovative mid-career recruitment programme of one international bank in Zimbabwe; Standard Chartered Bank. This programme allowed the bank to build skills and a broader knowledge base by recruiting non-traditional bank trained professionals (Table 15.3). This formed part of an Africa-wide initiative by Standard Chartered Bank Africa.

A senior manager who has since left the bank said this programme was a short-term strategic move to fill an identified skills gap. This seems paradoxical; an innovative and strategic approach which could have contributed a longer term strategy to generate risk analysis skills for project management and build capabilities was relegated to a short term measure. The senior manager argued that once the identified skills gap had been filled, they could revert to the usual graduate trainee programme and train in-house. He argued that the mid-career entrants

Table 15.3 Recruitment of non-traditional banking skills to build finance capability by one Zimbabwean international bank in 1998–2000

Intake	Skills Sets	Roles in the Bank
1	Engineers, Economists	Credit Risk Analysis, Monitoring and Management; Relationship Management; Processing; Global Markets; Retail Banking
2	Engineers (electrical, mechanical and civil), Scientist, Agriculture and Geo-Sensing, Computing Technology and Programming,	Credit Risk Analysis, Monitoring and Management; Relationship Management; Processing; Marketing; Treasury (Global Markets); Retail Banking; Direct Banking; Branch Management; Credit Operations; Interest Recalculation; Structured Trade Finance; Transactional Banking; Syndicated Lending
3	Accountant, Scientist	Credit Risk Analysis, Monitoring and Management; Finance; Treasury Back Office Operations

Source: Compiled by author from fieldwork in Zimbabwe (2010–13) and experience.

came in at middle-management level, were more expensive to the bank and so reverting to the cheaper junior level graduate trainees helped contain costs. However it is clear that these 'non-traditional bankers' had added value to credit risk analysis, management and monitoring, with their specialist skills and in-depth technical knowledge. They served as a knowledge bank that junior and senior management tapped into to understand once-opaque industrial operations. As Table 15.3 shows, many of these recruits' skills were used to build a deeper technical knowledge of industries that the bank funded. The short lived innovative programme (a flash of strategic brilliance) demonstrates the lost opportunity for long term skills and finance capability building.

Government interventions to assist companies to access investment capital

There is therefore a need for micro-level financial skills to be developed within the industry and within the financial community. However, it is also recognized that governments need to intervene to enable companies to access affordable investment capital. What types of interventions can governments employ to help resolve this critical issue? A government can provide soft loans, or it can use direct intervention to reduce

the cost of financing (e.g. interest subsidies). As well as such specific initiatives, it can intervene to create a conducive industry context that makes investment in the sector attractive to various providers of capital, thereby reducing perception of risk and theoretically increasing the availability of and reducing the cost of capital. Finally, a government can employ time-limited incentives to support industry investment.

Direct capital provision

Many industry actors and a number of trade associations have called for their governments to set up designated funds for low-cost investment in the pharmaceutical sector. One example is in Ghana, where in 2014 the President announced that Cedis 50 million would be set aside from the Export Development and Agriculture Investment Fund (EDAIF) for soft loans to the pharmaceutical sector (with recent currency depreciation this is now equivalent to less than USD$20 million). The government of Nigeria proposed a Naira 200 billion (roughly USD$100 million) fund to support the sector, but this has yet to materialize.

These limited examples to date suggest that for most countries, direct capital provision may not be viable or of sufficient impact to enable the transformation of the industry. Where countries (such as Ghana) have more than a handful of manufacturers, it is unlikely that governments have resources to create a fund of sufficient magnitude to tackle the capital funding gap for a meaningful number of companies. Furthermore, a government making direct capital provision must be equipped to make informed decisions, to ensure these scarce public resources are not wasted through poor investment. Public funding of investment capital for the pharmaceutical sector therefore demands the development of financial capabilities of the type just outlined within governments as well as private institutions.

However, where limited resources can be brought to bear, there is the potential for leveraging these public funds to assist a number of companies to achieve an affordable cost of capital. For example the proportion of individual investments that a fund supports could be limited to a certain percentage of capital required. A blended cost of capital combining public with commercial investment can be more affordable than pure commercial capital. Such leverage could be enhanced if governments consider taking a junior debt position, thereby perhaps reducing the risk coupon required by private sector investors.

Assuming that an investment fund can be regularly recapitalized, through a sustainable funding mechanism such as a levy on pharmaceutical imports for example, public resources could be allocated in tranches. In this way the capital requirements of an organization at one

particular time during a project lifecycle can be addressed without tying up resources required for total overall capital requirements, and therefore a greater number of companies can be supported simultaneously over a number of years.

Direct government expenditure to reduce the cost of financing

Governments can also facilitate access to affordable investment capital through subsidizing interest payments. Interest subsidies were made available to Indian pharmaceutical manufacturers to support their development. Using public resources to support the servicing of debt rather than providing the capital itself can be a more efficient use of public resources. However, limitations on the political acceptability of direct transfer of public funds to the private sector, given other pressing demands on public expenditure, may make such a model untenable for many countries. At the least, mechanisms are essential to control waste of resources and limit government financial liabilities.

Can criteria be established for companies to be eligible for such subsidies? There is widespread anxiety about governments trying to 'pick winners', or rather failing to spot losers, thereby backing unsustainable manufacturers and losing scarce funds to unintended uses. All industrial policy interventions require the development of industrial skills and capabilities within government.

Another concern may be that an interest subsidy approach can reinforce a debt-financing model, shifting the industry away from equity financing. Equity financing should form an element of the capital structure of firm in which the return on investment is necessarily long term. Hence, parallel mechanisms may be needed to encourage companies to seek some equity financing to cover some of the capital requirements for upgrading. These mechanisms could include facilitating repatriation of profits, to stimulate interest from foreign investors, or levelling the playing field between debt and equity financing through limiting the tax shields that debt conveys.

Interest subsidies provide an investment incentive, but have the advantage that they do not have a direct impact on revenues and operating profitability, unlike preferential pricing or other forms of market protection. They may therefore be a constructive means of support in that they do not encourage uncompetitive practices.

Creating an industry context that attracts capital

Creating a conducive context for pharmaceutical manufacturing involves the combination of multiple interventions, not all of which

are necessarily within the purview of individual governments. The importance of a regional market has already been highlighted. However, individual governments can tackle dimensions such as the overall business environment (corporate tax rates and special economic zones, for example), as well as sector-specific aspects such as strengthening regulatory oversight and developing human resources. While credible forward-looking statements from governments help, genuine impact does require observable developments and interventions.

The role of time-limited incentives

The PMPA Business Plan, regional plans and national strategies all call for time-limited incentives. Given the specific nature of the pharmaceutical industry, what is the purpose of these incentives, what are the tools available to governments and how do these vary by country context?

First, there is a clear distinction to be made between time-limited incentives and policies to induce structural change whether on the demand or supply side. For instance, resolving the widespread unequal tax and duty regimes applied to imports versus inputs for local production (Chapters 2–6) is a long-term structural approach that needs to be embedded. However, it is also possible to decide to adjust tax regimes for a limited period of time, to convey a temporary competitive advantage to local producers in competition with imports.

Examples of time-limited incentives that could be utilized can be drawn from the policy actions already implemented within Africa, on other continents, and for other industries. A major concern for manufacturers is funding their working capital requirements. For African companies this is a particularly profound problem, since they need to import the vast majority of inputs from abroad. Often, credit terms are used up before raw materials can even begin to be converted into final formulations. Such concerns can be addressed through provision of working capital credits, an approach that was used successfully in India, or through underwriting letters of credit enabling manufacturers to secure improved credit terms from their suppliers.

Other government incentives can focus on reducing the tax burden for which companies are liable, as a means to free up resources to fund investment. Effectively, this provides an additional margin that can make local products more competitive in the transition period, as companies learn to operate facilities more efficiently. Examples of incentives to achieve these intents are tax holidays and special depreciation provisions. The latter were once again used in India where companies

were able to include depreciation over time on the profit and loss statements up to 150% of the capital cost for plants and equipment.

Previous chapters have covered the use of procurement preferences and restricted lists and highlighted the potential for such approaches to give a boost to local manufacturers. There are acknowledged downsides associated with market protection, particularly if done at a national rather than a regional level, since it can, for example, reduce competition. Introducing preferential import tariffs on inputs for local production is another mechanism to provide a degree of protection for nascent industries. Again, a regional approach that consolidates markets can help to implement this while sustaining local competition.

This discussion is far from exhaustive in covering the range of industrial policy incentives available. The relative merits of the different tools depend strongly on context, but their fundamental purpose is to support the industry during a transition phase so that companies can build capabilities, develop plans for upgrading facilities and execute them, whilst continuing to compete viably during the transition. This transition period also provides time for policy makers to put in place longer term initiatives to sustain the economic and technical viability of high-quality manufacturing, including defragmenting markets and building the institutional capacities and skills within government and industry actors. Initiatives are under way to address these structural realities, but a much stronger push is still required, with the support of international technical assistance programmes to build government skills and accelerate industrial knowledge accumulation.

The importance of country context

Each country considering development of its pharmaceutical industry faces a unique context which determines what policies and initiatives are required and feasible. With a large domestic market, a government could employ protective measures to support industry growth, using import substitution as Ethiopia has done (Chapter 4). For smaller countries, however, regional exports are likely to be a critical part of the business mix for a sustainable industry. Botswana has an expressed desire to establish a pharmaceutical industry, but with a population of 2 million, its strategic positioning objective is to become a regional centre for pharmaceutical production.

Another key variable is the state of the public finances. All countries face choices as to where they invest public resources, and where such resources are severely constrained, the Ministry of Finance and the National Revenue Authority are likely to resist policy initiatives that will

reduce the contribution of current taxes levied on the sector to government income, or that increase expenditure through for example procurement preferences or industry subsidies. For example, at present, Ghana and Kenya face difficult public finance situations, making budget-neutral support mechanism such as domestic market protection an attractive option. While the options open to governments and their relative power vary according to the specific context, complementary regional initiatives such as tariff harmonization, regulatory harmonization and general collaboration between countries can increase the leverage that national government interventions have to stimulate upgrading and development of the sector.

Conclusion

We began by highlighting recent developments at regional, continental and international levels that have generated a new convergence of high-level political will to support the development of the pharmaceutical manufacturing industry in Africa. The chapter has sought to shift the understanding of the key challenge of investment finance within those strategies, from a focus on access to capital to a framework of collaborative financial capability building in firms, financial institutions and governments. The chapter outlines the shared political recognition of the need for time, protection and incentives to build the industrial base through upgrading and transition to higher skills and quality standards. Development of new skills within interconnected institutions, evolution of regional markets and firms making the requisite investments and learning to operate competitively at international standards cannot happen overnight. This final chapter, framed by the intensive international and regional collaborations that are now under way, also frames the detailed studies in this book as a timely contribution to those endeavours.

Note

1. See the World Trade Organisation website at https://www.wto.org/english/tratop_e/trips_e/trips_e.htm for more information on TRIPS.