CHAPTER 7

Pharmaceutical production policy

ILLUSTRATIONS

COUNTRY STUDIES

SUMMARY

Policy makers must be concerned about pharmaceutical production for the same reasons that underlie other policy and legal decisions: pharmaceuticals can be dangerous as well as lifesaving. Health professionals and patients have no ready way of making judgments about medicines without public surveillance as a guide.

The potential for national or local production of quality-assured, low-cost pharmaceuticals to meet national needs is an issue that has been debated and discussed for several decades. The justifications for local production have included the problems of lack of access, high prices for imported pharmaceuticals, and poor pharmaceutical quality. These challenges prompted public and political interest in considering local production to promote self-sufficiency, achieve independence from international suppliers, develop local industrial capacity, and create jobs. The changing landscape in the global pharmaceutical market, however, has made local production of pharmaceuticals in many countries unlikely as a viable option, except under certain circumstances, such as the existence of a large national market or a need to address specific requirements within a local market. Furthermore, self-sufficiency in pharmaceutical supply has proved to be a myth; because most active pharmaceutical ingredients are now sourced globally, even the most developed countries cannot be considered wholly self-sufficient in pharmaceutical production.

The globalization of the pharmaceutical sector and the advent of worldwide public health funding initiatives have led to a more competitive market for generic pharmaceuticals, resulting in significant decreases in the prices of some essential medicines. Domestic production operations have had difficulty achieving the high quality expected in the market at prices that compete with those of large-scale international producers, and many countries have limited capacity to monitor and regulate pharmaceutical production activities. Decisions regarding producing or importing pharmaceuticals are complex and involve health policy, industrial policy, a country's national development strategy, and related political pressures. Despite the argument that actual production decisions should be left to private-sector and market forces, policy makers must sometimes respond to pressures to become more involved in decisions about pharmaceutical production. The principal policy question now is often not whether to make or buy pharmaceuticals, but rather what pharmaceuticals to buy and where to buy them.

Three important points related to decision making about local pharmaceutical production guide this chapter—

- Pharmaceuticals are potentially lifesaving and life-threatening. Pharmaceutical production requires precise standards, quality control, a highly skilled labor base, capital, national regulatory capacity, and management. Modern pharmaceutical production often uses raw materials that are most economical in the international market, which means that high-quality, low-cost medicines are not likely to be produced from the raw materials stage in countries that do not have the required market size and resources in terms of skilled people, technology, and quality control.
- Section 7.1 describes several types of pharmaceutical manufacturers that operate in low- and middle-income countries, ranging from subsidiaries of multinational firms to small, hospital-based operations that repackage medicines into course-of-therapy packs. Policy makers must assess the feasibility for the range of production options, from the primary manufacture of raw materials to the packaging of finished products.
- Because consumers are unable to judge medicine quality on their own, policy makers must be concerned about regulating the production quality of medicines from either international or domestic sources. Regulatory policy should focus on assuring that manufacturers who supply products to the national market follow good manufacturing practices. Whether policy makers take an active or a passive role, they must recognize that the regulations and incentives existing in a country always affect pharmaceutical production. The most constructive stance is to shape policies and regulations that promote the goal of reliable access to effective, safe, and inexpensive medicines rather than to focus on where the production takes place. If preferences are given to locally produced medicines, the sick may pay directly or indirectly for these preferences through higher prices or poorer quality.

7.1 Levels and types of local production

Most countries are part of the global pharmaceutical market, but few try to be entirely self-sufficient. Raw materials, which form the backbone of the industry, are produced and traded as commodities worldwide. Almost all countries, even the largest ones, actively acquire at least some raw materials, machinery, and packaging goods abroad—at the most economical prices and at different stages of production—and then complete the process at home. It is a matter of competitive advantage, not imaginary independence, in an increasingly globalized economy.

Production standards known as good manufacturing practices (GMPs) are quality requirements that have been adopted as guidelines by the industry and the World Health Organization (WHO). The GMP system ensures that products are consistently produced according to quality standards appropriate to their intended use and as required by the product specification. Some countries require more-exacting standards to further ensure quality, and any hope for an export market increasingly requires compliance with international GMP standards.

The three different levels of production are primary, secondary, and tertiary.

Primary production

Primary production is the processing of raw materials to create active pharmaceutical ingredients (APIs) and ancillary substances used in pharmaceutical formulations. The final API, which is the biologically active compound in the pharmaceutical that produces the therapeutic effect, should meet pharmacopoeial or similar requirements. Primary manufacturing may involve either chemical or biological processes requiring different types of production facilities, technologies, skills, and knowledge. The manufacture of active ingredients is the most expensive aspect of pharmaceutical production because of the necessary investment in capital equipment, process development, and quality assurance systems.

The more modern or sophisticated the products, the more skills and greater capability are needed to develop and maintain the production processes. Few middle- to low-income countries will have all the infrastructure needed, including a pool of skilled workers (scientists and engineers), industrial technology, a research and development base, quality-control experience, capital, and reliable utilities—as well as the potential market size—to make primary production an initial goal. Rather, because these basic commodities are most efficiently produced in large volumes—much greater than the markets could absorb in many countries—they tend to be traded and bought as are other international commodities, such as steel, some foods, and other chemicals.

Secondary production

Secondary production is the large-scale processing of finished dosage forms, such as tablets, capsules, or injections, from raw materials or intermediate products, often from both local and imported sources. Production of sterile preparations (such as injections, antibiotics, and intravenous fluids) and nonsterile preparations (oral solids, liquids, and topical preparations) can be carried out with either locally produced or imported packing materials. Although less technically demanding than primary production, this stage must be completed to precise specifications. It requires modern, high-speed, precision equipment to produce pills, capsules, and liquids, often in large quantities and at very low unit costs, which are targets that small facilities find difficult to achieve, especially while also meeting international GMP standards.

Tertiary production

Tertiary production includes packaging and labeling finished products from primary and secondary sources into bulk packs, smaller dispensing packets, bottles, or course-of-therapy units for individual use. The initial quality of the pharmaceutical product established in the earlier phases of production must be maintained in the tertiary and final step, so ensuring high quality standards through rigorous operational procedures is important. This type of production can be developed first in many countries as a positive contribution that also builds industrial skill and experience. Tertiary production also addresses specific local needs for certain formulations, labeling, and packaging.

7.2 Trends in local production

During the 1970s and 1980s, some international organizations and governments were promoting the idea of creating or strengthening the pharmaceutical manufacturing capacity of developing countries under the assumptions that such initiatives would—

- Increase countries' self-sufficiency in pharmaceutical supply
- Improve medicine quality
- Produce foreign exchange through exports of domestically manufactured medicines
- Create new jobs

However, even with the enthusiasm about the potential role of pharmaceutical production in the developing world, a 1986 World Bank report (Lashman 1986) concluded that the economies of scale and technological requirements for manufacturing medicines made local production an unrealistic

option for most countries. The exceptions were countries with large local markets and the capacity to produce APIs, including Argentina, Brazil, China, Egypt, India, Mexico, and Thailand.

At that time, the pharmaceutical industry in most developing countries depended on production by multinational affiliates and the licensed production of generic products; very few developing countries were able to initiate any systematic pharmaceutical export (Balance, Pogany, and Forstner 1992). In addition, the increased market for generic medicines plus greater price competition led to significant decreases in the prices of many essential medicines. This market shift worked against domestic manufacturers, who were largely unable to produce medicines at prices that were competitive with those of large-scale international pharmaceutical producers. These factors led to a trend away from the promotion of local pharmaceutical production and toward more emphasis on quality-control and procurement issues (Kaplan and Laing 2005).

In a 2004 report, the World Health Organization estimated the worldwide pharmaceutical production capacity of 188 countries, which had changed little from the 1992 statistics—

- Ten countries had a sophisticated pharmaceutical industry and a significant research base (eight Western European countries, plus Japan and the United States). These countries—led by the United States and Japan—were responsible for 84 to 88 percent of the world's pharmaceutical production value.
- Sixteen countries had innovative capabilities: a sound production capacity and at least one new molecular entity marketed between 1961 and 1990 (including several European countries, Argentina, Australia, Canada, China, India, Israel, Mexico, and the Republic of Korea). India and China had seen huge growth in their pharmaceutical production over the preceding decade. India, in fact, had developed highly specialized manufacturing capabilities and had become one of the largest exporters of API raw materials for the production of generics (World Bank 2005).
- Thirteen countries produced both active ingredients and finished products (including Brazil, Egypt, Indonesia, Norway, and Turkey).
- Eighty-four countries from virtually every continent only produced finished products from imported ingredients.
- Forty-two countries and areas had no pharmaceutical industry (primarily low-income African and Asian countries).

Moving from one category to the next requires substantial technical and financial resources, and still, no country is completely self-sufficient in pharmaceutical production. Even countries that export more pharmaceuticals than they import still rely on imports of some finished products, APIs, or other materials.

Currently, several types of pharmaceutical manufacturers, with different business models, operate manufacturing facilities in low- and middle-income countries (World Bank 2005)—

- *Subsidiaries of large multinational companies* that manufacture patent-protected, branded products for local and regional markets.
- *Global manufacturers of generics* that focus on developed markets in the United States, Europe, and large middle-income markets such as India and China. Some have manufacturing operations in smaller developing countries or joint ventures with local manufacturers.
- *Generics companies with predominantly national operations* that focus on the domestic market with occasional exports into neighboring countries. Their ability to comply with good manufacturing practices varies.
- *Small-scale local manufacturers* that usually make a limited number of products, including traditional medicines, to serve local or regional markets. Most are not able to meet GMP standards.

In addition, most hospitals repackage medications in smaller, unit-dose containers and may compound specialty items, such as creams with special formulations, for their own patients and for satellite facilities. The type of small-scale production of pharmaceuticals in a hospital pharmacy could include secondary production from existing raw materials that are usually imported and the packaging or repackaging of finished goods into smaller dispensing packs and course-of-therapy packages (see Chapter 45).

National manufacturers vary widely in the scope of their operations. Some in larger markets may have substantial capabilities in primary and secondary manufacturing activities and extensive pharmaceutical distribution networks. Smaller countries may be limited to a few major companies that do basic manufacturing or formulation and packaging. Many developing countries may have only one or two local importing distributors who represent all the international manufacturers. Multinational manufacturers of proprietary medicines have used this pathway to globalize their operations, and as multinational generic producers grow, they will likely follow the same expansion model (Guimier, Lee, and Grupper 2004). Country Study 7-1 profiles three types of manufacturers operating in West Africa.

Finally, one of the most important global trends has been the rapid growth of active-ingredient manufacturing companies in India and China. India, especially, led the way in developing highly specialized manufacturing capabilities

that cover a large range of medicines, from antibiotics to antiretrovirals. Leading companies have invested in manufacturing facilities that meet the highest international standards for GMPs. Technical advances in China have caught up as it has entered into joint ventures with pharmaceutical manufacturers in developed countries as a way of acquiring technological expertise. China and India will probably maintain a competitive production advantage because of their skilled labor forces, low resource costs, and large, high-volume domestic markets, which will help them keep their pharmaceutical prices low (Attridge and Preker 2005).

7.3 The effect of globalization on local production

The creation of high-profile international initiatives, such as the Global Fund to Fight AIDS, Tuberculosis and Malaria, and increased funding for public health treatment programs are part of the growing momentum to increase access to medicines in developing countries (see Chapter 2). In addition, initiatives to reduce pharmaceutical prices, such as the Clinton Foundation's negotiations with multinational producers and global procurement mechanisms, such as the Global Fund's voluntary pooled procurement system, are expanding the number of procurement options for these countries. As a result, the market is growing for pharmaceuticals that treat diseases that disproportionately affect poor countries. In addition, the scale-up of public health treatment programs, such as antiretroviral therapy, is creating a large demand for pharmaceuticals in the public sector. Countries that are tempted to add to or expand their production of pharmaceuticals to fulfill the needs of such targeted public health programs must carefully evaluate the cost-effectiveness of global production compared with that of their procurement options. Global funding mechanisms require that products either be prequalified by WHO or approved by a stringent regulatory authority. So far, mainly

Country Study 7-1
Profiles of three pharmaceutical facilities operating in West Africa

A 2004 study looked at the pharmaceutical production capacity in West Africa using data available from interviews with key stakeholders and field visits to Ghana and Côte d'Ivoire. The following profiles illustrate the similarities and differences of three different types of pharmaceutical production operations.

The first firm is an owner-operated company that started small and grew into an operation employing more than 300 people, with production lines for tablets, liquids, capsules, syrups, and powders. The company sells most of its products to private-sector customers, but some sales go to the public sector. The firm does not export its products but has developed a large sales and distribution network covering the entire country. The company funded its expansion using sales profits that were supplemented by loans from commercial banks. Because the company already had significant domestic market share, it was looking for new markets and new products, including medicines to treat HIV/AIDS and malaria. Although the company's owner-operated status has probably helped keep costs manageable, strict control by the owners could discourage the recruitment of talented workers from outside the firm whose expertise could help the firm expand into a large-scale, international player.

Large European multinational pharmaceutical companies own the majority of the second firm, and it operates under licensing agreements with them and other international partners. The company's structure allows it to benefit from both the financial support and technical expertise of these experienced partners. However, because the firm buys most of its APIs through its parent companies, costs are higher than what the firm could achieve by procuring through open international tenders. Consequently, the prices of imported medicines from Asia are generally lower. The company is not planning on producing any new medicines to treat HIV/AIDS, tuberculosis, or malaria.

The third company is privately owned but run by professional expatriate managers brought in by the principal investors, who are based outside the country. On one hand, the company benefits from easier access to international financing and management expertise, but on the other hand, the expatriate management team is costly. The company is looking to expand its reach to export markets throughout West Africa and is planning to add an artemisinin-based combination therapy (ACT) product to its production portfolio.

The structure of each of these firms offers advantages and disadvantages to operating pharmaceutical production facilities in West Africa. The first and third companies, however, which plan on adding antiretrovirals and ACTs to their production, may have a difficult time meeting WHO prequalification requirements.

Source: Guimier, Lee, and Grupper 2004.

large, well-established companies have been able to achieve prequalification standards.

An additional factor affecting the globalization of the pharmaceutical sector is the World Trade Organization's Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). TRIPS allows countries affected by a public health crisis such as HIV/AIDS to bypass patent laws and issue a voluntary or compulsory license to a company to manufacture or import a particular medicine to ease the crisis. However, the consensus is that many smaller middle- and low-income countries lack the necessary infrastructure to take advantage of this mechanism by investing in and successfully operating pharmaceutical plants (although they may issue compulsory licenses to import such products). This situation may be changing, however. In 2010, WHO founded Quality Chemical Industries, Ltd., of Kampala, to be the first manufacturer in a least-developed country in compliance with GMPs—moving a step closer to achieving prequalification status in the WHO system.

Country Study 7-2
Health policy versus industrial policy: Rifampicin in India

The international market for rifampicin, an essential antituberculosis medicine, presented an example of rivalry between the pharmaceutical production sectors in China and India. In India, the cost of imported rifampicin from China, at 40 U.S. dollars (USD) per kilogram, was lower than the cost of Indian manufacturers, at USD 70 per kilogram. However, Indian manufacturers questioned the quality of the Chinese medicine and demanded that their government place restrictions on these imports. India already had an overcapacity for rifampicin manufacturing; therefore, this situation illustrates a typical schism between health policy goals and industrial policy goals. Because India was estimated to have 25 percent of the world's tuberculosis cases, the government had to decide which was more important: getting the cheapest rifampicin from China, which would presumably make the medicine more affordable for patients, or sustaining and developing national rifampicin manufacturers.

Source: Attridge and Preker 2005.

7.4 Issues that affect local production decisions

In some countries, national pharmaceutical policies promote local pharmaceutical production as a way of improving access to medicines and achieving national self-sufficiency. But decisions regarding which pharmaceuticals and how many should be imported or locally produced are complex and involve health policy, industrial policy, and a country's national development strategy. Sometimes, a health policy with the goal of increasing access to affordable and quality-assured medicines is pitted against an industrial policy with the goal of promoting a local industry whose products may be more expensive than those on the international market (see Country Study 7-2). Countries should consider their economic conditions and health services infrastructure when deciding on investments in the local pharmaceutical industry.

The greatest challenge for policy makers is often not the creation of a comprehensive policy on local production, but rather the creation of policy elements that function as constructive next steps and build on existing conditions and local institutional capacities. Many countries are limited in their capacity to monitor, supervise, and regulate pharmaceutical production. Policies need to take into account a country's capacity to implement and enforce appropriate regulations.

The Assessment Guide for this chapter lists many of the factors and policy issues that affect production decisions. Each issue contains elements that may favor or hinder the production decision or leave it unaffected. In general, policy makers should concentrate on promoting guidelines that support the essential medicines concept: improving the prospects of access to low-cost, quality-assured, effective medicines. Producers can make their own decisions about what and how much to make, and essential medicines program managers can concentrate on choosing to buy from the best sources, whether they are domestic or international.

Human and physical infrastructure

A primary issue in many countries, especially low-income countries, is the ability to find experienced and skilled staff, particularly scientists and engineers. Managing the issues of quality assurance, including regulatory compliance and meeting GMP standards, is key to ensuring high quality. In the current market, technical expertise to produce complex formulations, such as fixed-dose combinations, is critical. In the short term, human resources can be supplemented from external sources, but production decisions are long-term investments that require sustainable, local staffing.

In addition to human resources, the reliability of water, power, and environmental controls are central to the production decision. If materials, equipment, and spare parts are not available, items will have to be imported from countries with established pharmaceutical industries.

Market factors

Population size and distribution combine with per-capita income to determine how many potential customers in the national market will be able to buy medicines. Although aspirations for health are high, difficult economic times can lead to falling real personal incomes and low government capacity to provide health services, both of which limit actual market size in many countries. The national markets of most developing countries are too small to absorb all the outputs of domestic production if done at scale; therefore, a manufacturer producing essential medicines at a scale adequate to lower unit production costs to competitive levels will often have to consider exporting its products, which requires a more sophisticated distribution network and the ability to ensure that its products meet international quality standards.

Other local competitors and importers also need to be taken into account, along with the possibility of a preference in the public-sector market for local production. Barriers to importation of finished products may help local producers initially, but they will increase local prices paid by consumers (and public health organizations) and make the national producers uncompetitive internationally.

Regulatory and legal provisions

As discussed in Chapter 6, pharmaceutical registration requirements are rules that prohibit dangerous, unproven, or useless items and promote the availability of quality-assured and effective medicines. However, a cumbersome or corrupt registration process can limit a producer's incentives to offer a product. From the producer's viewpoint, the important issues related to registration are the transparency, speed, fairness, and expense of the process.

With the globalization of the pharmaceutical sector, an increasing movement exists to establish and enforce GMPs as common high standards for quality. The enforcement of these standards is through regular inspection of manufacturing facilities by authorities. Therefore, a strong regulatory agency in the home country facilitates an export business, because it provides a credible proof of quality.

A manufacturer's adherence to GMPs can add significantly to investment and operating costs. If the national drug regulatory authority is not strong enough to enforce GMPs, facilities may be tempted to relax their practices. Given the shift toward globalized quality standards in pharmaceutical production, however, the rationale for local production at some lower quality standard has shrunk, and such second-tier products will be exposed in the world market. Currently, developing countries vary greatly in their capacity to monitor GMPs, and pharmaceutical manufacturing should be encouraged only in countries that have an effective regulatory agency to enforce them.

Economic incentives and disincentives

Pharmaceutical production involves a worldwide marketplace, and the raw materials that constitute about half of production costs are traded widely as competitive commodities. Reliable, rapid access to foreign exchange is essential. The pharmaceutical industry is commonly one of the most price-controlled industries, which can help as well as distort a local production decision; price controls, by definition, distort the marketplace. (See Chapter 9 for more information on pharmaceutical pricing policies).

Tax treatment and local development incentives can affect the cost of production start-ups through direct subsidies, assisted capitalization schemes, training support, or tax abatement. However, evidence suggests that legislated incentives to promote exports from local production do not affect developing-country production: by 1999, less than 5 percent of low-income country pharmaceuticals were exported on average, a figure that had been on the decline for two decades (WHO 2004).

Duties and import controls

Differential taxation of pharmaceutical materials, both imported and local, can significantly affect the production decision. If the public-policy goal is to create a level playing field for producer decisions on what and where to produce, there should be no difference in the tax treatment of raw materials, both active and inactive ingredients, and finished

Table 7-1 Distribution by country groups of tariff rates for finished pharmaceutical products, 2009

Tariff rate (%)	Number of countries (n = 136)	Low-income countries	Low–middle-income countries	Upper–middle-income countries	High-income countries
0	62	16	13	12	21
0–5.0	32	9	14	6	3
5.1–10.0	28	5	9	12	2
10.1–20.0	13	3	5	2	3
> 20.0	1	0	1	0	0

Source: Stevens and Linfield 2010.

products. Heavy taxation of packaging materials and production will deter local industrial development.

The Organisation for Economic Co-operation and Development (OECD) countries have an agreement to impose zero tariffs on specified lists of active ingredients for medicines, which has facilitated internal OECD pharmaceutical trading. Average tariff rates have been decreasing; however, in a 2009 analysis, 54 percent of countries were applying import tariffs, down from 61 percent in 2005 (Stevens and Linfield 2010). As Table 7-1 shows, for many middle-income and low-income countries, substantial tariff barriers remain.

Many pharmaceuticals are classified as chemicals, with tariffs that have been levied to protect and promote a national chemical industry. Many countries, including India, use nontariff barriers to protect national industries from cheaper pharmaceutical-related imports, which may decrease their consumers' and health systems' access to inexpensive products. Such barriers include antidumping regulations, onerous systems of certification of origin and quality, and legislation requiring local pharmaceutical manufacture (see, for example, Olcay and Laing 2005).

To increase pharmaceutical access, countries may be better off focusing on reducing or eliminating their tariffs and taxes on pharmaceuticals. Markups added throughout the pharmaceutical distribution system may be far greater than import tariffs; additionally, such internal distribution tariffs could outweigh any price benefits achieved through local production. Chapter 9 discusses the effects of taxes and tariffs within the pharmaceutical distribution system.

Collaboration and public-private partnerships

The use of public-private partnerships in the research and development of pharmaceuticals has been growing. Efforts such as the Drugs for Neglected Diseases Initiative are described in Chapter 3. In addition, public-private partnerships and joint ventures can be mechanisms for developing countries to gain some of the benefits of local production, such as the acquisition of technical expertise, without taking on business risk. In fact, partnering with international companies is often the most common form of local production support, with joint ventures and majority or minority ownership shares depending on the strength of the local economy and the political and market potential. The potential for profit repatriation by the external partners is critical.

As pharmaceutical markets become more globalized on many levels, suppliers may be more likely to form alliances and partnerships that increase their capability to compete in the world market. Likewise, multinational pharmaceutical producers have developed a better awareness of the need to consider the social implications of their business practices, and as a result, to be more open to entering into collaborative arrangements that promote technology transfer in low-income countries (Chapter 3).

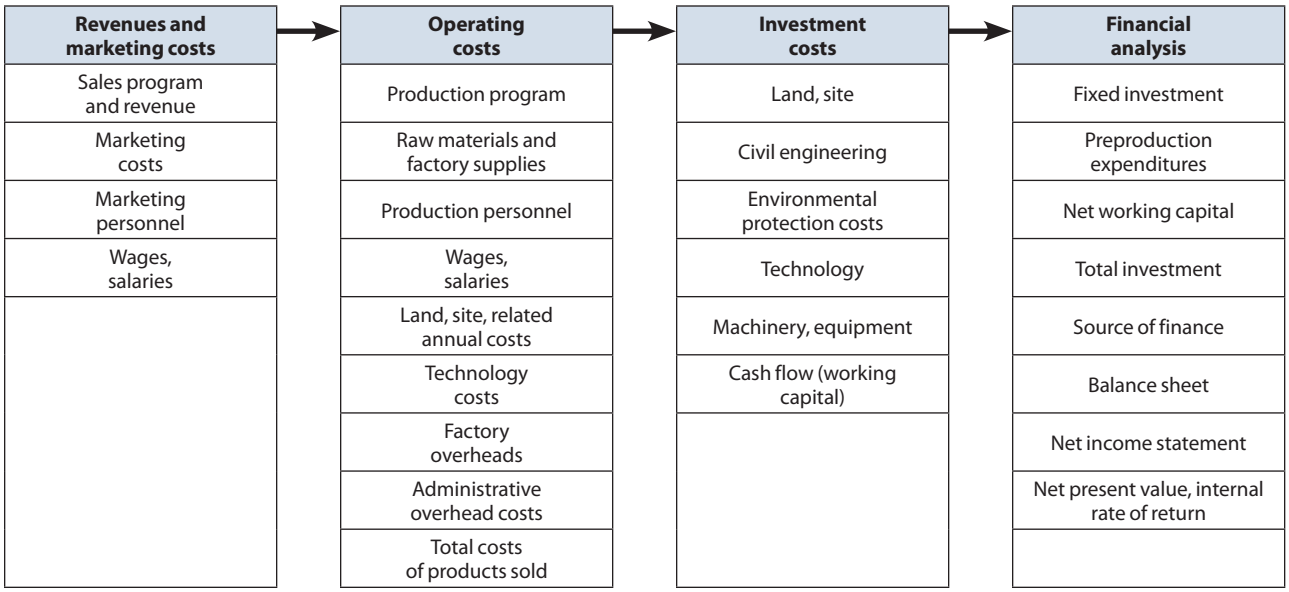
Figure 7-1 Preinvestment, investment, and operating phases of the project cycle

In addition to benefiting from collaboration between large multinational companies and smaller enterprises, small country markets can coordinate or join together to create economies of scale. Some African governments have adopted policies that favor local industrial development and investment and have created trading blocs in an effort to harmonize tariffs, currency, and medicine registration processes (Guimier, Lee, and Grupper 2004).

7.5 Assessing the feasibility of local production

Despite the argument that production decisions should be left to private-sector and market forces, policy makers must sometimes respond to pressures to become more involved in decisions about pharmaceutical production. A feasibility study may serve either to warn against a hasty decision to consider manufacturing locally or, if the decision is made to go forward, to establish an appropriate framework, timetable, and resource plan for analysis. Figures 7-1 and 7-2 illustrate the project investment cycle and the complexity of the analysis process *only* for the feasibility stage. The issues to be considered in a careful investigation include marketing analysis, raw materials and supplies, location, engineering and technology, organization and overhead costs, human resources, implementation planning and budgeting, financial analysis, and investment appraisal.

Figure 7-2 Information flow for an industrial feasibility study



Source: Behrens and Hawranek 1991.

When a project feasibility analysis is carried out in the public sector, many different government agencies (ministries of treasury, industry, and commerce, as well as the ministry of health) must be involved to appraise the forces and issues that will determine the outcome of the analysis. The complexity of these negotiations means substantial time commitments from senior analysts and policy makers. Nevertheless, the vast majority of worldwide production is done by private companies that have learned from experience how to manage the process efficiently. Country Study 7-3 illustrates the difficulties encountered by some public-sector production programs.

A feasibility assessment of how well sub-Saharan African countries could use local production to increase access to medicines concluded that a few countries appeared to meet the criteria for developing a successful pharmaceutical production industry; however, long-term financial viability was unknown because of major factors out of the companies' control, such as the price they would have to pay to import APIs and the stability of their market share (Guimier, Lee, and Grupper 2004).

As mentioned, new global public health initiatives have greatly influenced the pharmaceutical marketplace. Countries' desire to increase access to antiretrovirals, artemisinin-based combination therapies for malaria, and other essential medicines have renewed their interest in assessing the feasibility of local production, based on the assumption that domestically manufactured medicines would be cheaper than those bought from a foreign manufacturer. The World Bank (2005) points out that local manufacturing has the potential to strengthen political support for public health treatment programs and institute pride in a national industry. Under the challenging conditions for developing and maintaining a successful domestic production enterprise, however, national stakeholders will have to consider whether scarce resources should support local pharmaceutical production or be used to improve the health system infrastructure or other areas of pharmaceutical management, such as the distribution system and the pharmaceutical regulatory system. Investments in local medicine production will be cost-effective only if domestic pharmaceuticals can be produced more cheaply than they can be imported on the open market (Guimier, Lee, and Grupper 2004). For example, the institutions and governments that buy recommended medicines to treat HIV/AIDS, tuberculosis, and malaria must follow the procurement guidelines of their major donors. Therefore, domestic producers must meet international quality standards, such as WHO's prequalification standards, as well as be price competitive with large international competitors. If the cost of developing local production capacity is too high or the quality of the products is doubtful, local production must be viewed as probably not justifiable.

WHO, the United Nations Conference on Trade and Development, and the International Centre for Trade and Sustainable Development are collaborating on a project to promote local production of medical supplies and related technology transfer in developing countries. Started in 2009, the project is working to identify the challenges and obstacles of local production and make evidence-based recommendations on their feasibility and sustainability (WHO n.d.). ■

Country Study 7-3
Local public-sector production problems

- The Social Security Agency (CSS) laboratory in Panama had produced a number of pharmaceutical products for decades. The government gave the laboratory a permit to operate, but it did not require registry of the laboratory's products, which would entail instituting some quality-control measures. In 2006–2007, more than 120 people died after taking cough syrup contaminated with diethylene glycol, an industrial solvent, and the CSS treated more than 50,000 patients exposed to the contaminated medicines. The director of CSS explained that analyses are performed on the medications to guarantee quality, "but unfortunately in this case they did not detect the toxic substance." The laboratory was closed. Investigation showed that adulterated glycerin (which contained over 20 percent diethylene glycol) that a local firm sold the laboratory had come from China via Spain. More than a dozen people in Spain and Panama (but not China) were charged with crimes related to the incident.
- One Latin American ministry created an "in-house" pharmaceutical factory to produce essential medicines for its own system. Production had little connection with the ministry market, however, and the product line drifted into over-the-counter preparations and beauty aids, largely missing its original purpose.
- In another semi-autonomous government laboratory, production of essential medicines is usually two to three years behind schedule, throwing ministry purchasing into turmoil and resulting in higher prices because of emergency purchases.
- A parastatal company in East Africa faced multiple problems in producing pharmaceuticals at competitive prices. Inadequate capitalization and inadequate foreign-exchange allocation left the firm unable to purchase enough raw materials to operate at the break-even level of 60 percent capacity. For the pharmaceuticals that were produced, containers of inadequate quality—metal tins without aluminum coating—were all the local suppliers had, and these had to be lined with polyethylene bags, adding to production costs. Plastic containers were tried, but the lids fit poorly because a proper mold could not be obtained locally at reasonable cost. The cardboard used for boxes to pack intravenous fluids collapsed when stacked, and the containers broke when transported over rough roads. When the government attempted to purchase pharmaceuticals on tender from the company, it could not meet the competitive prices on the market, and as a result of a structural adjustment program, the company was put up for sale.
- For political reasons, a Latin American government was obligated to purchase a nonfunctional private facility as a means of expanding its production capacity. Originally constructed to produce small quantities of a large number of sterile injectable products, it had never functioned because of an inadequate water supply, which rendered it useless as a production facility. In addition, the plant lacked the production capacity, types of equipment, and storage capacity to produce the priority items required by the ministry.

References and further readings

★ = Key readings.

★ Attridge, C. J., and A. S. Preker. 2005. *Improving Access to Medicines in Developing Countries: Application of New Institutional Economics to the Analysis of Manufacturing and Distribution Issues.* Washington, D.C.: World Bank. <http://siteresources.worldbank.org/HEALTHNUTRITIONANDPOPULATION/Resources/281627-1095698140167/AttridgeImprovingAccessFinal.pdf>

Balance, R., J. Pogany, and H. Forstner. 1992. *The World's Pharmaceutical Industries: An International Perspective on Innovation, Competition, and Policy.* Brookfield, Vt.: Ashgate Publishers.

Bate, R. 2008. *Local Pharmaceutical Production in Developing Countries: How Economic Protectionism Undermines Access to Quality Medicines*. London: International Policy Network. <http://www.policynetwork.net/health/publication/local-pharmaceutical-production-developing-countries>

Behrens, W., and P. M. Hawranek. 1991. *Manual for the Preparation of Industrial Feasibility Studies*. Vienna: United Nations Industrial Organization.

CVI (Children's Vaccine Initiative). 1992. *Local Vaccine Production: Issues of Quality and Viability*. Geneva: World Health Organization. <http://whqlibdoc.who.int/hq/1999/CVI_99.02.pdf>

★ Guimier, J-M., E. Lee, and M. Grupper. 2004. *Processes and Issues for Improving Access to Medicines: The Evidence Base for Domestic Production and Greater Access to Medicines.* London: DFID Health Systems Resource Centre. <http://www.who.int/3by5/capacity/4)processes_issues_improvingaccess.pdf>

★ Kaplan, W., and R. Laing. 2005. *Local Production of Pharmaceuticals: Industrial Policy and Access to Medicines.* Washington, D.C.: World Bank. <http://siteresources.worldbank.org/HEALTHNUTRITIONANDPOPULATION/Resources/281627-1095698140167/KaplanLocalProductionFinal.pdf>

Lashman, K. H. 1986. *Pharmaceuticals in the Third World: An Overview*. Population, Health and Nutrition Technical Note 86-31. Washington, D.C.: World Bank.

ASSESSMENT GUIDE

Human and physical resources

- Are technical specialists available?
- Are skilled production staff available?
- Is there an educational system that can supply trained workers?
- What are the cost and reliability of water, power, construction, equipment, and other resources?
- Are there financial resources available to retain skilled workers and to support the maintenance of infrastructure?

Market factors

- What are the population size, geographic distribution, and income levels in the country?
- Is there existing local production capacity (competition)?
- What are the barriers to imported products (degree of protection)?
- Can the size, reliability, and preference of the public-sector market ensure economies of scale?
- Is there predictable demand for medicines?

Regulatory environment

- What is the status of laws on pharmaceutical registration?
- What is the status of product and process patent protection?
- Does the regulatory agency have systems and capacity to assure product quality through GMPs and enforcement of standards?
- Are there generic labeling, prescribing, and dispensing laws and practices?

Investment and industrial development environment

- How strong is the country's financial sector (banking and nonbanking activities)?
- Is there sufficient access to capital?
- Are tax or other investment incentives available?
- Are industrial development funds available (access to start-up capital)?
- What are the ownership requirements (limits on foreign ownerships, requirements of local ownership)?
- Are there restrictions on repatriation of profits (foreign investors)?

Economic incentives

- Does the government enforce price controls?
- Is there access to foreign exchange?
- Are there export incentives?

Duties and import controls

Are there duties or import controls on—

- Active pharmaceutical ingredients (versus finished products)?
- Inactive pharmaceutical ingredients and other raw materials?
- Packaging materials?
- Specialized pharmaceutical equipment?
- Nonspecialized equipment?

Mohammed, N. 2009. The Role of Local Manufacturers in Improving Access to Essential Medicines: The Case of Uganda. *Africa Health* November 2009:40–2. <http://www.medicinestransparency.org/fileadmin/uploads/Documents/MeTA-Uganda_AfricaHealth.pdf>

MSH (Management Sciences for Health). 2008. *International Drug Price Indicator Guide* (updated annually). Cambridge, Mass.: MSH. <http://erc.msh.org/mainpage.cfm?file=1.0.htm&module=DMP&language=English>

Olcay, M., and R. Laing. 2005. *Pharmaceutical Tariffs: What Is Their Effect on Prices, Protection of Local Industry and Revenue Generation?* <http://www.who.int/intellectualproperty/studies/TariffsOnEssentialMedicines.pdf>

Stevens, P., and H. Linfield. 2010. *Death and Taxes: Government Mark-ups on the Price of Drugs*. London: International Policy Network. <http://oi.org.mk/upload/Death-and-Taxes-web.pdf.>

UNIDO (United Nations Industrial Development Organization). 2003. *UNIDO's Manuals on Preparing Industrial Feasibility Studies*. Vienna: UNIDO.

World Health Organization (WHO). 2007. *Quality Assurance of Pharmaceuticals: Compendium of Guidelines and Related Materials*: *Good Manufacturing Practices and Inspection*. 2nd ed. Vol. 2. Geneva: WHO. <http://whqlibdoc.who.int/publications/2007/9789241547086_eng.pdf>

———. 2006a. *WHO Basic GMP Training Modules*. Geneva: WHO. <http://apps.who.int/prequal/trainingresources/pq_pres/gmptraining/GMPBasicTraining.htm>

———. 2006b. *A WHO Guide to Good Manufacturing Practice (GMP) Requirements: Part 3, Training.* Geneva: WHO. <http://whqlibdoc.who.int/hq/2006/WHO_IVB_05.24_eng.pdf>

———. 2004. *The World Medicines Situation*. Geneva: WHO. <http://whqlibdoc.who.int/hq/2004/WHO_EDM_PAR_2004.5.pdf>

———. 2003. Good Manufacturing Practices for Pharmaceutical Products: Main Principles. *WHO Expert Committee on Specifications for Pharmaceutical Preparations: Thirty-Seventh Report*. Annex 4. Geneva: WHO. <http://apps.who.int/medicinedocs/pdf/s5517e/s5517e.pdf>

———. 2002. Guidelines on Packaging for Pharmaceutical Products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations: Thirty-Sixth Report.* Annex 9. Geneva: WHO. <http://whqlibdoc.who.int/trs/WHO_TRS_902.pdf>

———. 1997a. *A Guide to WHO Good Manufacturing Practice (GMP) Requirements: Part 1, Standard Operating Procedures and Master*

Formulae. Geneva: WHO. <http://whqlibdoc.who.int/hq/1997/WHO_VSQ_97.01.pdf>

———. 1997b. *A Guide to WHO Good Manufacturing Practice (GMP) Requirements: Part 2, Validation*. Geneva: WHO <http://whqlibdoc.who.int/hq/1997/WHO_VSQ_97.02.pdf>

———. n.d. *WHO Project on Improving Access to Medicines in Developing Countries through Local Production and Related Technology Transfer*. Geneva: WHO. <http://www.who.int/phi/implementation/TotLCProject.pdf>

★ World Bank. 2005. *Pharmaceuticals: Local Manufacturing*. Washington, D.C.: World Bank. <http://siteresources.worldbank.org/HEALTHNUTRITIONANDPOPULATION/Resources/281627-1109774792596/HNPBrief_3.pdf>