

Overcoming barriers to access

The Working Group on Access to Essential Medicines has organized its analysis and recommendations into three main categories: availability, affordability, and appropriateness.¹ One or more of these elements will be missing or deficient in settings where access to medicines is inadequate (Liu 2003). The WHO includes a fourth category: reliable health and medicine supply systems. The working group addresses medicine supply systems in the discussions of availability and affordability and recognizes the importance of the larger healthcare system as the context in which medicines are prescribed and dispensed.

The degree of confidence that people invest into a local health system is determined largely by the ability of the system to respond in a timely and consistent manner to the needs of patients. This in turn will often be directly related to the existence of a sustainable supply of essential medicines. Critical shortages of trained personnel and severely deficient health system infrastructures will also impede the safe and effective prescription and movement of medicines that are available. This interdependence demonstrates the considerable and often dialectical interaction between all of the various components that will ultimately determine access to essential medicines in any given location.

Innovation

Treating priority diseases of the poor is greatly hindered by a fundamental problem: the medicines required for many of the diseases and illnesses most prevalent in developing countries do not exist because of a lack of therapeutic innovation (MSF 2001). Byström and Einarsson (2001) estimated that, between 1975 and 1997, only 13 of 1,223 new chemical entities found to have useful pharmacological properties were for treating diseases predominantly prevalent in poor countries. Similar estimates have been made by others (Yamey 2002; Troullier and others 2002).

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Another critical need is for new medicines to supplement or replace those to which microorganisms have become resistant, as is notably the case for malaria and TB.² A complementary approach to the resistance problem is to develop and employ new combinations of medicines. These combinations require proper investigation before they can be accepted and used, however, and again there is little commercial incentive to study them.

The lack of innovation in medicines needed to meet public health problems in poor populations reflects the fact that industrial research has been directed primarily toward treatments for diseases of industrialized countries, where chronic diseases associated with longer life spans (such as cardiovascular diseases and cancer) are the main causes of mortality and morbidity (Troullier and others 2002). While the *World Health Report 2003* (WHO 2003f) notes that chronic diseases are also becoming more prevalent in developing countries, the numbers of people affected are still far lower than the numbers affected by the major infectious diseases.

Despite substantial achievements, a dramatic ongoing need continues for new and innovative medicines and vaccines to fight current, emerging, and evolving health challenges. The need is likely to grow, and concerns exist that existing medicines, such as antibiotics, may be threatened by resistance before effective new medicines can be developed and that the incentives for vaccine development are failing. The research-based industry has started to respond, for example, by launching dedicated research facilities focused on TB, malaria, dengue fever, and other parasitic diseases. It would appear that public-private initiatives for the development of new medicines and vaccines may be a productive way of promoting innovative research, development, and financing within the current system.

Three of the most neglected diseases—African trypanosomiasis, Chagas disease, and leishmaniasis—for example, are now beginning to receive additional attention, in particular through new public-private initiatives. For African trypanosomiasis, an initiative by the WHO and three pharmaceutical companies—Aventis, Bayer, and Bristol-Myers Squibb—has been established.³ There are several products available for leishmaniasis, developed by pharmaceutical companies working with the Special Programme for Research and Training in Tropical Diseases (TDR), a joint effort of UNICEF, UNDP, the World Bank, and the WHO. For Chagas disease, Roche has donated rights and technology to manufacture benznidazole (the most effective medicine for this disease) to the Brazilian government. The only significant tropical disease for which there is no existing medicine is dengue fever. But even for this disease, five compounds are currently in stages of discovery and preclinical development, two are in Phase 1 trials, and one is in Phase 2 trials (IFPMA 2004).

A reorientation of medicines research is necessary to make it better attuned to the needs of the poor. This will require creative new research, development, and financing mechanisms. The for-profit private sector is not going to take

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up needed innovation for major infectious diseases in poor countries without major involvement and subsidy from the public sector and an appropriate and supportive policy environment. Provided this environment can be realized, it is hoped that the research-based industry would also be willing to increase their regular R&D budgets that are devoted to priority diseases of developing countries.

A rethinking of public and private R&D investments should include an analysis of the role of academia. Although a great many fundamental discoveries potentially relevant to therapeutics emerge from academic research, academia does not itself have the structure to carry these through to development and marketing. Many academic units, with restricted budgets of their own, cooperate closely with pharmaceutical companies and receive industry funding for research projects. To a large extent, though, those research priorities are determined primarily by the industrial partner, which has an eye toward potentially profitable markets. To date, much of the discussion has centered too much on the role of industrial country-based academia in research. The substantive involvement of research institutions and scientists in developing countries should become the norm in all stages of R&D.

Public-private initiatives for new medicines and vaccines, such as MMV, IAVI, DNDi, and GATB, appear to be offering useful new models for how R&D can be organized among major actors. They are a main way to increase the involvement of researchers and institutions based in developing countries and to establish and strengthen ties among industry, academia, and others to combat major diseases of poverty at regional and global levels. Well organized and managed public-private initiatives help maximize the comparative advantages of all of the participants. Since most public-private initiatives are relatively new, it will be important to monitor their progress and outcomes.

Meeting R&D needs for the poor means taking risks by the public and private sectors and—importantly—requires creative new thinking by major actors. For example, innovative, open-source arrangements for sharing knowledge should be investigated and developed as justified to meet R&D objectives. Proposals to reorient the way the financial burden is shared among countries deserve serious analysis and discussion. Another proposal is to promote increased public financing for biotech firms or academic units working on the medicines, vaccines, and technology needs of the poor. Yet another idea for creating research incentives is to establish international drug or vaccine funds that will be used to purchase guaranteed quantities of medicines for use in developing countries. Recently, the Bill and Melinda Gates Foundation offered financial rewards for the discovery of medicines for neglected diseases. That foundation has also provided a major grant to the first nonprofit pharmaceutical firm that has a stated mandate to develop medicines for diseases of poverty.

The principle of profit-based and patent-butressed incentives to enterprise and innovation is widely accepted. The principal drawback for medicines

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innovation of that approach is that 90 percent of this money still is spent on the health priorities of 10 percent of the world's population, according to the Global Forum for Health Research (GFHR 2004).

For new approaches to succeed, an adequate financing structure needs to be available that provides incentives to all major actors—governments, international organizations, academia, and industry. They all need to release themselves from longstanding notions about their roles and contributions and be willing to build trust and try new ways of working together.

New approaches should promote fresh strategic analysis, emphasizing a substantive role for representatives from affected countries. They should ensure technology transfer, development of research capacity, research leadership, and creation of manufacturing facilities in affected countries (Folb 2004).

The working group recognizes that successful innovation to help meet the Goals will require greater cooperation among all sectors (such as public and private sectors, academia, foundations, and the United Nations), substantially more financing from multiple sources, clearly setting priorities for research efforts, effective management, and promoting technology and knowledge transfer. WHO should take a leading role in promoting R&D that meets the public health priorities of developing countries. For instance, the WHO Commission on Intellectual Property Rights, Innovation, and Public Health should examine alternative international models to the current patent-based system for priority setting and financing of health R&D. Drug regulatory process reforms and harmonization—for example, the International Conference on Harmonization (ICH)—need to better reflect and serve the needs of developing countries. Traditional knowledge and medicines continue to be marginalized, to the detriment of consumers. Vigilance surrounding all aspects of pharmacological practice in developing countries needs to be strengthened.

The answers all point to the need for considerable change. The working group appreciates that the public must continue to support research-based firms. It would seem no less than equitable that these innovation costs should be borne primarily by the nations with the broadest shoulders, such as heavily industrialized countries with strong economies that are capable of sustaining relatively high prices for the medicines that they require.⁴

Production

Even medicines that have been developed may not be in production if they are considered unprofitable or if supply chain requirements are not sufficiently known. Some medicines developed virtually to the point of application are abandoned; others are discontinued because of disappointing sales. At present very few low- or middle-income countries are able to compensate for the unavailability of particular medicine substances on the world market by producing them at the national level.⁵

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Local production in such countries is rarely at a sufficient economic scale and technological level to take up such a challenge, as it is usually limited to processing imported active substances into finished form. From an economic perspective, medicine production requires considerable capital investment, adequate technical staff, and basic infrastructure. The cost of quality assurance systems is also considerable. All of this should be seen in the perspective of fierce global competition. Local production will usually be economically feasible and sustainable only above a certain turnover. More than a decade ago, consultations within the World Bank led to the view that, with certain well defined exceptions, new investment in medicine production in countries at a low level of development was unlikely to be justified. Quite apart from the difficulties in maintaining adequate staffing and ensuring sound quality standards, the products of this relatively small-scale production would be unlikely to compete in cost with generic products produced on a large scale in countries such as India and China.

But the political aspect of local production also needs to be considered. For example, Brazil was able to negotiate reduced prices of antiretroviral medicines by threatening compulsory licensing, because national production capacity was actually available. National production capacity also allows for voluntary licensing, as was recently the case in South Africa and in Kenya. However, voluntary licensing, especially if it is achieved under the threat of compulsory licensing, does not automatically result in the transfer of technology. In the absence of technology transfer, local production is at a disadvantage, as the development, testing, and registration of adequate formulations requires considerable technological skills and will usually take several years.

Even where there are sufficient reasons to reject the notion of creating new production capacity, manufacturing units that already exist may have a good reason to continue. Production units are frequently seen as strategic facilities with the capacity to promote economic development and to serve as training centers. In addition, even simple units may be capable of producing a limited range of finished products at reasonable cost. Where such units exist, for whatever reason, the authorities have a responsibility to ensure that production of medicines takes place according to GMP and that international quality standards are applied. Generics producers, especially exporters to developing countries (for example, India and China), have been playing a crucial role in ensuring price competition for key essential medicines, such as antiretrovirals. Ironically, within these two countries, domestic supply remains inadequate to meet current needs.

Financing

Problems in financing medicines supply exist at three levels. First, all poor countries experience a basic and chronic absolute lack of economic resources; second, resources that do exist are not always optimally allocated with sufficient

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consideration for health needs within a country; and third, support from the international community has often been inadequate to supplement currently inadequate national resources.

On average, during 1997–99, the Least Developed Countries spent \$11 per capita on health, compared with \$93 per capita for lower middle-income countries and \$1,907 for high-income countries (CMH 2001). Although the minimum cost of a basic set of health services is still a subject of debate and there is significant variance among countries, there is increasing agreement that \$30 per capita represents the lower bound. Thus, although many developing countries promise universal access to essential healthcare to their citizens, few can afford to deliver it to their populations. As a result, in many poor countries today, much of the funding for healthcare is in the form of direct out-of-pocket expenditures by patients at the point of care. In wealthier countries, the public sector can raise money through general taxation or through social health insurance (employment taxes).

The current lack of international support in the health field to poor countries was already noted in the introduction to this report. The Working Group on Access to Essential Medicines fully endorses the findings of the Commission on Macroeconomics and Health (CMH 2001) and others (Troullier and others 2002) that donor assistance for health needs to rise dramatically in order to have an impact on the health of people living in developing countries. Others have noted that significant additional funding will be needed to target specific diseases. For example, the Institute of Medicine (United States) recently estimated that instituting new malaria treatment (artemisinin combination therapy) worldwide would require \$300–\$500 million each year (Coleman 2003).

In addition to inadequate aid flow, there is also a serious lack of coordination and transparency in donor assistance. In many cases, it is even difficult to estimate the total amount of funding going to support essential medicines. The lack of transparency and multitude of donors create significant transaction costs for poor countries, which must devote scarce staff to managing the morass of reporting requirements.

At the national level, it is evident that the money available for healthcare in general, and for medicines in particular, will often be strictly limited for many years to come. As noted above, in the short and medium terms, only significant additional donor assistance can ensure that countries can afford to offer basic health services, including essential medicines, to their populations. In addition, addressing access to medicines and other health issues will, in many cases, require a reallocation of priorities so that healthcare and medicine supplies are allowed to rank more highly on the scale of government expenditure, bearing in mind both the humanitarian and economic benefits that will flow from improved access to medicines. Detailing concrete actions to promote import (or production), distribution, quality testing, and promotion of sound prescribing within national poverty reduction strategies will be a key strategy

Evidence on the effectiveness of community insurance is mixed

for securing government and donor commitment to dramatically enhancing access to medicines.

Because of the low levels of government spending on healthcare, many patients are forced to pay out of pocket for health services and essential medicines. Out-of-pocket payments are the least equitable method of financing healthcare, as they are a disproportionately greater burden (as a percentage of income) for the poor than for the wealthy, and they come at a time when families are most vulnerable to usurious interest rates for medical loans. Furthermore, user fees, whether the full payment or a copayment for services, can act, for the poor, as a direct barrier to accessing needed health services. Even with extensive out-of-pocket spending for healthcare, the absolute spending is not enough because of the low per capita incomes of much of the populations in poor countries. For the poor, healthcare competes with other necessities of life, such as food and water, schooling, clothing, and shelter. Thus financing for essential health services in much of the developing world today can be described in two words: insufficient and unfair.

Some experts advocate community-based insurance as an important mechanism to offset the financial impact of healthcare on the poor. “Community insurance” is a term usually used to describe village- or district-level schemes to pool risk across the members by collecting monthly premiums from each family, which are then used to reimburse providers directly for costs incurred. In some cases, communities may employ the providers or have direct agreements with providers on fees for services—both of which can help to ensure a higher quality of services. Community insurance is preferable to user fees in that prepayments or premiums are often lower and more predictable, and they protect the family from catastrophic one-time payments when illness strikes. By transferring resources from the wealthier to the poorer and from the healthy to the sick, community insurance is also a more progressive payment mechanism than user fees.

Evidence on the overall effectiveness of community insurance as a financing mechanism is mixed. A 2002 review of 45 published and unpublished reports on community financing indicates that, while community insurance improves access to health services and reduces out-of-pocket health spending for poor rural communities, it often excludes the poorest of the poor, who simply cannot afford the premiums (Preker and others 2002). Another limitation of community insurance is its limited funding base and consequently limited coverage, which subscribers often prefer to direct to common illnesses requiring relatively cheaper types of care. As a result, community insurance usually does not cover rarer, high-cost, life-threatening events—precisely the ones that carry the highest risk of impoverishing a patient’s family. Community financing schemes are also somewhat complex to administer, requiring a significant investment in management and oversight by communities. Community financing therefore is not, in the short term, a viable option for sustainable financing of primary healthcare in low-income countries (Ekman 2004).

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In view of this, the UN Millennium Project advocates for government-led financing of essential health services to ensure affordable access to a core set of services as guaranteed in the constitutions of many countries and in the Health for All initiative. User fees should be eliminated for essential health services and medicines. Financing is distinct from delivery of services, which can be done by NGOs and the private, for-profit sector, with appropriate regulation. Performance-based contracting is one promising tool for health service regulation. The UN Millennium Project also recognizes that current public health spending on healthcare is wholly inadequate in most low-income countries and meeting the Goals will require large inflows of donor assistance for health over the next several decades.

At the international level, there will often be a long-term need for donor support. Support itself should always (except in severe emergencies) have a development component and not be limited to supportive aid and the supply of consumables. Finally, as noted above, promises made about international aid need to be kept. Other factors that need to be addressed by the international community include punishing debt burdens and the imposition of social sector spending limits as a condition of loans from the international financial institutions. Support for debt relief in the Least Developed Countries has been gaining momentum in recent years, but responsive action on the part of the donor community has been inadequate. When seeking donor aid, states must quantify their needs for medicines and the extent of the shortfall in meeting those needs from national resources so that well documented requests for support can be developed.

Donors have traditionally been reluctant to fund recurrent costs, such as salaries. For their part, governments have been hesitant to rely on donors for such funding, given its lack of predictability. Yet providing adequate salaries for health workers is key to service delivery. A massive scale-up of services cannot happen without donor commitment to long-term sustainable funding for recurrent costs. The working group recommends that donors commit to funding salary and other recurrent costs for the poorest of developing countries over the short to medium terms.

Prices and affordability

Evidence of the role of price in obstructing access to medicines, in both the past and the present and in a wide range of countries, is abundant. Many institutions and authors have provided examples of gross discrepancies between the global prices of essential medicines and the ability of most ordinary individuals in developing countries to pay for them (Mossialos and Dukes 2001; WHO and HAI 2003). To cite a single example: in 2000, the costs of using didanosine for AIDS in the Côte d'Ivoire amounted to \$3.48 per patient per day, yet the GNP per person was only \$1.94 per day and the health services were able to make a contribution to the cost equivalent to only \$0.03 per day (Mossialos and Dukes 2001).

The levers for pushing prices downward are generics competition, price negotiation, differential pricing, and effective procurement

Whether the price of a medicine is reasonable or unreasonable from the point of view of a manufacturer or supplier, if the patient or the health system cannot afford it, it will not be bought and used.

The problem is least severe for those medicines (such as generic products) that are off patent and can be obtained from multiple reputable sources. For many of these medicines, the international wholesale prices, based on generics supplies, are today only a fraction above manufacturing costs, though still sufficient to finance quality control, overhead, and distribution. These prices render the medicines accessible to all except the indigent, who will remain dependent on whatever support the social system can provide. Only if there is entirely inept procurement or if retail or other margins greatly inflate the price to the consumer do these medicines become unreasonably expensive.

Once a medicine has been taken into mass production, the costs of manufacturing it are generally extremely low. When the wholesale or retail price of a medicine represents a serious obstacle to its use, this price is primarily determined by factors other than the expense involved in making it. This allows substantial room for negotiation with the manufacturer. Certain medicines are reported to have a prohibitively high manufacturing cost, but this information is not publicly accessible. The example has been cited of natural insulin, which, even at the best generics prices, is still out of reach for poor people. Even here, however, it is not clear that, if synthetic human insulin were widely used, the cost would decrease sufficiently to be within reach of impoverished people.

Because newer medicines will be protected by patent from low-cost competition for at least 20 years, impoverished populations may (and generally will) be deprived of these medicines for that entire period. On the one hand, in the case of hypertension, rheumatism, and diabetes, this will not be a significant problem; medicines developed in the 1980s are still effective. On the other hand, patents will affect the affordability of medicines for prevalent diseases such as AIDS, MDR-TB, and multidrug-resistant malaria. Although research-based companies are actively engaged in donation or discounting and treatment programs (such as the Accelerated Access Initiative, which is treating 300,000 people in developing countries with discounted antiretrovirals), the sheer scale of the problem for AIDS alone precludes donations or multicompany discounting as viable strategies over time to counter the magnitude of need for treatment, however well intentioned or implemented.

The main levers for pushing medicines prices downward are generics competition, price negotiation (which can include the option of resorting to compulsory licensing), differential pricing offered by companies, and effective procurement practices, such as bulk or pooled procurement.

In almost all countries, a public sector and a private sector for medicines provision exist in parallel. This means that, in theory, an individual has two channels through which to obtain medicines, with different prices and charges in each sector. The public sector, often subject to serious funding constraints,

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will more readily pursue purchase of generics medicines to maximize purchasing power. The generally lower costs of these medicines are in turn passed on to patients, who receive the medicines either at no charge or at relatively low cost, sometimes in the form of a prescribing fee. The private sector supplies originator drugs at prices similar to those charged in Western countries, though retail prices may be quite variable within a country; most private channels also handle a certain number of generic medicines.

The inadequacy of public sector supplies in many developing countries means that much of the population will be obliged to use the private sector if they are to secure medicines at all, and it is here that serious problems can arise. Although most developing countries have some affluent citizens, they usually constitute only a small minority of the population. The bulk of users of the private sector will be those who have been either driven to use it or persuaded to use it and who can generally ill afford the prices that are charged.⁶ A real risk is that high-cost originator medicines will be bought at the expense of other vital goods (such as food) or will be purchased in small quantities inadequate to serve their purpose, thereby perhaps doing more harm than good, for example, by inducing bacterial resistance (WHO 1998a).

Differential and equity pricing

The high prices charged in developing countries for essential medicines that are still under patent protection are a major barrier to accessing those products. Differential pricing, or tiered pricing, is widely practiced by the pharmaceutical industry as part of its marketing strategies. There are good examples of social responsibility leading to differential prices for essential medicines, including antiretrovirals. Yet it does not always result in lower prices for less affluent countries. For example, recent pricing surveys have shown that in many developing countries, such as Kenya, Morocco, and Peru, the prices of some originator products are much higher than they are in the originator countries (WHO and HAI 2003). In some countries, taxes and tariffs further increase the price.

Equity pricing is a concept launched by WHO in the late 1990s. It is based on the ethical notion that developing countries should not be asked to pay for medicine development cost, marketing, and shareholder returns. This view that medicines should be less expensive in poor countries than in wealthy ones is widely accepted; the broadest shoulders can well carry the heaviest burdens. Equity pricing is a much wider concept than differential pricing and encompasses all the active policy and administrative measures a government or procurement organization can take to achieve differential pricing related to purchasing power. These measures include price information and transparency, bulk or pooled procurement, reduced taxes and margins, price negotiations, voluntary licensing agreements, and, as an ultimate measure, compulsory licensing. Equity pricing is the political choice and action; differential pricing

TRIPS created a comprehensive global patent regime for WTO member countries

may be one of the results. Equity pricing has been successfully practiced for more than 30 years for children's vaccines and reproductive health commodities, although care must be taken to ensure that multiple suppliers continue to participate to ensure continuity of supply.

In differential pricing, industry needs to provide these medicines at production cost ("no profit, no loss") to national health systems in low-income countries. In middle-income countries, differential pricing should be pursued, although the prices will not be at marginal cost. In both sets of countries, negotiating differential prices should not be burdensome to the purchaser. Differential pricing should not result in price referencing or the re-importation of the lower priced products in high-income countries. Administrative and regulatory measures are available to prevent this from happening. A good example in this regard is the market segmentation strategy for Novartis' Coartem®, with separate products for developed and developing countries, and separate presentations for the public and private sectors. However, it must be borne in mind that that it is not a simple process to use administrative and regulatory measures to offset the negative consequences of differential pricing. There is a significant cost burden associated with maintaining separate brands, presentations, and packaging and other issues, in terms of both direct costs and human resources.

The need for timely pricing information

The WHO, in collaboration with HAI, has developed a price survey methodology that is an important step forward in understanding what patients actually have to pay. It is a useful tool for collecting and comparing prices, especially at country level, helping policymakers to address high and variable pricing of essential medicines. The WHO also collaborates with MSH and MSF to produce information on prices offered by various suppliers.

Intellectual property protection

The world's network of patent systems was, until late in the twentieth century, far from absolute or homogenous. Some nations had no patent systems at all, while in others patents were not consistently enforced. This enabled low-cost manufacturers in some countries to produce new medicines legally. They were sometimes manufactured purely for internal sale, but were also commonly exported. Following the establishment of the World Trade Organization (WTO) in 1995, its agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) created a comprehensive global patent regime for WTO member countries (WTO 1994; Drahos and Braithwaite 2002). Implementation of TRIPS began in 1995 for developed countries (which were also countries most likely already to have extensive patent protection). Less-developed countries were put on a rolling schedule of when they had to bring their national legislation into compliance. Least Developed Countries

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originally had until 2006; through subsequent negotiations, they now have until 2016 to offer patent protection for pharmaceuticals. TRIPS recognizes that some flexibilities would be required to allow governments the means to respond to domestic requirements, including for public health considerations.

As the UN Millennium Project Task Force on Trade has pointed out, the schedule for TRIPS implementation was probably not well grounded in economic and development realities for poorer countries:

There is perhaps more agreement about the extent to which the TRIPS Agreement provides sufficient flexibility for developing countries. As a basic matter, there is wide agreement that the time and resources required to implement the Agreement were greatly underestimated and that implementation has (and will, if nothing is done) put a considerable strain on many developing countries. Assistance from developed countries, and the additional implementation periods permitted developing countries, have not been commensurate with the size of the task. (UN Millennium Project 2005a, ch. 10).

Another problem the Task Force on Trade highlights is that of flexibility required to account for different levels of development and national priorities for development:

Additionally, in some cases, the substance of the Agreement provides insufficient flexibility, imposing a “one size fits all” model of [intellectual property rights] protection on countries at widely differing levels of development and requiring protection of the full range of [intellectual property rights], despite varying interests and priorities. In other cases, the problem may be not so much that the Agreement has no in-built flexibility. Rather, it is that some WTO members are not permitting others to take advantage of the existing flexibility. For instance, while the agreement provides for differing implementation periods, countries acceding to the WTO may not even have access to these normal flexibilities. Additionally, certain WTO members—the US on drugs, the EU on [geographical indicators]—are trying to impose strict (and thus unacceptable for a vast majority of the rest of the world) limits on the existing TRIPS flexibility. (UN Millennium Project 2005a, ch. 10)

It has been recognized for many years—and is today virtually unquestioned—that if enterprise and innovation are to be encouraged, the innovators must be in a position to exploit their discoveries so as to reap their due reward and finance future innovative work. To this end, the issuing of a patent on the discovery of a new medicine, generally for a period of 20 years, provides innovators with protection from competitors. In general, the patent system works well because the inventor will have every reason to make a discovery widely available to the community through production and licensing and to publish

Most countries allow the government to use patented inventions for public purposes with fewer bureaucratic obstacles than apply to the private sector

patent information free from the threat of competition; theoretically it will therefore benefit both the inventor and society.

Although the patent system has developed primarily in Western industrialized countries, it can also provide an advantage to emerging market economies and some developing countries in advancing R&D in various fields. Such considerations have led to an almost universal acceptance of the patent principle, whatever problems it may pose in particular situations.⁷ One of these problematic situations involve the issues surrounding inadequate or absent access to medicines.

The TRIPS agreement does embody a number of provisions for exceptions to be made to its rules, and these can be relevant to the issue of medicines pricing. These inherent flexibilities were endorsed in the November 2001 Doha Declaration on TRIPS and Public Health, approved by all 146 WTO member governments and endorsed by the research-based and generics industries (WTO 2001). There is every reason, where medicines are concerned, to exploit these exceptions—targeted to address the constraints of developing countries—to the full (Love 2000). It should be noted, however, that the interpretation of these exceptions in the field of medicines has been a matter of dispute since the Agreement was concluded, and that the extent to which these exceptions will be of value is still in doubt.

A potentially broad exception provided for by TRIPS itself is to be found in Article 30, which states:

Members may provide limited exceptions to the exclusive right conferred by a patent, provided that such exceptions do not unreasonably prejudice the legitimate interests of the patent of the patent owner, taking account of the legitimate interests of third parties. (WTO 1994)

An example of such an exception is the Bolar clause, which allows for fast introduction of a generic after the patent term by permitting technical preparation for registration of the same medicine from an alternative source before the patent has expired.

A further vital tool for the governments of developing countries to use in dealing with obstacles presented by patents is Article 31 of the TRIPS agreement, which sets out the procedures for compulsory licensing and government use of a patent. A compulsory license is an authorization by the government for itself or a third party to use that patent without the permission of the patent holder. Most or all countries—developed and developing—allow the government to make use of patented inventions for public purposes with fewer bureaucratic obstacles than apply to the private sector. A compulsory license authorizing the government to use the patent for its own purposes is also referred to as a government use authorization.⁸ In practice, compulsory licenses are not normally used. Most often, it is the presence of the ability in national legislation and the threat to invoke it that results in desired price concessions

**The Fourth WTO
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to protect
public health**

from suppliers. There remains an obligation to pay the patent holder “adequate remuneration in the circumstances of compulsory licensing or government use, taking into account the economic value of the authorization” (WTO 1994).

A limitation on the use of Article 31 is the requirement that governments proposing to exploit this exception seek in advance the agreement of the patent holder to use the invention on reasonable terms (such as to seek a voluntary license). A compulsory licence can be issued only if such agreement cannot be obtained “within a reasonable period of time” (clause b). However, this requirement may be waived by a member in the case of “a national emergency or other circumstances of extreme urgency or in cases of noncommercial use” (WTO 1994). Countries are free to determine what constitutes a national emergency and do not need to follow any official procedures.⁹ It is not, for example, obligatory to officially declare that a state of emergency exists.

Countries are also free to define what constitutes public noncommercial use. This can, for example, be defined as covering procurement or production of healthcare products for use in the public sector. In practice, this means that a procurement authority in a country can start the purchase of generic versions of needed medicines without prior negotiations with the patent holder. The patent holder will be informed of the decision to make government use of the patent and the government will have to offer to the patent holder adequate compensation, the level of which is determined by the government itself. Article 31 further rules that such use “shall be authorized predominantly for the supply of the domestic market of the Member authorizing such use” (WTO 1994).

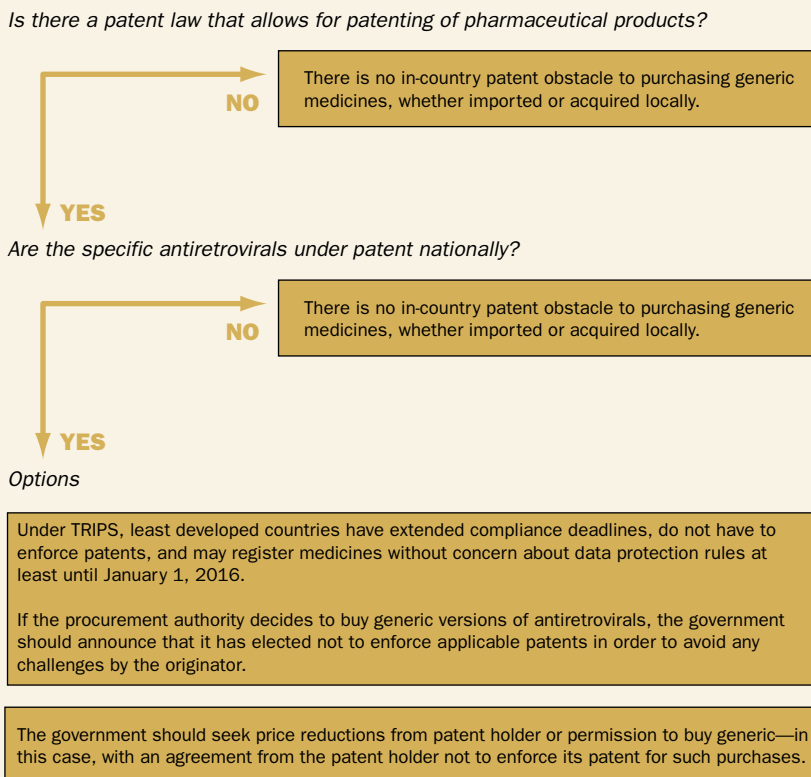
The Fourth WTO Ministerial Conference, held in 2001 in Doha, Qatar, adopted the Declaration on TRIPS and Public Health, which affirmed the right of national governments to take measures to protect public health and appeared to legitimize the broad use of these flexibilities, including compulsory licensing (Abbott 2002) where medicines were concerned (WTO Council for Trade-Related Aspects of Intellectual Property Rights 2001). With opposition from some industrialized countries, the declaration is weaker than originally proposed and is not legally binding. Nevertheless, from a legal perspective, it is an important document that will have to be taken into account by any WTO panel dealing with this issue in practice.

The Doha Declaration has also created new rights, for example, the right of Least Developed Countries to exclude pharmaceutical products from patenting until 2016. This right is legally binding and cannot be challenged (figure 2.1). It has been criticized by some defending the point of view of the research-based industry (Gillespie-White 2001), but others have seen it as a major step to protect the interests of developing countries (Correa 2002). The generics industry has welcomed this protection, while pointing to the problems that remain.

The latest developments are those resulting from a decision of the WTO General Council on August 30, 2003. A key issue that remained unresolved at Doha was how to ensure production for export to a country that has issued a

Figure 2.1
August 30 waiver
scenario for a Least
Developed Country

Source: World Bank 2004a.

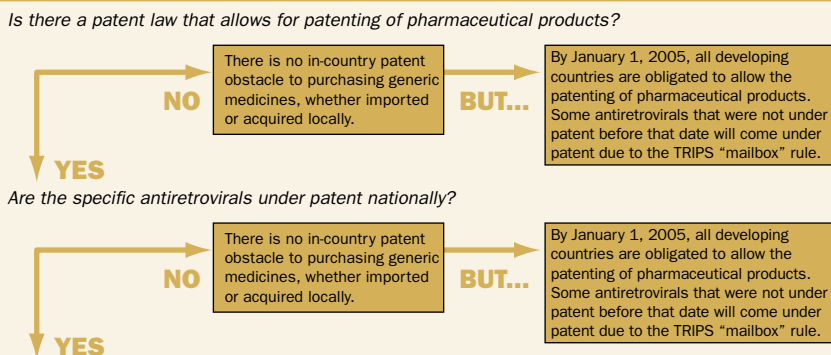


compulsory license but that does not have adequate manufacturing capacity. Since Article 31(f) of TRIPS limits compulsory licensing to uses that are predominantly for the supply of the domestic market, WTO members agreed that further action was necessary to ensure that countries without production capacity can use compulsory licensing provisions to the same extent that countries with production capacity can use them (WTO Council for Trade-Related Aspects of Intellectual Property Rights 2001). The Doha Declaration on TRIPS and Public Health acknowledges the problem in paragraph 6, and on August 30, 2003, the WTO adopted a decision on a waiver to the 31(f) requirement. Concurrent with this agreement was the requirement that exporting producing countries also have to issue a license (which will require amendments to their existing domestic legislation). Overall, the system appears to be very cumbersome, and it may be beyond the administrative capacities of many developing countries to use effectively (figure 2.2). More will be known about the usefulness of this agreement after 2005.

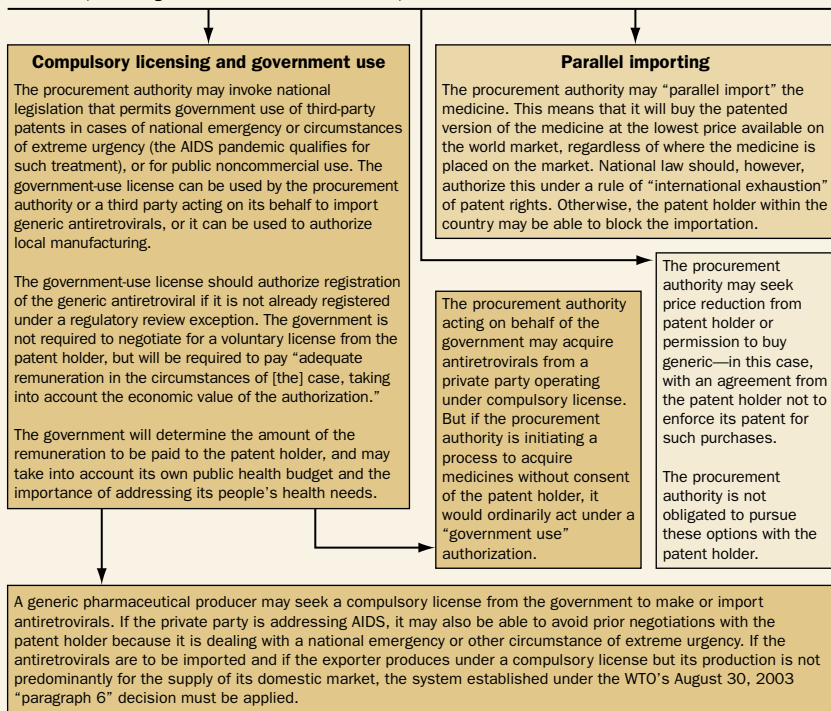
Since the adoption of the Doha declaration, the 32 Least Developed Country members of the WTO have been able to benefit from exceptions with regard to pharmaceutical product patents. Paragraph 7 of the Doha Declaration provides a special extension of the TRIPS transitional period for pharmaceutical products. Least Developed Countries do not have to “implement or

Figure 2.2
August 30 waiver scenario for a developing country

Source: World Bank 2004a.



The procurement authority should have several options under national law. If these options are not now part of national law, the procurement authority should encourage the government to adopt TRIPS-consistent rules that will assist it in purchasing medicines at the most favorable prices.



apply Sections 5 and 7 of Part II of the TRIPS agreement or to enforce rights provided for under these Sections until 1 January 2016" (WTO 2001). This means that Least Developed Countries do not have to grant product patents for medicines, provide protection of undisclosed test data, or enforce patents that have already been granted until at least 2016.

The UN Millennium Project Task Force on Trade has concluded that the impact of TRIPS on access to essential medicines will probably have a negative effect over time on developing countries:

From an economic perspective, the first-best approach to intellectual property in the drug industry would be to subsidize research and development and to grant no patent rights (or to grant patent rights

It seems clear that free trade agreements will negatively affect access to new patented medicines and vaccines in developing countries

and subsidize production up to the point where the patent-holder maximizes profits by setting price equal to marginal cost). However, this approach seems out of reach for a long time.

In fact, the international extension of intellectual property rights, as it applies to drugs, may progressively become (as the effect of TRIPS-induced patent protection will be felt mainly in the future) welfare-reducing from a world perspective and particularly from a developing country point of view. This is because most developing countries have virtually no ability to contribute meaningfully to the costs of developing major drugs, and there is little worldwide gain in terms of new product development funded by developing country purchases.¹⁰ By contrast, the cost of drug protection to developing countries may increase because the monopolies created by the extension of patent protection may progressively cut many developing countries off from essential medicines. In sum, no innovation gain may ultimately compensate the monopoly-related loss brought about by extending patent protection to the developing countries. (UN Millennium Project 2005a, ch. 10)

Regional trade agreements, TRIPS-Plus, and access to medicines

According to the UN Millennium Project Task Force on Trade, virtually all WTO members are party to one or more free trade agreements. The WTO estimates that, by the end of 2005 the total number of free trade agreements in force might well approach 300. The proliferation of free trade agreements is compounding concerns about the impact of trade agreements on access to medicines (UN Millennium Project 2005a). Box 2.1 summarizes the various ways in which free trade agreements are imposing TRIPS-Plus conditions that affect access to medicines.

In reviewing the evidence on the impact of trade agreements on access to medicines, it is a clear likelihood that these agreements will negatively affect access to new patented medicines and vaccines in developing countries. Although some steps have been taken to address undue limits on the existing TRIPS agreement (such as the waiver for Article 31[f]), it is likely that more will need to be done as more becomes known about the effects of implementation after 2005. At the least, developing countries will need more technical assistance from a range of expert sources to cope with the technicalities of trade agreements at the country level. While debate continues in some quarters about the impact of patents and trade agreements on access to medicines, it is safe to conclude that the proof will not be long in coming, since 2005 is a milestone year for the implementation of TRIPS in key countries and for the launching of some free trade agreements that impose further restrictions on how public health needs can be addressed. It will be important for the WHO,

Box 2.1
Examples of
TRIPS-Plus
provisions in free
trade agreements

Sources: Oxfam 2003,
 2004; Vivas-Eugui
 2003; Drahos 2004.

Extension of patent protection beyond the 20 years required under TRIPS. Patent terms should be extended to compensate patent holders for any unreasonable delays in granting the patent or unreasonable curtailment of the patent term as a result of the marketing approval process. There are not such requirements under TRIPS and thus the effective period of protection under TRIPS is usually less than 20 years.

Limits on parallel imports. The patent holder is permitted to restrict the possibility of parallel imports in the market. TRIPS is silent on parallel importation.

Test data protection. Test data of patent owners must be protected for at least 5 years for pharmaceutical products (10 years for agricultural chemicals) from the date of approval of the patent, delaying the marketing approval of generic drugs. Should this requirement continue to apply even where a compulsory license has been issued, it would effectively prevent the use of such licenses as the delay and costs would be too great. TRIPS requires protection of such data only against “unfair commercial use.”

Compulsory licensing. The grounds on which compulsory licenses can be issued are more restrictive than they are in TRIPS, and requirements for compensation to the right holder may be higher than required by TRIPS.

Marketing approval and the life of the patent. Requirements exist to disclose the request for marketing approval and identity of the applicant to the patent owner; patent holders are alleged to use frivolous lawsuits to unnecessarily delay marketing approval for generics. TRIPS permits generic producers to seek regulatory approval during the life of the patent with no conditions.

perhaps in cooperation with other agencies, such as the WTO, to monitor TRIPS implementation and free trade agreements as they pertain to medicines in coming years and to report, initially by the end of 2007, findings to date and recommendations.

Data exclusivity and evergreening

Although the degree of protection conferred by patents, generally for a period of 20 years, is clear, one must also take into account a number of techniques that originators have used or sought to use to defend or extend their rights.

A widely used way to obtain additional patent rights beyond the patent term for the original compound patent is to enhance the original product in some way so that a new patent may be granted on the new invention (NIHCM 2000; MSF 2003a). Sometimes the modification itself constitutes a significant innovation of importance in health terms; other times it may provide only marginal benefit in terms of usefulness, efficacy, or safety, and thus the modified product is unlikely to replace the original except to the extent that prescribers move to it.

There is also an ethical aspect of extended data exclusivity. Many patients voluntarily participate in clinical trials and accept the inherent risks associated with that participation, with the understanding that they contribute to the benefit of future patients and in the interest of the advancement of medical

Price transparency is an essential tool for designing public policy, promoting competition, and keeping prices in hand

science. However, they could be more hesitant to participate if they knew that the outcome of the trial would not become part of the public good and would only benefit one commercial company to the exclusion of all others. An increasing number of scientists and consumers are arguing that the data on which the efficacy and safety of medicines are being assessed by regulatory agencies should be open to public scrutiny. Some research-based companies are beginning to act to increase the transparency of clinical trials data, for example by participating in online registries.

Procurement

Countries with scarce resources use a variety of ways to procure medicines. Whenever a developing country does find ways to reduce the cost of the medicines it procures, it can pass the benefits on to its population through reduced prices or fees and broader access.¹¹

It is clear that governments and their agencies have a leading role to play in negotiating or agreeing to the prices at which medicines can be acquired. In developing countries, central medical stores or similar bodies commonly play that role.

In the public sector, procurement of medicines may be either insufficient because of lack of resources; inefficient because of lack of information, expertise, or negotiating power; or simply inappropriate to the country's highest-priority health needs. In the private sector, some medicines are also inaccessible for a given country because there is no commercial channel able or willing to import them. In such cases there may be no alternative to the public sector filling the gap insofar as it is capable of doing so.

Lack of information on prices and sources is a problem that can be solved relatively simply. For many essential medicines, various impartial bodies have issued compilations of the prices at which medicines and diagnostic supplies are available on the world market; such guides provide valuable support to procurement bodies.¹² Available evidence shows that price transparency is an essential tool for designing public policy, promoting competition, and keeping prices in hand. Special offers are available for some originator drugs. MSF has provided an overview of discounts, donations, and other offers available from manufacturers and the conditions attached to them (MSF 2003e); here too industry has criticized the data used, but at the country level, the positive impact of such documentation on procurement is evident.

Lack of information on the population's needs from district to national levels will require focused operational research and the use of available epidemiological statistics to overcome. Drug utilization studies providing data to guide procurement are needed everywhere and in a form that is relatively simple to carry out using readily available data (Dukes 1993). Technical support in this field can be provided by the various regional drug utilization research groups sponsored by WHO.

Box 2.2
Some conditions
for the success of
regional pooled
procurement
schemes for
medicines

Source: Adapted
 from SEAM 2003.

- Homogeneity of member states: size, range of needs, economic development, culture, political tradition, language.
- Harmonized national requirements: drug regulation, taxes, import duties.
- Financial stability: stable currencies, countries able to pay for pooled services and for supplies received.
- A common approach to quality: agreed quality standards, agreed procedure for control of suppliers and batches.
- Reasonably accurate prediction of needs.
- Competent and stable central staff.
- Reliable data on the patent situation of medicines.
- Loyalty of member states: national procurement agencies must not compete with the pool.
- Monitoring performance at pool and national level.

Lack of expertise in international procurement and in negotiating prices is a difficulty experienced in the public sector in many smaller countries. Donors have often provided support by training procurement officers. However, well trained and experienced individuals in this field are often lost to the private sector, where salaries are much higher. A novel approach to public procurement, which has been adopted in various parts of the world in recent years, is pooled procurement, an arrangement by which a number of countries jointly entrust their drug purchasing to a single body, generally working at the regional level.

The advantages of pooled procurement systems include:

- Access to experienced negotiating expertise and market knowledge.
- The ability to purchase medicines from the supplier on a larger scale, frequently resulting in significant bulk discounts.¹³
- Substantially widened access, since major suppliers that would not ordinarily tender for very small national markets are willing to tender to the larger regional procurement bodies.
- A provision of central financial guarantees to suppliers that will apply should any member state default on payment.

Essentially, a regional pool takes over the task of providing all medicines for its member states, either across the board or within a defined therapeutic area. The pool remains dependent on the individual member states for forecasts of need, if necessary assisting member states to undertake these forecasts, so that ordering is adjusted to real requirements. Some schemes go further: the regional procurement body operating in the Eastern Caribbean provides considerable support to its member countries in such matters as encouraging good prescribing by well constructed formularies, hence promoting the most efficient use of resources. (See box 2.2 for a list of conditions for success of regional pooled procurement strategies.)

The following excerpt is from the 134th Session of the PAHO Executive Committee, *Report on the 38th Session of the Subcommittee on Planning and Programming*, June 2004:

A range of specialized global funds and agencies have entered the field of global procurement

In examining options for pooled procurement, it would be important to review the experience with the PAHO Revolving Fund for Vaccine Procurement, applying lessons from that to the development of other procurement mechanisms. The Revolving Fund had initially, in 1979, been capitalized at \$1 million, with 19 countries participating, for the purchase of five vaccines. The corresponding figures now were \$24 million, 35 countries, and 12 vaccines, and the Fund had contributed significantly to the achievement of priority objectives in immunization in the Americas by supporting countries in commodity procurement, supply, and use. Another option for pooled procurement was the PAHO Strategic Fund, which had been established to help countries in the procurement of HIV/AIDS, TB, and malaria products. Although 11 countries had signed participation agreements with the Fund, it had been used in only a few countries to date. The Fund could become an effective instrument for ensuring continuous supply of public health products and building capacity in supply management, but in order for that to happen it would be necessary to reaffirm political commitment, redirect the technical cooperation package supporting the Fund, review the administrative procedures governing operation, and develop lines of communication with countries. (PAHO 2004, p. 20)

A different approach is involved in the global procurement of medicines. These initiatives have been undertaken at various times in order to meet a major worldwide need for a specific type of product. The best known of these involved procuring oral contraceptives and vaccines for a range of countries, with UNICEF and the Rockefeller Foundation taking the lead, and securing prices that represented only a small fraction of the supplier's usual market price. UNICEF has for many years maintained a nonprofit global supply system for drugs, vaccines, and other essential supplies, with its own procurement agency and its own warehousing and delivery program. UNICEF has claimed that, although it supplies some 40 percent of the vaccine market in unit terms, it covers only 5 percent of the market in financial terms (Jarrett 2003), which would indicate that its vaccines are procured at only a small fraction of the prevailing industrialized country market prices. It also indicates that they are supplying poor countries rather than pricing and supplying to markets in wealthy countries. More recently a range of specialized global funds and agencies have entered the field of global procurement, for example, for AIDS. Established in 2001 by the Stop TB Partnership, the Global TB Drug Facility provides grants in kind to some countries and technical support for procurement in others.

It has been argued that a very large pooled procurement scheme might actually exert excessive downward pressure on prices, thus rendering the market so unattractive that some suppliers would withdraw (Jarrett 2003). This

Technical pharmaceutical regulatory systems are essential means of ensuring that medicines attain the necessary standards of efficacy, quality, and acceptable safety

risk probably arises only in the case of a very large and powerful joint procurement agency with global outreach, but it should be borne in mind.

Regulation

The regulation of medicines exists to protect public health. In theory, regulation should not create a barrier against access to bona fide medicines, but in some circumstances it can do so. Bureaucratic delays can occur or excessive demands may be imposed, delaying distribution or increasing systemic costs. Regulatory regimes and measures are challenged on such grounds by both research-based and generics companies, and it can be helpful to consider some of the problems that arise.

Basic standards

Technical pharmaceutical regulatory systems are essential means of ensuring that medicines entering the market attain the necessary standards of efficacy, quality, and acceptable safety, and that the information provided with them is sufficient and reliable. In certain areas of the world (most notably the European Union, but also in parts of Africa and members of the Association of Southeast Asian Nations), collaboration between agencies has been established and has progressed toward regional regulation. Particularly where agencies are small and understaffed, as is the case in much of the developing world, it is likely that this development will reduce unnecessary delays.

National regulatory agencies need to be strengthened. They may wish to consider developing fast-track procedures for medicines for priority diseases in a given country. WHO prequalification offers national agencies a reliable source of information about priority medicines for AIDS, TB, and malaria.

Equivalent versions of medicines

Because of the commercial value to research-based companies of the medicines that they have researched, developed, and marketed, understandably bitter disputes have arisen around the licensing of generic versions from other firms. These medicines, developed by copying the active ingredient, allow firms to benefit from all the creative effort of the originator. Insofar as the original medicine is patented, exact copying will not be possible so long as the patent remains valid. It is not, however, the task of a regulatory agency to determine, when considering an application for regulatory approval, whether the medicine in question complies with patent law or not.

In general, the generic version of a product should be bioequivalent to the original. Not all agencies have a common policy regarding the evidence that will be required to demonstrate bioequivalence, and the level of proof required will depend to some extent on the nature and form of the drug.¹⁴ The essential principle is that bioequivalency can be said to exist only when the product in question will, beyond reasonable doubt, have precisely the same kinetics and

A national government must ensure that there are effective means of supplying and distributing medicines to the entire population

effects in an individual in the same dose as the original. This will usually require testing on a living subject. It would be desirable to arrive at clear and universally agreed criteria for determining when this bioequivalence can be said to exist.

Similar medicines

Regulatory agencies are regularly confronted with medicines based on new active substances that are so close in chemical structure to those already known that a hypothesis arises that they will have the same effect. As a rule, this can be no more than a hypothesis, since even slight differences in chemical structure can result in major differences in pharmacological activity and effects. While such a drug should be subject to full regulatory requirements, it is generally accepted that many agencies have, to some extent, applied less stringent criteria in the review process.

Taxation

Import duties or taxes, imposed by another government department, may lay an excessive burden on medical supplies. Delays at customs can also mean that medicines lie unused for long periods in port facilities, sometimes actually expiring during this time or being subjected to suboptimal storage conditions that can cause degradation in their quality because of exposure to excessive heat, cold, humidity, or light.

A value-added tax (VAT) is a revenue-raising instrument that can exist at several different levels of the system and may be applied to different classes of products, including, in many countries, essential medicines. A 2003 European Commission study found that VAT rates imposed on medicines averaged more than 12 percent (Irvine 2004). The combination of duties and taxes can significantly increase the retail price of medicines. While the global average increase is 18 percent, for many low-income countries the increase is higher; for example: India 55 percent, Sierra Leone 40 percent, Nigeria 34 percent, and Bolivia 32 percent.

Distribution

Medicines entering a country may be reasonably accessible only in urban centers because of a lack of a countrywide distribution system. Private distribution systems (through wholesalers and pharmacies) operate only in the urban areas in many developing countries. Public systems, set up to provide national coverage, often experience chronic or incidental problems: management and ordering routines may be poor; transport networks may be irregular or incomplete (especially in areas with poor communications); and losses may occur due to poor storage, theft, or corrupt practices at one level or another. Lack of qualified and dependable staff exacerbates all of these problems.

A realistic interpretation of the duties of a national government in this field is that it must ensure that there are effective means of supplying and

Taxes and tariffs on essential medicines should be eliminated; they negatively affect both affordability and competition

distributing medicines to the entire population. There is no conclusive evidence to support the superiority of public over private distribution systems or vice versa. In many countries the two co-exist; sometimes one has developed because of defects in the other. The entire balance between private and public operation must be subject to ongoing review, and the system of control adjusted as necessary to counter shortcomings identified in the system. Where a public supply system is proving unsatisfactory, the possibility of transferring operations to the private sector or subcontracting certain tasks (such as procurement, transport, or administration) may need to be considered.

A special place can often be accorded to faith-based NGOs with their own distribution systems. Some of these, such as Joint Medical Stores in Uganda, provide exemplary models for efficient, low-cost operation. Kenya is one of several countries where the most successful medicines supply system (that is, one providing medicines to the mission health sector) has been managed by an NGO rather than a government agency (WHO 1997; Kawasaki and Patten 2002). The country's Mission for Essential Drugs and Supplies was set up in 1986 by the Catholic Secretariat and the Christian Health Association to supply medicines to church-managed health units. Financial support has been provided by various bilateral donor agencies, but by 2002 the system was found to be financially self-sustaining. Supplies are procured in bulk from local agents and local producers and the system maintains its own facilities for storage, distribution, and quality control. Monitoring for efficiency is intensive, with operating expenses averaging only some 10 percent of total costs. There have been extensive training programs for health facility staff, though these cover only part of the training needed.

Competition

The means to promote and regulate competition normally operates at the national and local levels. On the national level, it will be heavily influenced, and to some degree regulated, by features such as national licensing policies, importation regulation, and other public policy tools. The degree to which this does or does not regulate competition will also vary (at times significantly) from country to country. Taxes and tariffs on essential medicines should be eliminated; they negatively affect both affordability and competition.

On the local level, manufacturers, importers, and distributors may or may not be constrained in setting the terms of commerce (Huttin 1994). Within any country, the promotion of competition is a potent tool to ensure that prices fall to a fair level. It should include competition between various therapeutic approaches and between originator and generic medicines producers. The prices charged for marketed medicines at all levels—imported, wholesale, and retail—must be published and constantly monitored so that excessive charges can be detected and eliminated; this is already the practice in many industrialized countries and it should be applied everywhere.

**Establishing
and maintaining
standards of
good quality
are critical for
reliable access
to medicines**

Supply and distribution in developing countries could, theoretically, be addressed by the private sector. However, in most low-income countries, the private sector is not robust enough to attract this type of investment. The public sector, in the form of central medical stores and similar bodies, arose precisely because the market was not responding to national needs in terms of imports, distribution, and price. It is worrying that the United States appears to be contracting private international firms to deliver medicines supplied through its PEPFAR program. Such approaches, while technically “private,” have a chilling effect on the development of local, private, competitively based distribution mechanisms.

In developing countries, it is not unusual to find a profusion of private retail pharmacies, often clustered within a single section of a major urban center, that have developed in response to the demand for expensive originator medicines by a wealthy minority. Beyond this urban setting, drugstores (which are often poorly stocked) may or may not exist. Despite rapid urbanization trends, the majority of the world’s poorest populations continue to live in rural, often very isolated, regions. Competition, for the most part, is nonexistent in these areas because there are no medicines to be obtained by any means. Competition is severely constrained because of a lack of demand (because people cannot afford to pay) and high costs of supplying physically isolated locations.

Patent protection can also be viewed as a barrier to competition (this assumes serious dimensions when a medicine is virtually unique and irreplaceable) during the period of patent protection. Unless or until a suitable alternative medicine enters the market, there will be no genuine competition capable of reducing prices. However, experience has shown that in some cases, good-faith negotiations with the patent holder have led to expanded access to needed patented medicines on acceptable preferential terms.

Quality

Once a product has been developed and approved, quality manufacturing is required to bring it to consumers. It is evident that if a medicinal product is of poor quality it cannot realistically be regarded as accessible. The failure to adhere to adequate quality standards may result in immediate or long-term injury to human health. The importance of establishing attainable standards of good quality (quality assurance) and of ensuring that these are maintained during production (quality control) becomes a critical factor in reliable access to medicines.

A problem from the global point of view is that the experiences of agencies in this matter are generally not published, and it is difficult to determine how watertight the methods are and where and to what extent problems are encountered (Kaplan and others 2003a, 2003b). The same applies to some excellent studies known to have been conducted by bilateral aid agencies; it would be helpful if these were to be made public. Certainly, however, there is abundant

**Only a minority
of medicine
manufacturing
facilities are as
yet producing
medicines to
GMP standards**

evidence that widespread quality problems persist even where some life-saving medicines are concerned, such as antimalarials in Africa (Maponga and Ondari 2003).

Quality standards

There can also be some difference of view on the quality standards to be applied. Standards for older medicines are usually to be found in national pharmacopoeias. During the last 20 years, the concept of GMP standards (supported by WHO) has come into use. There are also, however, stricter standards, such as those propagated primarily through the International Conference on Harmonization (ICH).

Representatives of drug regulatory agencies and the pharmaceutical industry from the European Union, the United States, and Japan first developed the ICH in 1990. First proposed as a regional initiative to eliminate duplication of regulatory efforts and achieve quicker access to new pharmaceuticals, global expansion of the initiative has been planned since 1997. During a meeting of the Neglected Diseases Group in Malaysia in February 2004, concerns about the impact of ICH regulation on access to medicines in developing countries was discussed. In addition to the use of the ICH as a global standard without any clear international mandate or any international harmonization, other concerns echoed those expressed during a meeting in Geneva in 2003. One of the main concerns was that it would increase the costs of raw materials and generic medicines without any quantified increase in quality and therefore without clear public health benefits (Bannenberg 2004).¹⁵ The standards are justified in certain situations, but they are often complex and disproportionately costly and have been criticized by independent experts as unnecessarily strict.¹⁶

Of the many thousands of medicine manufacturing facilities throughout the world, only a minority are as yet producing medicines to GMP standards. Many more must be induced to do so. Achieving GMP is often an incremental process that, given the economic and logistical constraints inherent in many developing countries, will take longer for some manufacturers to fully implement than others. This will be achieved only if procurement agencies are firm in insisting on these standards as a condition of purchase. Where these standards have not yet been attained, the decision will have to be made from case to case about whether a particular product or supplier offering lesser standards can, as a temporary measure, be regarded as acceptable. As noted above, much will depend on the nature of the medicine concerned; no flexibility can be allowed for medicines with a narrow therapeutic margin, but some flexibility may be tolerated for medicines with a broad safety margin.

Generic medicines

The misperception that generic medicines are inherently of lower quality than originator products still exists. In fact, generics must demonstrate the same

Quality controls exercised by manufacturers are complemented by those carried out by public authorities

quality standards as the originator version in order to be registered. Ongoing quality control criteria remain the same for either type of product. It is a fundamental fact that approved generic medicines are identical in their effects and usefulness to the corresponding products of originator companies. An approved, chemically derived generic pharmaceutical is thus medically interchangeable with the originator product and with all other generic clones of the original patented medicine. For many products, proof of this interchangeability will require a bio-equivalence study. For some products and in certain countries, this requirement may be bypassed where other guarantees of identity are considered sufficient. In this respect and in other regulatory matters it must, however, be acknowledged that some resource-short nations do not succeed in enforcing such standards. Where that is the case it is vital that the national authorities “stand tall” politically and allow, for as long as necessary, an international agency to assist them by coordinating and simplifying the regulatory and approval process, and where necessary assume some technical functions that they cannot perform themselves (for example, the inspection of foreign manufacturing plants and products, as is done by the WHO for antiretrovirals for AIDS, antimalarials, anti-TB medicines, and other essential medicines) (Haddad 2004).

Official quality controls

Quality controls exercised by manufacturers are complemented by those carried out by public authorities. Many countries maintain quality control laboratories of different sizes and levels of competence, both in order to examine quality standards at the time of registration and procurement, and to check suspect samples from the field.¹⁷ Any importing country should, in principle, be capable of protecting its population from generic products from unreliable sources by relying variously on its own regulatory approval systems and inspectorate and on international systems for cross-border inspection and prequalification of firms. The costs of maintaining such a system are not negligible, but they are likely to be modest when compared with the savings that can be achieved in terms of reduced waste.

Prequalification of suppliers and products

For many years, some national and other procurement agencies have limited their purchasing to prequalified suppliers, that is, firms or individual products that they have investigated in advance and found to be of sufficient standard. However, the fact that a supplier has been prequalified provides no absolute guarantee that the products that he or she supplies will in all cases meet the requisite standard; ongoing quality control at the time of supply remains essential. An ambitious prequalification scheme is currently operated within WHO to serve a number of agencies purchasing drugs for AIDS, TB, and malaria (Quality Assurance and Safety of Medicines 2003). Key steps in the process include assessing product dossiers for safety, quality, and efficacy and assessing

**Bona fide
quality generic
medicines have
sometimes been
erroneously
regarded as
counterfeit or
substandard
items**

manufacturers for compliance. Here, however, the same reservations apply: the WHO has had to remove certain prequalified products from its list when it has been found that they do not fully meet the required standards (some have been relisted after submitting more data on bioequivalence). Prequalification is thus an approach that can save time and can generally be reliable as a way to select suppliers and products for a particular order, but it should be part of a larger quality assurance strategy.

Substandard and counterfeit medicines

Though reliable statistics are hard to come by, the problems posed by truly substandard and counterfeit medicines are certainly widespread, particularly where governments and their agencies are weak. Counterfeiting and substandard medicines can also proliferate when countries are undergoing a difficult transition from a centralized to a market economy, but the necessary regulatory checks and balances have not yet developed.

This is unfortunately an area in which (as noted in chapter 1) the debate has sometimes been confused because of problems of nomenclature; bona fide quality generic medicines have sometimes been misrepresented or erroneously regarded as counterfeit or substandard items. The issues are entirely distinct.

Substandard is a term applied to those medicinal products that have an inadequate standard of quality because of incompetence, negligence, or dishonesty on the part of the manufacturer (Newton and others 2002).¹⁸ The problem exists with both originator and generic items. Although sound procurement practice can counter this problem to a large extent, constant vigilance through inspection is needed once a medicine has been procured or admitted to the market. The long-term solution must primarily lie in strengthening procurement, regulatory, and inspection systems, backed up by policing and judicial structures that ensure that regulations are truly enforced and that sanctions are imposed where necessary. Promoting the transfer of manufacturing technology from the developed to the developing world and providing technical assistance would be an effective way to counter the problem of substandard medicines quality.

Counterfeit medicines represent deliberate forgery and constitute an equally serious problem.¹⁹ A counterfeit medicine will be produced so that both the packaging and the contents resemble the originals in their color, shape, name, and typography. Such a medicine will often be smuggled into the supply chain at some level where vigilance is lacking. Since the contents are usually of no medicinal value, such products represent a real risk to public health. Because they also present a threat to the turnover of the bona fide producer, this is an area in which recognized manufacturers and the public health authorities have sometimes worked together successfully to track down and eliminate the sources. As in the case of substandard medicines, the policing and judicial systems must provide the backing needed to ensure that the law is enforced.

For donations to be effective, recipient countries must have the capacity to manage and distribute the donated medicines

Medicines donations

The research-based industry has long been active in providing medicine donations that address priority diseases of poverty. Since 1998, 10 major companies in the Partnership for Quality Medical Donations have donated products worth \$2.7 billion, which constitute only a portion of total contributions made by the industry. Merck, Pfizer, and GlaxoSmithKline have large, long-term donation programs to control and eliminate onchocerciasis (river blindness), lymphatic filariasis, and trachoma (box 2.3). Key elements of success are the effective involvement of and collaboration with governments and civil society; involvement of the community in treatment delivery; open-ended commitments of donated medicines supply; company interest in promoting learning and improvements in program implementation; and adequate administrative support and training.

A constructive development in the area of donations has been the publication of *Guidelines for Drug Donations* (WHO 1999a). The WHO led this effort, which was supported by the pharmaceutical industry. The guidelines were reviewed in 2000 and the findings show that the approach has been beneficial for recipient governments. A key aspect of the guidelines is the emphasis on donations being made only in response to recipient country requests, based on their assessments of need. A recipient should have the capacity to manage and distribute the donated medicines.

Large, well financed, and well managed global disease control programs aside, most donations at the national to local levels are short term and not sustainable for meeting ongoing medicines needs. Inappropriate donations are those that do not meet the needs of the country or that use medicines close to their expiration, which imposes the additional burden on countries of properly disposing of unusable medicines (Hogerzeil, Couper, and Gray 1997). A recent review of the effectiveness of donations by Autier and others (2002) found that inappropriate donations commonly came from small organizations with little or no field presence or experience in the pharmaceutical sector and from re-donations (often by developing countries themselves, passing on surplus items, and local in-country distributors unable to sell their medicines in the market). All of these errors are avoidable, and various attempts are being made to address them.

Even large-scale approaches have their limits. For example, the GFATM has not endorsed medicines donations, in part because the scale of need for treating AIDS, TB, and malaria is simply too great to rely on donations as a major means of medicines supplies.

Prescribing and dispensing

Inappropriate use of medicines is both wasteful and dangerous. A 1994 study conducted by the World Bank reviewed the causes of medicine waste in Africa. It suggested that for every \$30 of medicines reaching the periphery, \$15 could

Box 2.3
Community-
directed treatment
with ivermectin
(Mectizan®):
An example of
an effective
medicines
donation and
distribution
strategy

Source: Oswald, Leontsini,
and Burnham 2004.

According to WHO, onchocerciasis (river blindness) is endemic in 30 African countries. It also occurs in specific locations in six Latin American countries and in Yemen. An estimated 18 million people are infected with onchocerciasis. Among these, approximately 0.3 million persons are already blind from the disease. The recently developed and introduced community-directed treatment with annual doses of ivermectin could make it possible to largely eliminate this blinding disease burden from the affected countries in Africa and Latin America by 2010.

In 1987, Merck declared its commitment to donate ivermectin (Mectizan®) free of charge worldwide “to all that need it for as long as needed.” Because it requires only an annual dose and it can be easily administered, the provision of this donation is a crucial element in efforts to control and eradicate this debilitating illness. In the mid-1990s, studies were undertaken to assess the most effective means for distributing and delivering ivermectin in the community.

Community-designed distribution systems achieved better coverage than those designed by control programs. Furthermore, they appeared to have a greater potential for sustainability, as demonstrated by a number of factors: the commitment of community leaders and distributors, the high level of community involvement and a willingness to commit available resources, the perceived benefits of ivermectin and a high demand for treatment in endemic communities, and the community’s ability to determine and rectify problems within the distribution methods.

By 1997, community-directed treatment with ivermectin was adopted as the “principal method” for onchocerciasis control in Africa. The components of this protocol are as follows: the selection of the distributors; the mode of procurement and collection from the central supply; the form of communication used within the community; the method of dispensing the medicine; cost sharing; and the level of supervision and referral of adverse reactions.

The flexibility inherent within community-directed programs makes them suitable to the variety of circumstances in which treatment programs are required. The convenience of treatment, and thereby coverage, is increased by allowing the community to determine when, where, how, and by whom the medicine will be dispensed.

A review of the ivermectin distribution program in Uganda showed problems with delivery and treatment prior to the adoption of the community-based model. Studies also showed changes over time, consistent with changes to the community-directed approach, in the involvement and empowerment of women as distributors in the program. Initially, few women were chosen. Reasons cited included lack of interaction and trust among women, too much other household work, meeting sites being too far away, not being informed about meetings, sickness, restrictive husbands, and lack of information. However, when gender-responsive approaches were used in the community-directed activities, information and knowledge changed, trust increased, and more women have become distributors. Women have performed very well in this role. It has been empowering for them, in part because community-directed treatment builds on an understanding of gendered roles in providing healthcare and health-seeking decisionmaking in the community.

The success of community-directed treatment with ivermectin has been carried over into other donation and disease control and elimination programs, including the extension of ivermectin donations to treat lymphatic filariasis (in conjunction with a GlaxoSmithKline donation program for albendazole) and Pfizer’s donation of azithromycin (Zithromax®) to treat trachoma. These disease control programs have produced important advances in knowledge about what approaches are successful in ensuring medicines delivery and use at the community level.

Even when a medicine reaches isolated populations, appropriate treatment may be out of reach because of a prescriber's lack of knowledge

be squandered as a result of poor prescribing, and a further \$3 as a result of noncompliance by the patient (World Bank 1994).

Inappropriate use can and does also result in injury. In infectious disorders, such as malaria and TB, it can also result in a massive increase in resistance to treatment. In one study in Tanzania, 75 percent of health workers were found to be dispensing subtherapeutic doses of malaria regimens to stretch inadequate state funding, a practice that is notoriously prone to induce resistance (Mnyika and Kilewo 1991).

The WHO introduced the use of international nonproprietary names in 1950. The existence of several names for the same substance can be a source of potentially dangerous confusion; the use of a universally recognized and accessible name can reduce the confusion and potential for error. To date, more than 7,000 international nonproprietary names for generic and newly developed products have been selected, published, and translated into five languages (WHO 2004d).

Prescribing medicines

Even when a medicine reaches more isolated populations, appropriate treatment with it may be out of reach because of lack of knowledge on the part of the prescriber (inappropriate prescribing). Inappropriateness may involve, for example, over- or underdosage, the use of several medicines where one would be sufficient, or the use of an entirely unsuitable agent (Pavin and others 2003). It can also involve prescribing an expensive patented medicine despite the fact that a virtually identical generic product is available free of charge or at fraction of the price.²⁰ In impoverished settings, this wastes already scarce resources.

Several developing countries have attempted to promote generics prescribing as a general policy. Such campaigns are directed to prescribers and the public. As a rule, the introduction of simple prescribing guides for health workers (such as standard treatment guidelines and formularies) in which the recommended medicines are listed primarily or exclusively by generic name, has had a significant effect, especially where these generic products are readily available countrywide through a national supply system. However, in various countries (and in the urban and private sectors in most countries) resistance to this concept has been experienced and there has been relatively little impact, so that originator products often remain dominant.

Efforts to promote generics use in Nigeria, Pakistan, the Philippines, and some parts of Latin America are undermined by the deeply rooted professional and public perception that “lower-priced pharmaceutical equivalents . . . are necessarily of a quality inferior to the brand-name products sold by large, well-known firms” (Velásquez, Madrid, and Quick 1998). This failure is striking in view of the relative success of generics prescribing schemes in a range of countries, such as Denmark, Germany, the United Kingdom, and the United States. However, in these countries, very firm measures have been required to

Some excellent work has been done on examining the quality of prescribing in particular countries

change prescribing habits. It seems obvious that the successful introduction of generics prescribing requires good public relations and persuasion (if not compulsion), and not merely favorable prices.

Some excellent work has been done on examining the quality of prescribing at the country level so that corrective action can be taken where necessary (Laing 2001; Pavin and others 2003). A simple method is the ABC analysis of the medicines procured nationally, which is likely to point to certain gross faults in prescribing. The following summary is from *Drugs and Therapeutic Committees: A Practical Guide* (WHO and MSH 2004, p. 82):

Most pharmacists and managers know that only a few drug items account for the greatest drug expenditure. Often 70–80 percent of the budget is spent on 10–20 percent of the medicines. ABC analysis is the systematic study of annual medicine consumption and cost in order to determine which items account for the greatest proportion of the budget. ABC analysis can:

- Reveal high usage items for which there are lower-cost alternatives on the EML [essential medicines list] or available in the market. This information can be used to:
 - a. Choose more cost-effective alternative medicines.
 - b. Identify opportunities for therapeutic substitution.
 - c. Negotiate lower prices with suppliers.
- Measure the degree to which actual drug consumption reflects public health needs and so identify irrational drug use, through comparing drug consumption to morbidity patterns.
- Identify purchases for items not on the hospital or clinic essential medicines list (i.e., the use of non-formulary medicines).

ABC analysis can be applied to drug consumption data over a one-year period or shorter. It can also be applied to a particular tender or set of tenders.

Other sources on country-specific prescribing practices can be found in Ph.D. theses or work conducted by bilateral aid agencies. Supplementary evidence of faults in prescribing may be found by comparing orders received from comparable districts or institutions (which may point to overconsumption or to variables such as the training of the prescriber and local and cultural preferences). Studies carried out in comparable countries can suggest common features of prescribing practices.

More sophisticated methods for the study of prescribing include establishing a prescribing and patient care survey, using WHO's healthcare facility medicine use indicators (Hogerzeil 1993, updated 1997) and country progress indicators (WHO 2000a). Where sufficient resources are available, one may establish a series of periodic medicine-use surveys, such as those carried out biennially in Zimbabwe (Trap and Lessing 1995), or monthly

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self-monitoring at health centers or district level, as developed successfully in an area of Indonesia (Sunartono 1995). In all these respects, however, it is necessary to consider carefully how much investment in research is justified before proceeding to action, particularly since some of the faults in the existing situation may be entirely obvious or may have been documented in previous studies.

It is tempting at first sight to attribute much irrational prescribing to the fact that, in much of the developing world, prescribers commonly do not have full medical training. While it is beyond doubt that basic training is commonly inadequate, this does not sufficiently explain the fact that remedies are poorly selected and applied. At the primary care level, the number of essential medicines likely to be available and in regular use is quite small. So it is not an impossible task to provide prescribers who have a basic education in nursing or as medical assistants with sufficient guidance to diagnose the most common conditions likely to be encountered and to prescribe with a reasonable degree of competence. Fully qualified prescribers may prove to prescribe irrationally, especially where their prescribing is linked to an income from dispensing, which creates a temptation to overprescribe as a means of increasing earnings (Trap, Holme Hansen, and Hogerzeil 2002).

In some countries, there is intensive commercial persuasion to prescribe newer and more expensive remedies even in situations where they offer no advantages over older, much cheaper products. However, there are evident risks in aggressive promotion in an environment where educational standards are low, objective sources of data are hard to come by, and no resistance to advertising has developed.

Physicians in developing countries actively seek peer-reviewed, evidence-based data on medicines to improve their prescribing. Improving this situation as a matter of policy will provide valuable assistance to physicians in developing countries (Hafeez and Mirza 1999).

Guidelines on the relationships between members of the medical profession and representatives of the pharmaceutical industries are currently the focus of recommendations—in some cases regulation—by professional organizations. In a brief review that examined routine professional exchanges of goods and services from industry representatives to physicians in both developed and developing countries, Ann McGuaran (2002) noted an increasing trend toward regulation of such exchanges by physician organizations to ensure their professional appropriateness. The Royal College of Physicians (United Kingdom) recently issued updated guidelines that covered a wide range of situations, including the following:

- No conditions should be attached to gifts, items of equipment, or aid.
- Under no circumstances should cash or objects in kind be accepted by individual physicians, and gifts, honorariums, or hospitality received must be declared.

**Improving
prescribing
will require
both short-
and long-term
efforts**

- Speakers at company-funded meetings should not be chosen solely by the firms, and the hospitality firms provide at meetings with an educational purpose should be modest.
- The payment of reasonable expenses and honorariums is acceptable for larger and overseas meetings but should be handled through the independent scientific body and not paid directly to individual physicians.
- All research must be cleared by the doctor's research ethics committee, and all financial matters should be managed by institutional finance departments (RCP 2004).

Realistic and cost-effective approaches for developing rational prescribing according to WHO standards have been documented (Laing, Hogerzeil, and Ross-Degnan 2001). Not all have been tested under strictly controlled conditions, but the teaching methods tested over a period of years at Groningen University and McMaster University, partially summarized in a handbook available on the Internet, have a creditable record of success and have, through the medium of WHO, been widely adapted for use elsewhere (De Vries and others 1995).²¹

Improving prescribing will require both short- and long-term efforts. Recognized approaches are documented in the literature and a considerable fund of experience is available through the International Network for Rational Use of Drugs, which works in many developing countries as well as organizes training courses (INRUD 2002). Short-term methods include the development of national standard treatment guidelines (often based on the numerous established handbooks of this type), formularies, and bulletins. There are many excellent publications of this type that can be adapted to national needs; for example, the International Society of Drug Bulletins is a valuable source of advice, support, and draft texts. Some well known textbooks and reference volumes, such as the *Merck Manual* (consumer and professional editions) are provided throughout the developing world (in local languages) by the International Pharmaceutical Federation Pharmabridge Program and the International Council of Nurses trunk library program.

In hospitals and other institutions, therapeutic committees, with the full participation of medical and pharmaceutical staff, are capable of setting and maintaining high standards, in order to both improve patient care and economize on resources. The reorientation of the pharmaceutical profession can provide a promising new resource working toward the better use of medicines.

When seeking to influence prescriber behavior, it is essential to use means that will not be resented by those concerned. Physicians, in particular, are most likely to be responsive to efforts to improve their standards of practice if they emanate, at least in part, from within their own profession instead of being imposed upon them. The creation of therapeutics committees, noted above, is an important step in this direction. A national medical association and a nursing association should participate in developing these approaches and should

The retail pharmacist, dispenser, or drug seller is often the patient's primary source of information about medicines

be encouraged progressively to assume responsibility for them. When medical training is extended and upgraded, efforts must also be made to encourage the development of the professional's communication skills as well as his or her technical abilities. In particular there is a need to develop skills in communicating with patients, including the provision of facts and advice relating to medicines.

Finally, the issue of advertising and promotion for medicines will need to be tackled, generally in line with international ethical standards but also taking into account the particular susceptibility to commercial persuasion that a population may have when it is exposed to these influences for the first time.

Dispensing medicines

Much of what has been said above regarding the prescriber applies by analogy to the retail pharmacist, dispenser, or drug seller. The drugstore, whatever its nature, is often the patient's primary source of information about medicines, and in matters of self-medication it is likely to be the only one. Fully trained professional pharmacists will not be available for retail duties in all countries in the foreseeable future. But much can be done through basic training and follow-up documentation to ensure that the retailer, whatever his or her level of education, provides reasonable assistance to the purchaser of a medicine to understand its nature and how to use it appropriately. In some cases, trained pharmacists may be available but are not fully utilized in a manner consistent with their level of training (Professor R.R. Chaudhury, personal communication, 2004).

Use of medicines in the home

A medicine is not always used as instructed by the prescriber or indicated on the package. The verbal instructions may not have been clear or they may have been misunderstood. The text on the package may be in a foreign language or the patient may be illiterate. Common misunderstandings ("two doses are better than one") may call for correction. Gender issues can also play a role in determining the extent to which medicines are used appropriately in the family. It is often the woman who brings home the medicines and administers them. Women must thus have sufficient knowledge to select those medicines that are available without prescription, and to ensure that the medicines entering the home are used appropriately. Inequality in educational systems typically is to the disadvantage of women and girls. As in the case of health professionals, it is necessary to envisage both short-term and long-term approaches among the general public in order to promote the rational use of medicines.

Short-term approaches can be constructed around the fact that irrational use commonly reflects popular misunderstandings regarding the nature and use of medicines. Poster campaigns in clinics and brief messages transmitted by radio and TV have proved effective in correcting some of these misconceptions.

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They can also encourage the consumer to seek the advice and information that he or she needs to understand the proper use of a medicine, especially where no written information is accessible or the user is illiterate. In the longer term, the main solution must lie in improved standards of education, particularly where there is a need to correct a lag in progress in educating girls and women. The proper use of medicines should be a component of popular health education.

Promoting Rational Drug Use (2000) is an online compilation of course materials and references available on the Boston University website.²² Included in this collection is a session on “Effective Community Education” by Professor Anita Hardon that describes a systematic approach to providing information to patients and to correcting widely held misconceptions (detailed information is available online²³):

Step one: Investigate

The investigatory stage is essential and at the core of the communication process. It should address the following issues:

- What is already known about the problem?
- What new kinds of information are needed?
- What are the characteristics of the target audience?
- What development communication resources are there?
- How should data be generated? (both quantitative and qualitative)

Step two: Plan communication activities

Step three: Develop communication materials

Step four: Test and revise materials

Step five: Implementation

Step six: Monitor, evaluate and revise

These efforts must be complemented by others, especially those concerned with the information provided to the consumer at the point of sale. Both pharmacists and other medicine sellers need to become accustomed to providing information and advice to all customers purchasing medicines, whether over the counter or by prescription. Finally, as noted earlier, there needs to be an ongoing effort to involve the public and its representatives in developing better standards of medicine use and improving the accessibility of information and advice to the individual patient.