Chapter 1

The problem

A very large part of the world's population has inadequate or no access to essential and life-saving medicines. Along with skilled and dedicated health-care providers, medicines[1] are the most significant means that society possesses to prevent, alleviate, and cure disease. Most illnesses, especially infectious diseases, are either preventable or to some extent treatable with a relatively small number of medicines. Combined with appropriate public health interventions, appropriately prescribed essential[2] medicines and vaccines could, in principle, massively reduce the impact of disease on communities. Despite this fact, a large proportion of the world's population today still has either only limited access to appropriate medicinal treatment, or no access at all.

The consequences of this inadequacy include an enormous loss of life from preventable or treatable diseases (such as tuberculosis, pneumonia, acute respiratory infections, malaria, diabetes, and hypertension) and significant human suffering, particularly among the poor and marginalized populations of the world. The lack of access to life-saving and health-supporting medicines for more than 2 billion poor people stands as a direct contradiction to the fundamental principle of health as a human right. Illness is a major reason that the nearly poor slide into profound poverty. Illness decreases people's ability to work (be it remunerative or not). Illness orphans children and prevents them from getting the education they need. Women and children make up the majority of the poor, and their low status in many societies often means that they have even less access to medicines. Improving access to medicines must be a key component of strategies to strengthen healthcare.

Increasing access to medicines in developing countries, especially for the poor, offers many challenges. These can be crystallized into two main areas:

- How to increase access to affordable existing medicines in resource-poor settings, which countries can do by improving the selection and use of

The World Health Organization estimates that a third of the world's population lacks access to the most basic essential medicines

essential medicines, taking steps to ensure affordable prices, increasing sustainable financing, and strengthening reliable supply systems.

- How to find new ways to promote the development of new medicines and vaccines to treat diseases of poverty.

The World Health Organization (WHO) estimates that a third of the world's population lacks access to the most basic essential medicines, while in the poorest parts of Africa and Asia this figure climbs to one-half (WHO 2000f, WHO 2000a). WHO has also estimated that, in Africa and Southeast Asia, prompt diagnosis and treatment with appropriate medicines could save approximately 4 million lives annually (DFID 2004b). Moreover, it is often the poorest who are paying the highest out-of-pocket expenses for medicines because the public sector in developing countries is unable to provide affordable medicines reliably. Medical insurance schemes cover less than 8 percent of the population in Africa (WHO 2004a), and these schemes may not cover prescription medicines on an outpatient basis. Consumers often judge health systems primarily by whether or not they get medicines when they seek treatment. Participatory assessments during national poverty reduction strategy processes often find that the availability of medicines is a primary indicator of the effectiveness of healthcare delivery.

Though access to essential medicines has improved in recent years, WHO reports that delivering "the right medicines to the people who need them at the time they need them remains a major challenge" (WHO 2004a). The analysis contained in the WHO's 1999 *World Medicines Situation* showed that roughly two-thirds of the world's population have regular access to essential medicines, up significantly from 1975, when this proportion was just under one-half (WHO 1999). However, global population growth has meant that the absolute number of people without access has remained nearly constant, at approximately 1.7 billion.

The lack of access to medicines in most developing countries reflects both the lack of sufficient incentives for the development of new medicines to target those communicable diseases that disproportionately afflict the poorest countries, as well as the inability to pay for and effectively distribute those that do exist. The result is what the U.K. government has called a "mismatch between pharmaceutical needs in developing countries and the current nature of the global pharmaceutical market" (DFID 2004a, p. 14).

Tuberculosis (TB), once regarded as a receding public health problem that had become containable in the developed world, provides a clear example of the challenge of reemerging diseases (WHO 2004b). It is a well documented threat:

> [T]oday TB is making a comeback. One in three people in the world are infected with the Tuberculosis *bacillus*—they have latent TB. Normally only a small proportion—roughly eight million people per year—of these progress to the clinical disease known as active TB, in the vast majority of cases, characterized by a lung infection. Those with active

The world has the aggregate financial means to provide all people with basic medicinal treatment, but those means are not evenly distributed

> pulmonary TB are the most likely to spread the TB bacilli to others. . . . TB kills roughly two million people every year. Around 95 percent of all patients with active TB live in the developing world, where 99 percent of all TB deaths occur. Exact data are hard to come by, but at least 4 percent of all TB patients worldwide are resistant to at least one of the current first-line drugs. In parts of Eastern Europe, nearly half of all TB cases resist at least one first-line drug. Multidrug-resistant (MDR) TB, defined as resistance to at least rifampicin and isoniazid, the two most powerful TB drugs, might be spreading as fast as by 250,000–400,000 new cases each year (Dye and others 2002).[3] Their treatment relies on second-line TB drugs that have far lower efficacy and require even longer administration periods (18–24 months)—with much higher cost and much higher rates of adverse effects (MSF 2004a, p. 3).

The response to the global TB pandemic requires innovative technology: new medicines, new diagnostics, and new vaccines. It also requires innovation in the ways that new medicines are developed and made available in the regions bearing the heaviest TB burden. The Working Group on TB (one of the other working groups within the UN Millennium Project Task Force on HIV/AIDS, Malaria, TB, and Access to Essential Medicines), has identified the issue of new medicine development as a critical focus of analysis and action. The Working Group on TB recommends the following steps to increase access to TB medicines in their final report (UN Millennium Project 2005b):

- Donor agencies should increase their investments in the research and development (R&D) of new and affordable TB diagnostics, medicines, and vaccines through public-private partnerships, and in related projects such as the strengthening of clinical trials capacity in DOTS programs.
- The Stop TB Partnership and WHO should advocate for these investments to complement their access and treatment efforts. Advocacy should be based on a clear definition of the economic and social justifications of investing in new tools.
- Regulatory agencies should assist in harmonizing streamlined regulatory requirements to introduce new TB diagnostics, medicines, and vaccines.
- The network of Stop TB partners should work to ensure that new tools respond to the greatest demands of users, and should expedite testing and rollout in high-burden settings.

The most frequently cited cause of inadequate access to medicines is that individuals cannot afford them. The world has the aggregate financial means to provide all people with basic medicinal treatment, but those means are not evenly distributed (Attaran and Sachs 2001).[4] Even an adequate national financial base is no assurance that these health issues will be adequately prioritized within countries. For example, a country with very limited resources may prioritize primary education over health services; a country may make military spending

In 1999, roughly 80 percent of the global population without access to essential medicines was living in low-income countries

a priority over social sector financing; a country may fail to tackle corruption. Most developing countries demonstrate substantial internal inequalities; these can be exacerbated as they strive to fulfill repayment obligations and meet conditionalities of powerful international financial institutions, such as the International Monetary Fund and the World Bank. Finally, within the medicines sector itself, available resources may be poorly managed or misappropriated. The fact that medicines are items with a small volume, high unit value, and universal demand makes the sector susceptible to pilferage and corruption.

Definition of access to essential medicines

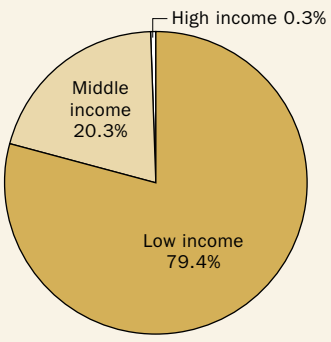
The Working Group on Access to Essential Medicines incorporated the WHO definition that provided the basis for the Millennium Development Goals indicator used to assess access: the proportion of population with access to affordable, essential drugs on a sustainable basis is the percentage of the population that has access to a minimum of 20 of the most essential drugs. Access is defined as having drugs continuously available and affordable at public or private health facilities or drug outlets that are within one hour's walk of the population (WHO 1999b). The working group qualified accessibility to apply only to products that are effective and of consistently good quality, that have no financial obstacle to a patient receiving it, and that have available the knowledge and guidance needed to use them properly.

Despite the progress made in the last decades, the likelihood of a person having access to essential medicines is still affected greatly by that person's income level. The *World Medicines Situation* found that people in poorer countries were much less likely to have access to these medicines (WHO 2004a). According to WHO, in 1999, roughly 80 percent of the global population without access to essential medicines was living in low-income countries (figure 1.1). This is a disproportionate share of the global burden, given their estimates that low-income countries account for approximately 60 percent of the world's population (WHO 2004a). In contrast, only 0.3 percent of those lacking access to essential medicines lived in high-income countries, which account collectively for about 15 percent of the world's population. In a global context,

Figure 1.1

Distribution by country income group of people without access to essential medicines, 1999

Source: WHO 2004a.



Together, India and Africa account for 54 percent of the world's population without access to essential medicines

that 15 percent of the world's population consumes 91 percent of the medicines produced (WHO 2000a). Of people living in low-income countries, nearly 40 percent did not have access to essential medicines in 1999 (WHO, 2004a).

Geographically, the lack of access to essential medicines is especially severe and concentrated in Africa and India (figure 1.2). In fact, 38 percent of the people without access to essential medicines live in India. Another 15 percent of the people without access live in African countries (WHO 2004a). Together, India and Africa account for 53 percent of the world's population without access to essential medicines (WHO 2004a). Although the disease burden and mortality from preventable or curable illness is highest in African countries, pervasive poverty means that the continent's share of the global pharmaceutical market is only slightly more than 1 percent.

India's and Africa's inordinate share of the global population without access is not entirely a function of population. India accounts for only 17 percent of the world's population. Similarly, Africa has roughly 10 percent of the world's population. This translates to very high absolute numbers of people without access in these two regions. Sixty-five percent of Indians and 47 percent of Africans lack access to essential medicines (figure 1.3), while the equivalent proportion is 14 and 22 percent in Europe and the Americas, respectively (WHO 2004a).

The lack of access to medicines throughout large proportions of the populations of most developing countries reflects both the lack of sufficient incentives for developing new medicines to target the communicable diseases that disproportionately afflict the poorest countries, as well as the inability to pay for and effectively distribute those that do exist. The result is what the U.K. government has called a "mismatch between pharmaceutical needs in developing countries and the current nature of the global pharmaceutical market" (DFID 2004, p. 14).

When examining access to essential medicines for the poor, the Working Group on Access to Essential Medicines identified a number of fundamental problems common to many countries. What is very clear, however, is that the basic knowledge and technical information already exist to increase access to

Figure 1.2

Distribution by region of people without access to essential medicines, 1999

Source: WHO 2004a.

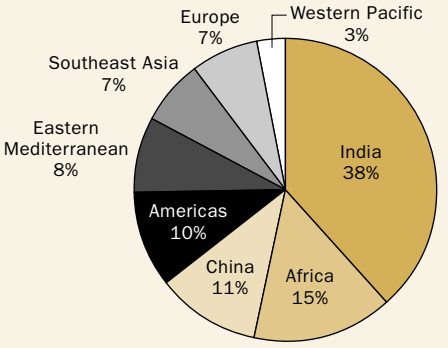
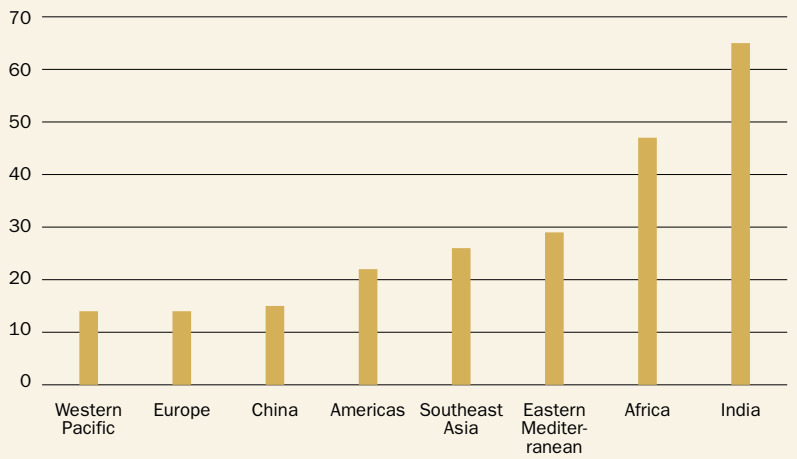


Figure 1.3

Share of people without access to essential medicines by region, 1999

Source: WHO 2004a.



all segments of a population. Furthermore, the world possesses the resources to fund adequate access to essential medicines and functioning health systems in the developing world.

Ideally the working group would have wished to propose a simple approach to improving access to medicines. Because obstacles to access are many and diverse, and because they differ in nature and degree from one country to another, this is not possible. The issues surrounding access are complex, at times culturally specific, and often fluid; the solutions can be no less. Some will need to be applied at the global level, while others need to be selectively employed in particular countries or regions depending on the situation and its context.

Overarching barriers

At the risk of overshadowing the other vital issues presented in this report, the Working Group on Access to Essential Medicines would however point to six of the most important barriers to access that merit special attention and action at this time. The first four relate to barriers to existing medicines, while the last two constitute barriers to the development of affordable and available new medicines and vaccines.

Barriers to existing medicines

1. *Inadequate national commitment* to making healthcare a priority from the national to the local levels remains one of the greatest barriers to increasing access to existing medicines. There are many reasons for this lack of prioritization. Key among them are a lack of political will by policymakers to make the needs of the poor a priority; donor programs that can skew or limit national governments' abilities to set health policy; debt servicing and conditionality for loans from international financial institutions that can further limit government responsiveness to basic social service needs of citizens; and, unfortunately, the threat of corruption that continues in the healthcare sector at all levels.

Most poor countries will require significant donor funding to achieve universal access to essential medicines

2. *Inadequate human resources* for health, including pharmacists and pharmacy technicians, is a growing problem that, if unaddressed, threatens to undermine all efforts to strengthen health systems and improve healthcare in much of the developing world. Education, information, and in-service training remain potent tools to change that situation. More needs to be done to identify what is needed to retain skilled workers, especially in the face of mounting demands for health workers, such as nurses and pharmacists, in developed countries. Retention plans and compensation schemes for countries that lose health workers should be investigated.
3. The *international community has not provided adequate finance nor consistently fulfilled its existing promises to developing countries.* Some proposed actions have not been carried out at all and others have not been carried out effectively. To achieve progress, there will be a need for political will, in both industrialized and developing countries, as well as a need for transparency on all fronts. Above all, there will be a need for increased levels of long-term financial support from the world community. It remains an unfortunate ongoing reality that some of the world's wealthiest countries remain the farthest from achieving their longstanding commitment to the international development assistance target of 0.7 percent of gross domestic product (GDP).
4. A persistent *lack of coordination of international aid* reduces access to medicines. Most poor countries will require significant donor funding to achieve universal access to essential medicines. They will also need much better aid coordination to avoid unnecessarily heavy reporting requirements and to avoid resource-wasting duplication of efforts. Sectorwide approaches should be used to promote improved coordination. Donors should commit aid that strengthens existing systems, that proactively targets the poorest and rural areas, and that avoids vertical programming by disease or by a given donor. A need exists at both the international and national levels for a great deal more transparency and coordination of effort between the large number of organizations that have already become involved in one way or another in this field. The involvement of so many bodies can and does lead to duplication of effort and to waste, and both are unacceptable. In some situations, there is every reason to merge complementary ventures. Pharmaceutical companies can and should contribute in their own particular way to the advancement of national medicines policies and the development of capacity in this field.

Barriers to the development of affordable new medicines

5. *The Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement may block access to affordable new medicines and vaccines.* After January 2005, generic production in India, the source of many vital existing medicines for developing countries without productive capabil-

WHO should be mandated to monitor the impact of TRIPS compliance by major developing country exporters on access to medicines

ities, will be fully subject to TRIPS provisions (WTO 1994). Concerns also exist that the August 30, 2003, decision reached by the WTO General Council concerning a waiver for TRIPS Article 31(f) (which would allow a compulsory license to be issued by the country in need and by the country that can produce the medicine for export) will be too cumbersome for developing countries to exploit (WTO 2003). Finally, the growing number of bilateral and regional trade agreements with major trading partners, such as the United States and the European Union, may often contain provisions that limit developing countries' use of existing flexibilities under TRIPS to protect public health (such as restrictive compulsory licensing conditions and parallel importation provisions, extended data protection, and forcing medicines regulatory agencies to take on national patent office oversight duties).

A major recommendation of this working group is for the WHO to be mandated, perhaps in coordination with the WTO or other trade bodies, to monitor the impact of TRIPS compliance by major developing country exporters and, in particular, to monitor the use of the August 30 decision over the coming two years as it concerns access to medicines. A report to the World Health Assembly and the WTO General Council, with recommendations, should be delivered no later than the end of 2007.

6. *The current incentive structure is inadequate to promote research and development of medicines and vaccines to address priority health problems of developing countries.* For a number of the most neglected diseases (such as African trypanosomiasis, Chagas disease, leishmaniasis, and dengue fever), which occur primarily in developing countries, new medicines need to be developed (WHO and IFPMA 2001). For others, new medicines are needed to address shortcomings of existing treatments, such as safety, efficacy, appropriate dosing, length of treatment, and the ongoing threat of drug resistance. Despite progress in funding research and development (R&D) for new medicines for neglected diseases, with notable contributions from philanthropic foundations and some governments and pharmaceutical companies, more financial resources need to be mobilized in a sustainable way to create a strong and sustainable pipeline of new products. New thinking, different means of financing and organizing medicines development, and other reforms are needed. For example, 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.

Finding solutions

Since the issues surrounding barriers to access have many causes, a single solution to improving the provision of medicines cannot be expected to succeed;

National medicines policy cannot succeed in isolation from broader health policies and government policies

it must be complemented by others. What this means is that every developing country should have an overall national medicines policy and strategy founded on the essential medicines concept. The aim of such a policy has been succinctly defined as existing to ensure that "safe and effective drugs of good quality are available and affordable to the entire population and that they are rationally used" (World Bank 1993). The most important step is to develop a model that meets national needs and to employ it as a basis for developing and managing the system as a whole.

National medicines policy cannot succeed in isolation from broader health policies and government policies in general. A ministry of health is unlikely to succeed in this area unless it has clear and acceptable understandings reached with other government departments dealing with such matters as finance; the training curricula for health professionals; the salaries of public employees; and practices regarding trade, taxation, and customs duties, all of which are likely to have positive or negative impacts on the supply of medicines.

Health sector strengthening and development to reach the UN Millennium Development Goals should be done in the context of the national poverty reduction strategic planning being adopted in poor, indebted countries. A recent WHO review of national Poverty Reduction Strategy Papers (PRSPs) and health pointed out that much good information is being generated about health system needs, including access to medicines, in analytical phases of the PRSP process (WHO 2004a). However, it would appear that when government responses were formulated, there was a tendency to rely on existing health policy approaches and budgets, which rarely included any community or civil society participatory processes. Instead, they tended to reflect top-down prioritization shaped by international financial institution conditions and a lack of political commitment to reorient government focus more toward the social sector. A need exists, therefore, to examine how health sector and other social sector needs can be better addressed in the poverty reduction strategy planning processes, including how information and needs assessments gained in participatory analysis can be better translated into government planning and budgets.

The goal of achieving universal access to essential medicines in developing countries will require creating and strengthening primary health systems along with the myriad specialized administrative and functional features needed to maintain a sustainable supply of all essential medicines. Firm priorities must be set, including an urgent need to reassess the importance of health sector investments by donors and recipient governments and to increase resources substantially through greater political will on both sides.

The lack of adequate and accessible pharmaceutical treatments for HIV/AIDS, malaria, and TB has received wide attention. But the problem extends to many other illnesses, and it is much wider in scope because it emerges from the failure to provide adequate healthcare overall. Poverty,

Access to medicines merits urgent study because it is a challenge that can be solved

lack of political will, social disruption, inconsistent aid and trade policies, and weak institutional supports have left poor countries with fewer tools to fight chronic, acute, and newly emerging and remerging illnesses. Overall, attention and innovation has been concentrated on diseases found predominantly in industrialized countries.

This situation—which is worst among the urban poor and the populations of isolated rural areas—has serious repercussions for human health and welfare. It will also have a profoundly negative impact on local, national, and regional economic growth and the general development of societies (CMH 2001). Widespread displacement of large populations, internal and international migration, and global exchange and commerce are features of globalization in the twenty-first century. The failure to address infectious diseases such as multidrug-resistant (MDR) TB systematically will ensure that their patterns of transmission will evolve from relatively circumscribed areas to global dispersion.

Context

Access to medicines merits urgent study because it is a challenge that can be solved (Quick 2003). Its various causes are known, and many of them can be eliminated with adjustments in government policies; economic, scientific and commercial priorities; and individual behavior with respect to medicines. These are attainable objectives, if sufficient focus is paid to them. UN Secretary-General Kofi Annan (Annan 2001) has defined a specific strategy of engagement through the framework for implementing the UN General Assembly's Millennium Declaration; this approach and others are considered in this report. It should be noted that access to essential medicines is closely linked to the achievement of other Goals and should be seen in that broader context. Table 1.1 outlines some of the main linkages between access and some of the other key Goal strategies elaborated by the UN Millennium Project.

Human right to health

The promotion and protection of human rights are principal mandates of the United Nations. The earliest global statement on human rights and health is in the WHO constitution, adopted in 1946. This includes the following relevant passages:

> The States parties to this Constitution declare, in conformity with the Charter of the United Nations, that the following principles are basic to the happiness, harmonious relations and security of all peoples:
>
> - Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity.
> - The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition.

Table 1.1

Key intersections between access to medicines and other Millennium Development Goal themes

Health systems	Consistent supplies of safe, reliable medicines are critical to the success of health interventions. Patient confidence and trust in health services are frequently and heavily influenced by the reliable availability of essential medicines at the point of care. The creation of new (and expansion of existing) primary services is required, including dispensing free or extremely low-cost medicines, with particular focus on poor people and geographically isolated communities.
Trade	Monitoring international, regional, and national trade, tariff, and intellectual property policies is required to ensure that the production, importation, and use of essential medicines is not obstructed.
Education	Education and literacy programs promote individual and collective empowerment and increase awareness of ways to prevent and treat a wide range of diseases, acute illnesses, and preventable injuries. These programs should include the appropriate use of over-the-counter and prescribed medicines. Expanded access to higher education will increase the number of healthcare workers (including pharmacists) at all levels of care.
Gender equality	Women's empowerment leads to more informed and focused demand for available treatment options. Women are often the first line of care for their families. Outreach on the safe use of medicines that is targeted to women can benefit large numbers of family and extended family members.
Slum upgrading and urban planning	Slum upgrading and urban planning improves access to general health services and disease-specific interventions.
Science and technology	Research should increasingly target the discovery and development of new and effective medicines, vaccines, and diagnostics to prevent and treat diseases associated with poverty. Improved communication technology can facilitate efficient procurement of medicines and inventory control of stock.
Energy	Reliable, sustainable, and modern energy services simplify and greatly improve the quality of diagnostic and treatment services across the healthcare spectrum.
Transport	Improved transport infrastructure reduces the cost of medicines and diagnostics and critical supply distribution. Improved geographic access, especially in isolated rural areas, will facilitate access to care. Improved transport infrastructure can facilitate movement of healthcare workers and reduce systemic obstacles to working in rural areas.

The right to health was subsequently recognized in a series of other global instruments. The Universal Declaration of Human Rights affirms that "everyone has a right to a standard of living adequate for the health of himself and his family, including . . . medical care" (United Nations 1948). The International Covenant on Economic, Social, and Cultural Rights, adopted in 1966 and ratified by 147 states, and other international and regional treaties recognize "the right of everyone to the highest attainable standard of physical and mental health" (UNHCHR 1966). In May 2000, the Committee on Economic, Social, and Cultural Rights specifically elaborated that Article 12

By 2001, all 193 countries in the world had signed at least one international or regional treaty that confirms the right to health

of the covenant included the right to essential medicines (WHO 2002a; Hogerzeil 2003). In 2002, the International Guidelines on HIV/AIDS and Human Rights (OHCHR and UNAIDS 2002) were updated to address the right to medical treatment, including access to medicines, as a specific right.

The right to healthcare facilities, goods, and services mentioned in the covenant includes a right to appropriate treatment of prevalent diseases, preferably at the community level. The covenant provides for progressive realization of the right to health and acknowledges the limits of available resources. It states that parties have an immediate obligation to guarantee that the right to health will be exercised without discrimination of any kind, and to take deliberate and concrete steps toward its full realization, with emphasis on vulnerable and marginalized groups such as children, women, and elderly people. By 2001, all 193 countries in the world had signed at least one international or regional treaty that affirms the right to health; more than 90 countries have included it in their national constitutions.

Increasingly, there is a consensus that human rights should incorporate the ability of individuals to maintain and restore good health through access to at least a basic level of primary care, including essential medicines. WHO, the World Bank, and major international development NGOs all promote rights-based approaches to poverty reduction and health development. However, the right to health is not reflected in the current global situation, in which entire populations—particularly the poor and underprivileged—commonly have little or no access to essential medicines or other basic health services.

Role of gender and women's status

At various points in this report it will be necessary to consider the extent to which gender issues affect drug access.[6] Understanding why more women and girls are infected with and affected by HIV and AIDS, comprehending the fact that many women do not and cannot seek treatment or buy medicines for their illnesses, and even explaining the manner in which medicines ordinarily enter the home, demands a consideration of the role of gender and the need for change in its construction. No health intervention can be completely successful without gender analysis of the problem and—crucially important—adequate translation of that analysis into strategies, financing, and implementation.

Gender analysis involves a systematic examination of the socially constructed roles played by women and girls and men and boys, and the power relationships arising from and reinforced by them. It includes looking at the division of labor, productive and reproductive activities, and access to and control over resources and benefits, and examining the socioeconomic and environmental factors that influence women and girls and men and boys differently. Such an analysis requires gender-disaggregated data (such as sex as an independent variable and information on how labor is divided and valued). Gender analysis

In India and China, 75 percent of those without access to essential medicines are women and children

takes into account the variable and intertwined factors of race, class, ethnicity, sexual preferences, and age.

Gender analysis also takes into account a woman's role in the household. "According to the World Bank, women, although they are not recognized as health care workers, are in fact responsible for between 70 and 80 percent of all health care provided in developing countries" (Bisilliat 2001, p. 17). This role extends to the use of medicines in the home. Yet within a household, women responsible for family healthcare and decisionmaking about care often do not control household money, so they may not be able to access needed finances to get transport to a facility or pay for treatment. In some societies, they may not be allowed to seek treatment unescorted by a male family member, which is a constraint on treatment-seeking behavior. One challenge that women face is that their healthcare needs differ from those of men and boys because of their reproductive roles. One aspect of gender inequality is that women may be limited to accessing only those healthcare services directly related to maternity or childcare. This neglects a broad spectrum of life-span health issues that will also arise.

The inequality between women and men has never been more starkly evidenced than by the link between violence, economic deprivation, social roles, age, and the risk to women and girls of being infected with HIV. The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that 58 percent of adults infected with HIV in Sub-Saharan Africa are women (UNAIDS 2002). UNAIDS has highlighted the urgent need to tackle women's inequality and to have gender-sensitive health responses if progress is going to be made against the pandemic. A gender-blind HIV and AIDS intervention is assuredly a key indicator for failure. AIDS has stretched traditional caregiving roles to the very limit. Notably, HIV-positive women retain this responsibility, even when they themselves are sick.

Concerted efforts must include increasing access to treatment for girls and women. According to WHO, of the 50 percent of the populations that do not have access to essential medicines in Africa and Asia, 75 percent are women and children (Bisilliat 2001, p. 17). According to a survey of antiretroviral medicines use by Oxfam in Uganda (Oxfam 2002), "Women are severely disadvantaged in gaining access to this life-saving treatment." The survey showed what has been well established concerning other health decisions: if choices have to be made, women are denied access in deference to others in the family. Poverty and this household discrimination explain why many women are not tested, even when the partner is HIV-positive. It is accepted that they would not be treated, even if their status were known. The Oxfam report provides a useful example of the untenable choices people are forced to make every day:

> John, a local fisherman near Kampala, has felt much better since he started antiretroviral therapy. He can work and provide for his family. John's wife has also recently been diagnosed with HIV. "I do not have the money to

pay for medicines for both of us." If he pays for his wife, his children cannot go to school and "they will not have a future" (Oxfam 2002, p. 2).

Recent WHO country-level surveys of the pharmaceutical sector show that inadequate labeling is a problem, especially in rural areas, in a number of countries. Illiteracy rates in developing countries normally are higher for women, due in large part to the discrimination against girls in accessing education, especially in poor households. So even with proper labeling, the inability to read the instructions can create a health risk. Moreover, illiteracy means that broad campaigns using printed medical educational materials will be of no practical use to the most vulnerable populations.

Medicines policies and programs at country level need to be gender responsive. This means that they must be based on an adequate gender analysis that informs strategies, plans, and budgets. It means that women must be consulted and substantively involved in health sector planning. For example, the revision of essential medicines lists should include, at a minimum, the recommendations from the United Nations Population Fund (UNFPA) and WHO for contraceptives (box 1.1).

Box 1.1

Essential reproductive health medicines and supplies

Source: Adapted from UNFPA and WHO 2003.

UNFPA and WHO have collaborated on a list of drugs and commodities to be procured for key needs in the area of reproductive health.

The list addresses various needs to provide:

- A full range of contraceptives (such as hormonal methods, intrauterine devices, barrier methods, and subdermal implants).
- Maternal and neonatal healthcare commodities (anesthetics, analgesics, antibacterials, anticonvulsants, antiseptics/disinfectants, oxytocics, vaccines, and vitamins, among others, including equipment for emergency obstetric care).
- Reproductive tract infection commodities (diagnostic tests and first-line drugs).
- HIV prevention commodities (male and female condoms and drugs to prevent mother-to-child transmission).
- General equipment and supplies for providing primary and secondary healthcare (sterilizing equipment, lighting, anesthetics and their equipment and supplies, oxygen, postoperative medication, operating theater equipment, ward equipment, drugs for gastric acidosis, muscle relaxation, and anaphylaxis, and cholinesterase inhibitors).

The list of essential drugs and other commodities for reproductive health services concentrates on those drugs that are necessary at the primary healthcare level. The appendixes provide detailed specifications. However, for certain components of reproductive healthcare, most notably maternal care, it is absolutely crucial that services are accessible at the first referral level and the necessary commodities for this level have also been included where appropriate. The list is not intended to be comprehensive; however, it includes those items that are most important for providing the core components of reproductive health primary care.

The list is principally intended for people involved in planning and implementing reproductive health programs, including program managers and development assistance agencies and organizations.

In purely economic terms, the return on investments in essential medicines is substantial

Essential medicines lists should not be gender blind. For example, the WHO model essential medicines list includes only condoms, without mention of female versus male condoms or sizes. Nor should essential medicines lists or procurement policies exclude treatments for women based on political, cultural, or religious perspectives of policymakers (such as contraceptives or medical abortifacients). National medicines policies need to recognize and reflect gender analysis in policy formulations. Monitoring and evaluating health policies(including medicines policies) should have both sex- and gender-disaggregated indicators.

To help meet the Millennium Development Goals, all parties engaged in developing new medicines needed to fight diseases of poverty should ensure that these processes and the medicines that result from them are gender responsive. For example, contraceptive implants (provided they are safe), can protect women who might be beaten by partners who knew that they were using family planning. A fixed-dose combination antiretroviral increases ease of compliance, thereby reducing fears of one's status being exposed in the family or community. More needs to be known about the differential responses to medicines based on biological differences between women and men. Research methodologies and clinical trials need to be gender responsive.

Economic dimensions

The investments needed to ensure access to medicines for all are often portrayed as an insurmountable hurdle. In fact, since essential medicines alleviate the burden of disease and reduce morbidity and mortality, universal access to them would yield significant and measurable economic returns through improved health outcomes. When assessing the merits of a particular project to improve health, the costs of resolving access barriers can often be set directly against the anticipated or proven returns in terms of the amount saved on healthcare and disability. In purely economic terms, the return on investment is substantial (Rankin 2003). Viewed in this way, essential medicines more than pay for themselves. The World Bank's pioneering report *Investing in Health* delineated the economic effects of improving the health of populations, and some of the most striking examples it provided related to medicines and vaccines (World Bank 1993).[7] The loss of disability-adjusted life years in Sub-Saharan Africa in 1990 alone totaled 7.4 million years for TB and 16.1 million years for malaria, both diseases, in principle, being curable by medication. Treatable childhood diseases, such as polio, measles, and pertussis, account for 5.2 percent of disability-adjusted life years in high-mortality, low-income countries (WHO 2002g), even though vaccines for these diseases have existed for at least 50 years.

A study of TB in Eastern African countries showed that the cost per life-year saved was between $1 and $3. Improving people's health and prolonging lives translate directly into gains in worker productivity, improved use of natural resources, reduced costs of medical care, and other economic benefits,

The amount that a country spends on medicines ought to be decided in a manner consistent with clearly articulated health policy priorities

some of which are directly measurable (Brazil, Ministry of Health 2001).[8] Out-of-pocket costs of medical treatment, including medicines, combined with loss of work due to illness, frequently reduce disposable incomes and deepen levels of poverty (CMH 2001).[9]

In the poorest developing countries, the money to fund health services and to provide medicines is simply not available.[10] Moreover, in these countries, donor support underpins substantial portions of national budgets. In Uganda, for example, donor financing accounts for 52 percent (see also appendix 1). For these countries, the inescapable fact is that increased donor support will be required to provide even a minimally sufficient primary care package.

However, some developing countries have aggregate national resources sufficient to meet all the primary healthcare needs of their citizens, yet non-health priorities are given precedence. The WHO Commission on Macroeconomics and Health (CMH) demonstrated that many middle-income countries already have the internal resources needed to raise the level of financing for a minimum universal package of health interventions, including access to the most essential medicines. For others, including many in Sub-Saharan Africa, significant additional donor funding will be required to provide a minimum package (CMH 2001).

The amount that a country spends on medicines ought to be decided in a manner consistent with clearly articulated health policy priorities. Actual per capita outlays on medicines can—and should—differ from one country to the next. For the poorest, most heavily indebted countries, an expedited, expanded system of debt relief will prevent the added value of additional donor support from disappearing into the quagmire of effort to meet impossible loan repayments. Once a country has advanced on the road to development, the key issue will be one of efficient allocation, balanced by the exercise of political will and the empowerment of ministries of health.

Cultural dimensions

There are culturally based differences between and within countries that will determine access to medicines and the utilization of healthcare in general. In addition to gender issues, other culturally specific factors include class-mediated relationships; patient and physician compliance; traditions of authority, dominance, and resistance; variable degrees of illness stigmatization; ethnicity; generational shifts; and culturally mediated perceptions of illness, health, and healthcare interventions. The history of a community also plays a major role in determining how access might best be supported.

Increasing the availability of essential medicines in settings in which biomedical treatments have been either absent or only nominally available carries the responsibility of providing appropriate training and educational resources to both healthcare providers (including pharmacists and pharmacy technicians) and the public. The commercial advertising and promotion of medicines

The role traditional medicines play in complementing Western medicine is often overlooked in discussions of access

differs both in its approach and in its effects from one culture to another. It calls for regulatory vigilance in regions that have not previously been exposed to these commercial pressures and have therefore not had an opportunity to develop a critical approach to them. Regulations, prescriber practices, dispensing systems, and patterns of home use must also be part of an evaluation of prescribing and consumption practices.

The case study in appendix 1 on access to medicines in Uganda provides a snapshot of this issue's intersections with poverty. By providing a context to the issue of access to medicines within the larger socioeconomic frame in which it is occurring, the case study seeks to demonstrate the interrelated nature of the obstacles and challenges facing Uganda today and to propose some solutions targeted to addressing access to medicines.

Traditional medicines

The role traditional medicines play—and could play in the future—in complementing Western medicine and relieving the burden on the health services has often been overlooked in discussions of access. Many developing countries have a rich flora and a long tradition of using these plants to prepare medicinal products. In these same settings, a large proportion of the population relies heavily on traditional practitioners using their knowledge to make and provide natural medicines. Traditional healers commonly enjoy a greater degree of popular trust than the official health services and often provide care to those unable to provide monetary payment; payment in kind is often the standard. There seems little doubt that many of the remedies used in traditional medicine have at least symptomatic and sometimes curative value. Some, ranging from digitalis to vinca, have in the last two centuries been assimilated into Western biomedicine for this reason. The fact that traditional healers are trusted enhances their ability to provide support and relief (WHO 2002d).

Beyond a fairly extensive study of traditional Chinese medicine, there has been little in the way of comprehensive attempts to examine traditional herbal medicines and identify new therapeutic opportunities that could be exploited in biomedicine. Some major pharmaceutical companies do from time to time examine the possibility of identifying new active substances on the basis of indigenous remedies, but it is not clear to what extent such efforts are productive compared with other approaches to innovative research.[11] Many substances of plant origin, once isolated and tested, prove to be similar to others already in use in a medicine, so that their further development is not justified. The effectiveness of traditional Chinese medicine (and many current indigenous systems) is based as much on a philosophical and cultural ethos as on specific natural ingredients. The efficacy of these treatments cannot be completely evaluated within the biomedical positivist model, yet no new methods to evaluate them have been developed that accommodate this holistic approach to medicines and therapies.

A large number of international organizations are committed to pressing the case for improved access to medicines

WHO has promoted a positive approach through its traditional medicines program, now closely associated with its main essential medicines activities. The "Global Strategy for Traditional and Complementary Medicine 2002–2005" (WHO 2002d) was released in 2002. The objective of the strategy is to discuss the role of traditional medicine in healthcare systems, the current challenges and opportunities, and WHO's role and strategy for traditional medicine. In a statement that accompanied the release of the document, WHO recognized that the use of traditional medicine is quite different from country to country and region to region. For example, in the African and Western Pacific regions, the member states consider that traditional medicine is a priority for healthcare in their regions, but in other parts of the world, traditional medicine is treated as complementary or alternative medicine (WHO 2002d).

Both patients and healers often have a clear understanding of the appropriateness of biomedical or traditional therapies for specific illness symptoms. The critical issue becomes the extent and quality of access to biomedical health services and supplies when traditional remedies do not exist to treat a specific disease such as AIDS or TB adequately. The belief that indigenous people will consistently first seek traditional modalities and the assumption that these patterns emerge from local (and immutable) systems of belief, rather than from economic and geographic exigencies, must be viewed with critical caution.

Unjustified assumptions about costs and the prospect of savings must be avoided. For example, herbal medicines prepared by patients or their families from the local vegetation may be available at negligible cost. However, the complexity of this issue is illustrated by the fact that people will often pay more for the services and medicines of a traditional healer than they would pay to seek biomedical treatment. This draws attention to the importance of understanding and trust between patients, their families, and practitioners. It also frequently shows the need for culturally appropriate communication and approaches to interventions.

Overview of major actors

A broad spectrum of specialties, interests, and levels of engagement have characterized international responses to access to medicine issues in recent decades. From issues of safety, quality, and efficacy to those of financing, infrastructure, and human resource needs, increasing attention has been paid to the complexities of getting the medicines from the manufacturer to the patient. Behind the scenes, the focus is on the R&D of new medicines and vaccines.

Today a large number of international organizations of various types are committed to pressing the case for improved access to medicines or working to bring about progress. There is a concern that these groups are in a sense competing with one another and with established donor agencies for funding. The emergent AIDS Medicines and Diagnostics Facility within WHO, if it develops as anticipated, may provide a model for coordinating efforts, as could

It is difficult to obtain a clear overview of the current levels of assistance for medicines because of a lack of coordination and transparency

the existing interagency coordination group for pharmaceutical issues (Boatin 2003; IAPCG 2000). The Global Drug Facility (GDF) was an initiative developed and implemented in 2001 by WHO, the Global Partnership to Stop TB, and the governments of 20 high-burden TB countries. The GDF, originally funded by the Canadian government, funds and facilitates movement of high-quality, generic anti-TB medicines into the countries most in need of them.

The CMH and agencies working on health in developing countries have been consistently recommending a drastic increase in the levels of aid provided for health in poor countries. The working group strongly agrees, but notes that it is difficult to obtain a clear overview of the current levels of assistance for medicines because of a lack of coordination and transparency among and between all of the major actors in this effort (CMH 2001; Troullier and others 2002).

Multilateral agencies

This section provides a brief history of efforts to improve access to medicines and some of the national and international institutions that began and developed these initiatives. The recent advent of public-private initiatives to address health and medicines challenges are also highlighted. Donation programs are considered in their own section. Although these actors should be congratulated for all they have done to bring medicines issues to the forefront in countries and in international forums, much remains to be done to make a substantive and lasting difference.

World Health Organization. Created in 1946, WHO limited its involvement in the area of medicines during its first quarter century to purely technical issues, particularly standards of manufacturing and quality control (Quick 2003). In the mid-1970s, then Director-General Dr. Halfdan Mahler introduced a broad change of policy in the organization as a whole, directing it toward improvement in basic health services and coverage; the concepts of "Health for All" and reliance on primary healthcare were introduced. To some extent this change in policy was a reaction to demands advanced by the growing membership of newly independent developing countries (Lunde 1984). In 1975, WHO introduced the Essential Drugs Concept as one of the basic components of primary care. Essential medicines were initially defined as "those considered to be of utmost importance and hence basic, indispensable, and necessary for the health needs of the population. They should be available at all times, in the proper dosage forms, to all segments of society" (WHO 1977). Expanded and revised, but not essentially different, definitions were adopted a quarter of a century later, in 2002 and 2003 (Laing and others 2003).[12]

Following the introduction of the concept of essential medicines, WHO went on to detail which specific medicines were safe, cost effective, and affordable, with particular consideration given to meeting the most pressing needs of the developing world. This approach led to the publication of the first model list

The WHO has become closely involved in measures to promote the appropriate use of medicines

of 224 essential medicines in 1977, largely based on similar lists developed in countries ranging from Papua New Guinea to Cuba to Mozambique. The WHO list was explicitly intended to serve only as a model for member states, and many national lists developed since that time have closely adhered to it. The model list has undergone regular review and revision, but it has only gradually expanded in size. The principal difference today is that a number of recently developed medicines, still under patent protection, have been included where they represent important innovations, notably in the treatment of AIDS. The list is now complemented by the existence of a model formulary providing basic prescribing information for all of the medicines listed on the model list (WHO 2003b).

The increasing need for medicines policies within developing countries by other UN organizations, notably the United Nations Industrial Development Organization (UNIDO), the United Nations Conference on Trade and Development (UNCTAD), and the United Nations Children's Fund (UNICEF), led WHO to create its own Action Program on Essential Drugs in February 1981. This expanded program forms the primary component of what is now the WHO Department of Essential Drugs and Medicines Policy.

The WHO has become closely involved in measures to promote the appropriate use of medicines (WHO 2002c) and has development standards in many fields, such as tools for developing national medicine policies (WHO 2002d); means of measuring medicine utilization and needs (WHO 1988, 2000f; Dukes 1993); and informative aids to critical procurement (MSH and WHO 2000). Training courses for national staffs are also provided in relevant areas. In these and other matters relating to pharmaceuticals, WHO currently works closely with a series of other global organizations, including UNICEF, UNCTAD, UNFPA, UNAIDS, and the World Bank, while an interagency coordination group for pharmaceutical issues has operated for several years (IAPCG 2000).

In 2001 the WHO, in collaboration with UNICEF, UNAIDS, and UNFPA and supported by the World Bank, started the Pilot Procurement Quality and Sourcing Project (known more commonly as the prequalification project or scheme[13]) for antimalarials, anti-TB medicines, antiretrovirals, and HIV and AIDS diagnostics. One of the most important achievements of this project was to standardize the criteria for assessing the pharmaceutical product dossiers and site inspections used by the participating UN agencies. Using a voluntary process, an increasing number of priority medicines for AIDS, TB, and malaria are now being assessed by the WHO and a team of international inspectors for their compliance with these standards. A list of prequalified products is published and updated every two months; some products have also been delisted on the basis of additional information. Although not intended for this purpose, the World Bank, the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), and many national procurement agencies are increasingly considering this information in their procurement decisions.

In 2003, the WHO announced the 3 by 5 Initiative to expand antiretroviral treatment for AIDS to 3 million people in developing countries by 2005

On World AIDS Day 2003, the WHO announced the 3 by 5 Initiative to expand antiretroviral treatment for AIDS to 3 million people in low- and middle-income countries by 2005.[14] As part of this effort, the WHO has established the AIDS Medicines and Diagnostics Facility, which aims to improve the supply of quality, effective HIV/AIDS diagnostics and medicines in developing countries. The World Bank and the GFATM increasingly rely on the WHO prequalification scheme or registration in Pharmaceutical Inspection Cooperation Scheme countries to identify good-quality medicines for AIDS, TB, and malaria.

World Bank. The World Bank has been significantly involved in medicines policy, procurement, and supply in low- and middle-income countries for many years. A pharmaceuticals group operates within the Health Systems Development component of the Health, Nutrition and Population department. According to a strategy paper on World Bank pharmaceutical policy and financing published in 2000, the focus of the bank's activities in medicines should be in the following areas: pharmaceutical sector reform; comprehensive national pharmaceutical sector assessments during project development in the health, nutrition, and population lending sector; support for greater transparency and accountability in pharmaceutical lending activities; lending that promotes policy and systems development and targets the poor; use of public-private partnerships to promote access to new essential medicines for the poor, including increased use of the private sector as a technical resource; and increased incentives for R&D aimed at diseases of the poor. The World Bank is a member of the Interagency Pharmaceutical Coordination Group, along with UNAIDS, UNFPA, UNICEF, and WHO. The Multi-Country AIDS Program (MAP) is the bank's long-term (12–15 years) program to scale up existing interventions to fight the AIDS pandemic. MAP projects include medicines procurement and supply. The bank recently published a very useful technical guide to HIV/AIDS medicines procurement (Taylor 2004). Among other relevant information, the guide promotes pro-generics procurement approaches and WHO prequalification, and offers important information for improving procurement, supply, and distribution of medicines in developing countries.

Global Fund to Fight AIDS, Tuberculosis, and Malaria. The GFATM was created as a pioneering financing mechanism for country-level efforts to combat AIDS, TB, and malaria. It is the largest health-related public-private partnership. It is an independent entity, governed by a board of directors that includes representatives from donors, the UN, civil society, and the private sector. Following an approved, focused application process, fund money can be used to purchase medicines to address any one or all of these three major diseases. The fund contributes to key access needs in two ways. First, it provides needed financing for medicines purchases that countries otherwise could not afford.

A number of bilateral agencies have been particularly important in funding related to medicines

Second, it has laid down very specific criteria for countries to meet concerning procurement, supply, and distribution of medicines to help ensure that quality medicines are bought and that those medicines get to the people who need them. It is hoped that these requirements will serve as a catalyst for governments to improve their current regulatory, procurement, supply, and distribution systems, all of which are key to improving access to medicines for the entire health system. A major problem, as noted by many public interest nongovernmental organizations (NGOs), recipient governments, and the fund management itself, is the continued failure to receive adequate donor financing, sometimes despite donor promises for funds.

Bilateral donors

All donor support to the health sectors of developing countries is necessary and appreciated. However, current funding is falling far short of what is needed. For example, Médecins Sans Frontières (MSF) estimated in 2002 that donors had pledged just 8 percent of the estimated funding needed to scale up the global response to AIDS. As mentioned above, the GFATM remains seriously underfunded. The WHO 3 by 5 Initiative is not adequately resourced. According to the UN Millennium Project Working Group on Malaria, the estimated funding needs to deliver antimalarial combination therapies is $300–500 million per year in Sub-Saharan Africa alone.

Within the bilateral donor community, a number of agencies have been particularly important in funding related to medicines, either by the size of their funding allocations, their prioritization of medicines issues and provision, or both. All bilateral donors that have significant commitments to health development strongly support the development and launch of effective AIDS treatment plans in all countries that need them. For example:

- The Danish International Development Agency (Danida) has a long history of supporting the establishment of essential medicines programs and strengthening medicines regulatory and supply systems. This longstanding commitment is under pressure, though. Since 2001, the government has been adopting a much more conservative approach to development aid.
- The U.K. Department for International Development (DFID) has a well-rounded aid program for medicines. It has just launched a new major commitment to increasing access to essential medicines (DFID 2004b).It is the second largest bilateral contributor to the GFATM. DFID money can be used to purchase medicines in national programs.
- The Dutch Directorate General for Development Cooperation (DGIS) is also a large contributor to international and national organizations, including WHO and many NGOs, for activities related to medicines. Over the last 15 years, it has been the largest cumulative contributor to the WHO Department of Essential Drugs and Medicines Policy. DGIS

Foundations have played leading roles in public-private initiatives for medicines and vaccines development

been a major supporter of efforts to improve the quality of medicines information, including medicines promotion and improving methodologies for collecting and analyzing medicines prices.

- The Swedish International Development Cooperation Agency (Sida) has provided similar health systems support in Southeast Asian countries, such as Lao People's Democratic Republic and Viet Nam, as well as selected countries in Africa, such as the setting up of the first essential medicines program in Angola in the late 1990s.
- The U.S. Agency for International Development (USAID) will certainly have an impact on access to AIDS treatment in the 15 developing countries it selected to receive funding from the $15 billion President's Emergency Plan for AIDS Relief (PEPFAR). Already the plan has sparked tremendous controversy by initially forbidding PEPFAR money to be used to purchase generic fixed-dosed combination antiretrovirals. In response, the U.S. government has initiated a special U.S. Food and Drug Administration approval process for generic medicines produced outside the United States. This move was adopted by the United States in lieu of the WHO prequalification project for antiretrovirals, TB medicines, and antimalarials. WHO prequalification standards are stringent and include regular quality monitoring, as well as prompt notification when a medicine is removed from the prequalification list.

Private foundations

Foundations that support health development also play a very important role in health funding. In particular, foundations have played leading roles in public-private initiatives for medicines and vaccines development. A few examples relevant to a discussion of access to medicines include the following organizations:

- The Bill and Melinda Gates Foundation has health as a major focal area in its strategic funding efforts. The Gates Foundation promotes the public-private initiative model. It has made large contributions to the GFATM, as well as to initiatives to promote the development of new medicines and vaccines. The foundation provides funding to the WHO 3 by 5 Initiative. It is a major funder of the Strategies for Enhancing Access to Medicines program at the U.S.-based consulting firm, Management Sciences for Health (MSH), which supports local public-private initiatives and public health–oriented private sector interventions.
- The William J. Clinton Foundation was responsible for a breakthrough in antiretroviral benchmark pricing in 2003. The foundation was able to secure agreements from manufacturers to supply selected countries with antiretrovirals for $140 per person per year (which is roughly half of the previous lowest price for treatment in developing countries). However, the arrangement has stringent conditions, including a three-year,

Because of severe problems of affordability in poorer countries, the role of nonprofit wholesale suppliers is very important

noncancellable contract; demonstration of purchaser financing to pay for supplies over the three years; and very high purchase volumes with each order. The arrangement demonstrates the important role that ensured demand and payment can play in setting delivery prices. The extent to which purchasers, often developing country governments that rely on donor financing that is not administered in a manner amenable to such arrangements, can avail themselves of these agreements and at what scale remains to be seen.

- The Rockefeller Foundation for several years has provided support to promote research and discussion in the area of access to essential medicines. It been a key player in the product development initiatives of the Global Alliance for TB Drug Development (GATB) and the Medicines for Malaria Venture (MMV). It has funded a policy series initiative on access to affordable medicines, bringing together leading experts for policy discussions in workshops at its Bellagio center. It is one of the funders of the WHO–Health Action International (HAI) pricing survey methodology initiative.

Supply organizations

Because of the severe problem of affordability in poorer countries, the role being played by nonprofit wholesale suppliers is very important. Supplies are obtained from low-cost sources, including research-based pharmaceutical manufacturers, and are distributed to developing countries either directly or through development finance programs.

- The International Dispensary Association (IDA), based in the Netherlands, has been supplying quality (mainly generic) medicines to governments and other public or nonprofit sector clients in developing countries for more than 30 years. Its routine publication of drug price lists has increased market transparency to the benefit of procurement specialists seeking the best return on their (often limited) budgets.
- Missionpharm in Denmark primarily supplies missionary health organizations.
- UNICEF Supply Division maintains a global warehousing and supply system to deliver medicines to developing countries at favorable prices. They engage in direct negotiations with manufactures and suppliers to secure patented or generic medicines at highly favorable prices to developing countries.

Emergence of a global access to medicines advocacy campaign by nongovernmental organizations

No single NGO can be credited with having first recognized and tackled the size of the access to medicines problem. The Consumer Project on Technology (CPTech), a public interest group founded by Ralph Nader in the United

No single NGO can be credited with having first recognized and tackled the access to medicines problem

States, was one of the first NGOs to recognize that TRIPS was going to have a negative impact on public health. Soon after TRIPS came into effect in January 1995, it launched a project focusing on TRIPS and healthcare, with specific concerns about the impact of TRIPS on medicines prices.

By 1998, HAI, a public interest network working exclusively on medicines issues, became actively engaged on a regular basis with the issues of intellectual property and access to essential medicines. HAI and CPTech were influential in pressuring the WHO to address the impact of TRIPS on access to medicines in the World Health Assembly in May 1998. The intense fight over language about trade and medicines in the proposed WHO Revised Drug Strategy foreshadowed what was to happen with intellectual property, the WTO, and access to medicines. The outcome eventually allowed the WHO to assume a more central role in gathering information and informing public debate about access to medicines and intellectual property issues.

By 1999, MSF, having just won the Nobel Peace Prize and deciding to devote the prize money to finance a global access to medicines campaign, became the de facto leader in the access movement, joining CPTech and HAI to organize a large conference on access issues just prior to the WTO ministerial meeting in Seattle. In 2000, Oxfam also launched a major access to medicines campaign, and Third World Network played a key role in developing technical assistance to developing countries on how to formulate pro-public health intellectual property legislation as they become TRIPS compliant. The Kenya Coalition for Access to Essential Medicines was successful in getting pro-public health TRIPS safeguards into Kenyan intellectual property legislation in 2001.

Linking among NGO groups working on access to medicines issues, especially those focused on access to affordable antiretrovirals in developing countries, was spurred by a lawsuit by 39 pharmaceutical companies against the South African government to prevent it from enacting a new piece of medicines legislation that permitted parallel importation of medicines (parallel importation is a flexibility permitted under WTO rules). Eventually, the pharmaceutical companies withdrew their complaint, due in no small part to the impact of a global and local advocacy campaign against their position. Treatment access groups in developing countries, for example the South African Treatment Access Campaign, have become effective advocates to pressure governments to increase AIDS treatment and provide affordable medicines. A Pan-African Treatment Access Movement has been launched. MSF continues to produce valuable information for policy debates at the international level and works to increase access to medicines through its many developing country-level programs.

It is clear that the emergence of a strong and ongoing global advocacy NGO network on access to medicines, especially antiretrovirals, has been a crucial boost to everyone working to increase access to medicines in developing countries. The impact of the network has been felt especially at the international

The emergence of a strong and ongoing global advocacy NGO network on access to medicines has given a crucial boost to work on access to medicines

policy level in new ways. For example, the substantive participation of a public interest civil society voice has influenced WTO actions on TRIPS and medicines (such as the Doha Declaration on TRIPS and Public Health [WTO 2001]); helped prompt two major international commissions on intellectual property (the U.K. Commission on Intellectual Property Rights and the current WHO Commission on Intellectual Property Rights, Innovation, and Public Health); helped support an increased role for the WHO on medicines issues; and helped influence legislation and treatment policies at the country level. Strong support for generics competition, independent monitoring of medicines prices, and other valuable supply information has helped lower medicines prices, particularly for antiretrovirals. Probably most importantly, especially at the country level, has been the way in which access to medicines issues have catalyzed and empowered citizens to engage in the political and policy process in new and important ways within the health sector.

Many well established NGOs provide essential health service delivery in developing countries. Some are also involved in advocacy on health and medicines issues. However, many are not. It is important to acknowledge, then, the vital role such organizations as the Red Cross and Red Crescent, CARE, and the many ecumenical organizations such as national Christian health associations, the Medical Mission Sisters, Catholic Relief Services, and others play in providing healthcare in developing countries.

Pharmaceutical industries

Pharmaceutical industries are key actors in ensuring the availability of needed medicines. The sector is not homogenous. It can be divided most easily into two main categories: the generics industry and the research-based industry. It should be kept in mind that even within either of those categories, the companies involved vary significantly in how they respond to medicines needs in developing countries.

It is beyond the scope of this report to provide comprehensive overviews of each company. The focus here will be on the provision of medicines in developing countries and the respective roles of the industries and the issues surrounding those roles. Notably, the role of the pharmaceutical industry is probably the most contentious and complicated of any in the discussions surrounding access to medicines for the poor. The debate about the pharmaceutical industry is very often very charged and misrepresentations are made by both critics and supporters.

The challenge for this working group has been to address the pharmaceutical industry's crucial role in a way that can be balanced and yet still call on all major actors to rise to the undeniable requirement to change the way they respond to the need for medicines in developing countries. It is very likely that the scale of need will demand fundamental rethinking of how medicines and vaccines are developed and marketed. Expectations and new approaches should keep in

The generics industry is the largest supplier of medicines to the developing world

mind the fundamental nature of these industry actors: they are in the medicines business to make a profit. The extent to which pressures and realities will cause a shift to include a socially responsible component remains to be seen.

Generics pharmaceutical industry. The generics industry is, in unit terms, the largest supplier of medicines to the developing world and to countries in transition. According to WHO, in low- and middle-income countries in 2000, the generics market share was at least 50 percent; the largest low-income country generics market share was Bangladesh at 70.9 percent. It is generics manufacturers that have been responsible for ensuring the wide availability of affordable generic versions of essential medicines in developing countries. Notably, more than 90 percent of medicines listed on the WHO essential medicines list are off patent.

Historically, generics producers have concentrated on replicating originator products once they were off patent. Innovation was very limited for many reasons. However, the generics sector is changing, and more R&D is being undertaken. For example, Zithromax®, a key antibiotic now licensed to Pfizer, was discovered and developed by a Croatian generics firm that was working with a U.S. subsidiary. The National Association for Rare Diseases produced the first medicines under the U.S. Orphan Drug Act. Generics firms have developed combination antimalarials.

Many generics firms concentrate on the large-scale production of medicines at low cost, and their prices, under international nonproprietary names, are commonly only a small fraction of those charged by originator companies (International Drug Price Indicator Guide 2003).[15, 16] In the case of antiretrovirals, price competition from generics has been responsible for pressuring originator medicines prices downward, to compete comparably with them in some cases. Low generics prices are low partially because these firms do not bear R&D costs. They also reflect the fact that unit profits are usually lower and that these firms do not, as a rule, engage in advertising or promotion for their products. Furthermore, production is, to a large extent, undertaken in countries where manufacturing overhead costs are also lower.

Major generics manufacturers are quite similar in their staffing, facilities, and product quality to the staffing, facilities, and product quality of research-based companies. In fact, the largest generics manufacturer in the world, Sandoz, is a subsidiary of the giant research-based transnational company, Novartis. The best firms adhere fully to internationally recognized standards of good manufacturing practice (GMP). Some are based in industrialized countries. A number actually choose to provide their products with brand names.

Quality generics are fully equivalent to originator versions in terms of quality, safety, and efficacy and are usually less expensive. Again, it is important to stress that neither the generics nor the research-based industries are monolithic. In addition to the internationally competitive generics manufacturers

Without generics competition, the availability and affordability of key essential medicines in developing countries would suffer

there are at least two other kinds of production mechanisms that exist within the context of developing countries. In middle-income countries, such as Brazil, state-controlled generics firms produce medicines to meet national requirements. And, in low-income countries, such as Kenya or Zimbabwe, local generics manufacturers may supply the local market with essential medicines, with some form of preferential government subsidy.[17]

In recent years, research-based and generics manufacturers have pursued voluntary licensing agreements for key medicines. This avenue is one way for local firms in developing countries to produce quality medicines in cooperation with the license holder. The arrangements for this production should include technology transfer and capacity building of local staff to be sustainable.

In some cases, generics producers in low-income countries do not comply with GMP, limiting themselves to simple, high-profit formulations. These firms do not want to have to meet bioequivalency requirements, which are required for WHO prequalification for medicines to treat AIDS, TB, and malaria. This approach limits the contribution of local generics manufacturers in developing countries to compete in the markets for these essential medicines. Producers wishing to ensure quality standards can avail themselves of WHO technical assistance to meet GMP and prequalification requirements. They can also pursue cooperative agreements with larger manufacturers that can provide technology transfer and staff training.

Key achievements for the generics industry include taking the lead in providing price competition for antiretrovirals that prompted real reductions in the price of antiretrovirals offered from originator manufacturers. Before increased generic competition on antiretrovirals, originator companies set price discounts as they saw fit. While voluntarily discounted originator prices, such as those under the joint UN–Industry Accelerated Access Initiative, did lower costs from $12,000 to $2,000 per person per year in selected developing countries, the costs were still unaffordable for poor governments and for the majority of the population in need. It took generics competition to bring the price below $1,000 and eventually to $250–$300. It is clear that without generics competition and their robust involvement in developing country markets, the availability and affordability of key essential medicines would suffer.

Research-based pharmaceutical industry. The research-based industry is the dominant supplier of medicines to industrialized countries. The most significant contribution the research-based industry can make to the goal of expanding access to essential medicines is to discover and develop new medicines. Most of these companies are also fully committed to working in partnership with others to ensure that these medicines are then available as broadly as possible. Private research-based pharmaceutical companies have produced the overwhelming majority of new medicines now on the market. For example, three-quarters of medicines now on the WHO essential medicines list,

The development of medicines that target the health problems in developing countries requires innovative approaches

although discovered in the public sector, were brought to market successfully by research-based companies.

The principal characteristic of these companies is the presence of innovative research. Much of this creative work is undertaken in-house, but these companies have also been increasingly successful in drawing on the output of publicly funded academic and institutional research. In fact, research-based industry recognizes the important relationship it shares with academia and public sector research agencies. Although scientists in research-based pharmaceutical and biotechnology companies contribute significantly to basic research, it is also true that publicly funded investigators have traditionally conducted the bulk of basic biological research. However, the research-based pharmaceutical industry continues to lead in the more applied research activity that ultimately results in the discovery and development of most new medicines.

The research-based industry is headquartered almost exclusively in industrialized countries and is increasingly engaged in a series of large and generally multinational enterprises. It is highly profitable: in the United States, the pharmaceutical industry has been by far the most profitable corporate sector over the past 30 years. Although it is an industry engaged in providing vital public goods, it remains driven by its corporate mandate to maximize profits. Therefore it is not surprising that its focus is on developing products for affluent markets. As a result, the research-based industry has come under criticism for not responding adequately to medicines needs of the poor in developing countries.

However, indications are growing that research-based companies, by and large, are doing more and wish to do still more. To promote the development of medicines that target the health problems in developing countries, innovative research, development, and financing arrangements are needed. Some examples of this include recent collaborations between the WHO, industry, and other stakeholders to lower the prices of key medicines, such as antiretrovirals, and those for treatment of MDR-TB. Originator companies have also expanded public-private alliances and interactions, donation programs, and technical assistance to help fill the capacity gap. A few examples include the African Comprehensive HIV/AIDS Partnership in Botswana, where 26,000 patients receive antiretrovirals donated by Merck; Uganda's first Infectious Disease Institute built by Pfizer in Kampala to provide a training site for physicians and technicians and a laboratory for monitoring and testing patients undergoing AIDS treatment; AIDS programs initiated by Bristol-Myers Squibb in five Southern African countries that provide antiretroviral medicines, as well as inputs into health management, medical research and education, community education and outreach, and capacity-building programs for women and children. The Accelerated Access Initiative is a cooperative endeavor of seven research-based pharmaceutical companies, UNAIDS, WHO, UNICEF, the

Public-private initiatives hold promise as a way for pharmaceutical industries to contribute positively on a variety of important fronts

UNFPA, and the World Bank to negotiate price discounts for antiretrovirals and provide treatment in selected developing countries.

The research-based pharmaceutical industry has indispensable scientific expertise to help solve the problem of access to essential medicines. However, it cannot do this alone. Leadership from the global public sector (including donors, multilateral organizations, and academia) will be required to create the necessary conditions to develop medicines for priority health conditions in low-income countries.

Public-private initiatives

One of the key challenges in achieving any development goal is to effectively harness the contributions of major actors. Meeting the health needs of developing countries is daunting and complex and requires finding new ways for major actors to work together. The pharmaceutical industries have a vital role to play and resources to contribute. However, the conundrum has often been finding a framework that allows disparate public and private actors to work toward common goals successfully. The rise of public-private initiatives in recent years is a trend that holds considerable promise as a way for pharmaceutical industries to contribute positively on a variety of important fronts. Since these types of interactions are diverse and new, it will be important for all of the actors to monitor and learn from initial experiences. Initial experiences point up much hope for the evolution of public-private initiatives as an effective means of collaboration, as well as pointing out inevitable limitations to be managed.

It is important to note that the term *public-private initiatives* is not entirely straightforward (box 1.2). In addition to coming in varying shapes, sizes, and modes of operation, public-private initiatives are being created to address a range of public health needs. Global interactions relevant to medicines can be divided into four main categories:

- Public-private product development interactions, (such as GATB, MMV).
- Donations (such as Mectizan®).
- Public-private coordination or financing mechanisms (such as Stop TB and the GFATM).
- Public-private interactions for strengthening health systems (such as the African Comprehensive HIV/AIDS Partnership in Botswana).

Public-private initiatives typically comprise various combinations of international and multilateral organizations (such as WHO, World Bank, and UNICEF), philanthropic foundations, research-based pharmaceutical companies, academic institutions, bilateral donors, and NGOs. These collaborative efforts, when successful, deliver the following positive outcomes:

- Deliver critical funding.
- Draw attention to health threats that may not be widely known.
- Share knowledge and resources.
- Build the numbers needed to facilitate volume-related discounts.

Box 1.2

What are public-private partnerships?

Source: Richter 2004.

The literature on global public-private partnerships is confusing for at least two reasons. First, even though public-private partnerships have been promoted for several years, there is no one single, agreed-upon definition. Second, most discussions do not distinguish between public-private partnerships as a policy model and actual examples of public-private partnerships and interactions that have been undertaken. According to the 2003 report of the UN Secretary-General on "Enhanced Cooperation between the United Nations and All Relevant Partners, in Particular the Private Sector," partnerships are commonly defined as voluntary and collaborative relationships between various parties, both state and nonstate, in which all participants agree to work together to achieve a common purpose or undertake a specific task and to share risks, responsibilities, resources, competencies, and benefits.

Many of the relationships that are currently called partnerships are not in fact new. Researcher Ann Zammit, who reviewed UN-business partnerships extensively for the United Nations Research Institute for Social Development, remarks in *Development at Risk,* "The term [partnership] covers a multitude of activities and relationships, perhaps best conceptualised as a special case of 'close' rather than 'arms-length' relationship between government and business" (Zammit 2003, p. 5).

The three levels of analysis about public-private partnerships are often blurred because the term "public-private partnership" is used to describe

- A policy paradigm (including its underlying framework of thought and ideology).
- Various categories of public-private partnerships or interactions, such as donations of pharmaceuticals or legally independent global health alliances.
- A specific public-private partnership or interaction, such as the Malarone® Donation Programme or the Global Alliance for Vaccines and Immunization (GAVI).

It is critical to make a theoretical distinction between these three uses of the term.

- Achieve specific public health disease management objectives (such as the Global Polio Eradication Initiative).

The private sector, by its very nature, seeks interactions and investments that deliver a clear and substantial return, financially and/or through branding or expanded influence in policy spheres or markets. In theory, the private, for-profit sector can and should assist the public sector in identifying ways that progress toward the essential goal of access to medicines can benefit from private sector, competitive initiatives. Room exists to increase the pharmaceutical industries' contributions to solving the problem of access to medicines. For example, using a joint venture model as the organizing framework for an alliance permits some formal separation of the for-profit and not-for-profit activities. This is indeed the case in many agreements negotiated by public and private institutions—in particular in the area of developing new medicines and vaccines.

A 2002 report by the Bill and Melinda Gates Foundation illustrates the application of a business model in the development and operation of global health alliances (Bill and Melinda Gates Foundation 2002). The report notes that more than 80 percent of the past and present alliances that were reviewed were deemed to be successful. The authors lay out an operational framework

A public-private initiative approach appears to be particularly effective in the area of new medicines and vaccines development

for analyzing an alliance's effectiveness that includes the existence of clear and compelling goals and clear scope (as defined by geography, patient populations, functional activities, and time). Other elements such as the nature of alliance structure, agreement on success metrics, milestones, partner contributions, and sufficient number of staff are discussed (Bill and Melinda Gates Foundation 2002).

Given all of the challenges facing the world community to reduce poverty and disease in developing countries, it is very welcome that the private sector's expertise and resources can be harnessed in new ways. Research-based industry is embracing the public-private initiative approach as a way to increase their contributions substantially in programs targeted at the poor in developing countries. The Partnership for Quality Medical Donations reports that its partners contributed $1.4 billion in donated medicines in 2003. It is clear that long-running large-scale public-private initiatives for the elimination of priority diseases of poverty, which involve sustained medicines donations and collaboration with partners in management, training, and implementation, have been successful. Examples are the Merck Mectizan® donation program (for onchocerciasis and lymphatic filariasis, the latter in conjunction with GlaxoSmithKline's donation of albendazole), Pfizer's donation of Zithromax® in the Trachoma Initiative, and Boehringer Ingelheim's now open-ended donations of Viramune® for the prevention of mother-to-child transmission of HIV.

A public-private initiative approach also appears to be particularly effective in the area of new medicines and vaccines development. This is especially true for the diseases strongly associated with the consequences of poverty, including AIDS, malaria, TB, sleeping sickness, Chagas disease, leishmaniasis, Buruli ulcer, dengue fever, leprosy, lymphatic filariasis, and schistosomiasis. Below is a list of major initiatives that focus on developing new medicines or vaccines, all of which include multiple public and private actors working often in innovative ways together within the interaction:

- *Aeras Global TB Vaccine Foundation.* Aeras was founded in 1997. Since 1999 it has focused exclusively on the development of an effective TB vaccine. Formerly the Sequella Global TB Foundation, Aeras has worked closely with the Bill and Melinda Gates Foundation.
- *Drugs for Neglected Diseases initiative (DNDi).* Conceived and organized by MSF, members include research institutes in Brazil, India, and Kenya, the Malaysian Ministry of Health, and the Pasteur Institute. The WHO Special Programme for Research and Training in Tropical Diseases (TDR) is an observer. The initiative aims to develop medicines to combat neglected and most neglected diseases. Current work includes the development of two fixed-dose combination artesunate antimalarials and seven projects to develop medicines against visceral leishmaniasis, Chagas disease, and trypanosomiasis.

It is important to monitor public-private initiatives, to measure their effectiveness and learn from experience

- *Global Alliance for TB Drug Development (GATB).* GATB was formed to accelerate discovery and ensure that there are better and more affordable agents to fight TB. The alliance makes support to institutions in TB-endemic countries a priority. It works with research-based companies to identify promising substances and move them along the development pipeline.
- *International AIDS Vaccine Initiative (IAVI).* The main aim of this initiative is to support and find ways to speed up discovery and development of an effective HIV vaccine. IAVI receives major financial support from a number of major philanthropic foundations, the World Bank, and nine national governments.
- *Medicines for Malaria Venture (MMV).* MMV selects, guides, funds, and develops research done by others and works in partnership with research institutions, ministries of health, disease control programs, research-based industry, academia, and NGOs to improve the availability of safe, effective, and affordable antimalarials. Two related initiatives include the Malaria Vaccine Initiative and the European Malaria Vaccine Initiative.

Without going into detail on all product development public-private initiatives, it is worth noting the following initiatives and projects to illustrate the range of activities under way: the South African AIDS Vaccine Initiative, the International Partnership for Microbicides, the Global Microbicide Project, the Microbicide Development Project (for anti-HIV microbicides), the Institute for OneWorld Health, the Pediatric Dengue [Fever] Vaccine Initiative, the Human Hookworm Vaccine Initiative, the Rotavirus Vaccine Accelerated Development and Introduction Plan, the Pneumococcal Vaccine Accelerated Development and Introduction Plan, and the Consortium for Industrial Collaboration in Contraceptive Research.

Global public-private coordination and financing mechanisms include the Stop TB Partnership, the Roll Back Malaria Partnership, the Global Alliance for Vaccines and Immunization (GAVI), and the GFATM.

As already pointed out, public-private initiatives, with the exception of a few long-running donations programs, are relatively new and diverse. It will be important to monitor the various types, measure their effectiveness, and learn from experiences. Monitoring and further operational research should cover the more objective and quantitative aspects mentioned above as well as the following process issues:

- *Sustainability.* Public-private initiatives should have timelines and funding commitments tied to reaching public health objectives, which may take many years to achieve. They may, therefore, need to be very long term or even open ended in initial phases. Short time horizons, for example, within GAVI or for GFATM project funding (five years, with no guarantees of further funding), are often counterproductive. Even if

With the global scale of recent health sector initiatives, transparency and decision-making processes are critical

actual allocations are yearly and subject to regular review and evaluation, sustainability is enhanced when resource commitments are known and driven by health needs.

- *Power inequities.* Inherent in many partnerships or interactions is that the developing country partners have no power to insist on the continued support and participation of either the private-sector partners or the international institutions.
- *Pro-poor focus.* Public-private initiatives, which are often very complicated to manage and implement successfully, may tend to default to commitments that are the most manageable and likely to succeed rather than those that reach the greatest number in the greatest need. Principles of equity and setting as a priority reaching the poor should be at the forefront of planning, implementation, and budgeting.
- *Competing initiatives.* Multiple initiatives in a single country or region will rely on the same (often overwhelmed) health system infrastructure to identify and diagnose patients and to deliver medicines.
- *Governance and accountability.* With the global scale of recent health sector initiatives, issues of transparency and decisionmaking processes have become critical. Democratic process is not the rule, and decisionmaking often is controlled by the multilateral institutions and the private-sector participants. GAVI is one example of an interaction that has come under scrutiny on these issues (Hardon 2001). Public-private initiatives need to be accountable to intended beneficiaries as well as the public-private initiative managers and funders. At the national level, government representatives should play leading roles in decisionmaking and accountability. These roles can be difficult when the government involved is relatively weak and dependent in relation to other participants.