

# Ensuring Supplies of Appropriate Drugs and Vaccines



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In 1988, the World Health Organization (WHO) reported that 30 percent of the world's population, some 1.725 billion people, lacked regular access to essential medicines. By 1999, the 15 percent of the population who lived in high-income countries purchased and consumed 90 percent of all medicines, by value (WHO 2004f). Again as of 1999, a recent WHO report estimates that 30 percent of the world's population, including 47 percent of Africans, 65 percent of people in India, 29 percent of people in the Eastern Mediterranean, and 26 percent of Southeast Asians (excluding those from India), had no access to essential medicines (WHO 2004f). So although access has significantly improved in a number of countries, a large fraction of the world's population still has no effective access to modern medicines or vaccines. The majority of these people are either extremely poor or are living in remote rural areas where the supply of drugs is limited or nonexistent—or both.

Many diseases can be effectively treated, managed, or prevented with pharmaceuticals and vaccines. The WHO figure of 30 percent of the world's population lacking access understates the reality; even within countries with apparently good services, some populations lack access. Similarly, immunization coverage globally has remained static for more than a decade at about 75 percent of children fully immunized, with about 27 million children born every year with no access to immunization services. Some effective vaccines, such as hepatitis B (HepB), are still not in routine use in many countries.

Medicines and vaccines are developed as a result of innovation by researchers and pharmaceutical companies. The global pharmaceutical market was worth more than US\$400 billion in 2004, and more than 80 percent of this market is in North

America, Europe, and Japan. Lipitor (atorvastatin), a cholesterol-reducing drug and the world's best-selling drug in 2002, had sales of US\$8.6 billion, and growth was 20 percent annually. Zocor (simvastatin), another cholesterol reducer and the second-best seller, had sales of US\$6.2 billion and was growing at 13 percent (IMS Global Learning Consortium 2003). These figures contrast with the dearth of research on neglected diseases prevalent in developing countries. For example, of the 1,325 new medicines launched between 1975 and 1997, only 11 were specifically for tropical diseases (Trouiller and others 2002). Médecins Sans Frontières (MSF) in 1999 initiated its advocacy program, Drugs for Neglected Diseases, which has highlighted this gap (<http://www.accessmed-msf.org/>).

Access to effective medicines and vaccines requires a complex and coordinated system. It must encompass production that ensures good quality, selection, procurement, and distribution; correct prescription and dispensing and correct use by patients; adequate financing; and effective monitoring of the system. Multiple delivery systems involving public, private, and nongovernmental organization (NGO) sectors frequently coexist, and patients are very likely to use multiple systems to access these products.

## DRUG POLICIES

In any country, many stakeholders are interested in the national policy on pharmaceuticals. In broad terms, they can be characterized as producers, importers, distributors, prescribers, finance providers, and consumers. Each has a different set of

interests, which in some cases are contradictory and in other cases congruent. To reconcile these disparate interests, many countries have developed a national drug policy. Managers of disease control programs need to be involved in these discussions at an early stage to prevent policy decisions from adversely affecting their programs. Any national drug policy broadly relates to three key objectives: increasing access, improving and ensuring quality, and ensuring rational prescription and use by providers and patients.

The primary components of a drug policy are selection of essential medicines; assurance of affordability, which includes issues of pricing, taxation, generic competition, and policies related to the Agreement on Trade-Related Aspects of Intellectual Property Rights (WHO 2001a); financing options; supply systems; regulation and quality assurance; rational use; operational research and drug development; clinical research, including clinical trials; human resource development for pharmaceutical policy and program management; and monitoring and evaluation. WHO has developed manuals and has provided technical support to countries to develop such national policies (WHO 2001b, 2003a).

## VACCINE POLICIES

Every country has a national vaccine policy, usually laid down in a national health policy or through the establishment of well-defined elements of such a policy. WHO defines global frameworks and produces policy documents to advise developing countries (WHO 2002b). At the national level these guidelines may be adapted to fit national needs and capacities. Standards and norms for vaccines are also set by WHO and are generally adhered to worldwide (WHO 2003b).

WHO's creation of the Expanded Program on Immunization (EPI) in the 1970s established a policy for selection and use of vaccines that the vast majority of developing countries adopted. Only three vaccines—HepB, yellow fever (YF), and *Haemophilus influenzae* type B (Hib)—have been added since then, and the overall program directions remain largely intact.

In recent years, WHO has published a set of policy guidelines for vaccines not included in the global recommendations. These position papers are regularly updated. Three guiding principles provide the pillars for any national vaccine policy:

- Every eligible child must have equal access to nationally adopted vaccines regardless of religion, caste, or economic status.
- Vaccines require active government financial participation to ensure that they are provided and used in adequate quantities, thus ensuring the benefit of their considerable externalities. For example, the benefits to society of an individual's being vaccinated are greater than those to the indi-

vidual, because vaccination prevents transmission. It can also be argued that the elimination or eradication of a disease as a public health problem has public good characteristics: the benefits of the absence of disease are available to everyone, and all persons benefit at the same time. Therefore, governments must take an active role in ensuring that adequate vaccines of assured quality are available for comprehensive immunization programs within the country. The recent flu vaccine shortage and resulting rationing problems in the United States have illustrated this principle clearly.

- Countries should strive toward financial sustainability for the national immunization program.

A vaccine policy normally has six specific objectives:

- To provide a coordinated approach to national vaccines and equipment needs, including national vaccine production where applicable
- To provide criteria for vaccine selection and introduction, including burden-of-disease studies where relevant
- To develop a financial sustainability plan that ensures availability of vaccines in the longer term
- To define guidelines for private-public partnerships, including vaccine research
- To define national research priorities
- To support the implementation of the national immunization programs.

Policy setting is a continuous process that must keep up with global developments and changing national needs. Countries will normally formulate policies that are based on the technical work of a national committee of experts, who meet regularly under the auspices of the ministry of health. Bilateral donors and the Global Alliance for Vaccines and Immunization (GAVI) may influence policy setting, such as the timing for introduction of new vaccines, where they contribute significantly to the national immunization programs.

## SELECTION OF DRUGS

Selection of a limited list of essential medicines that should always be available is necessary both for supply officials who work on procurement, storage, and distribution and for clinicians who aim to use medicines most effectively.

In 1977, WHO defined the first Model List of Essential Drugs (WHO 1977); since then it has updated the list 14 times. The latest list defines *essential medicine* as follows:

Essential medicines are those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and

comparative cost effectiveness. Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford. The implementation of the concept of essential medicines is intended to be flexible and adaptable to many different situations; exactly which medicines are regarded as essential remains a national responsibility.

In 2003, the WHO Expert Committee on Selection and Use of Essential Medicines decided to define the criteria for core and complementary lists, as follows:

The core list presents a list of minimum medicine needs for a basic health care system, listing the most efficacious, safe, and cost-effective medicine for priority conditions. Priority conditions are selected on the basis of current and estimated future public health relevance, and potential for safe and cost-effective treatment.

The complementary list presents essential medicines for priority diseases, for which specialized diagnostic or monitoring facilities, or specialist medical care, or specialist training, or all three are needed. In case of doubt, medicines may also be listed as complementary because of their consistently higher costs or less attractive cost effectiveness in a variety of settings (WHO 2003d, 28).

At its 2002 meeting, the WHO Expert Committee changed its attitude toward fixed-dose combinations (FDCs). The committee stated that most essential medicines should be formulated as single compounds. Fixed dose combination products are selected only when the combination has a proven advantage over single compounds administered separately in therapeutic effect, safety, adherence or in delaying the development of drug resistance in malaria, tuberculosis and HIV/AIDS (WHO 2002c). This change reflected the interest in preventing the development of resistance and in promoting adherence. Although controversial, these FDC products will very likely be the main form of treatment for AIDS, tuberculosis (TB), and malaria.

The number of medicines on the WHO list has increased over time. The 2003 WHO list has 320 drugs in 559 formulations (Laing and others 2003). At country level, the essential drugs list is used as a guide rather than as a template. A study of 17 national lists of essential drugs showed that 68 percent had fewer than 300 drugs. The number of drugs per list ranged from 108 in Liberia to 389 in Karnataka state, India. Nine of the drugs on the WHO list were not on any of the 17 national drug lists in the study (Laing and others 2003).

At the first stage of identifying common diseases and complaints, managers of disease control programs are in a strong position to provide epidemiological information about the incidence or prevalence of a condition. At the second stage, the

selection of treatments would ideally have already been undertaken on the basis of available evidence or clinical trial data from the country. The medicines identified within these guidelines would thus become the medicines on the essential medicines list. This list would then serve as the basis for procurement, storage, and distribution activities. The evidence-based treatment guidelines would define treatment practices and be the basis of training (including examinations and licensing) and supervision.

## SELECTION OF VACCINES

Developing countries select vaccines used in national immunization programs primarily on the basis of WHO policy guidelines. Most countries have adhered strictly to the six original vaccines—Bacillus Calmette-Guérin (BCG), oral polio, diphtheria, pertussis, tetanus, and measles. On the recommendation of the WHO Global Advisory Group on Immunization, HepB vaccine was included in the global guidelines in 1987, and YF vaccine was added in 1988; Hib vaccine was added in 1994. These remain the only vaccines recommended by the WHO for national use, and the recommendation presupposes that a disease burden of public health importance is present (see table 72.1).

A few vaccines, such as YF and Japanese encephalitis (JE), have regional importance in accordance with the prevalence of the disease. These vaccines are used in only a small number of developing countries. WHO has not generally recommended JE, although no evidence indicates that the disease burden of

**Table 72.1** Current Vaccines Recommended by the World Health Organization

Vaccine	Age				
	Birth	6 weeks	10 weeks	14 weeks	9 months
BCG	X				
Oral polio	X <sup>a</sup>	X	X	X	
Diphtheria-tetanus-pertussis		X	X	X	
Hepatitis B <sup>b</sup>		X	X	X	
<i>Haemophilus influenzae</i> type B <sup>b</sup>		X	X	X	
Yellow fever					X <sup>c</sup>
Measles					X <sup>d</sup>

Source: WHO 2002d, 88.

a. In endemic countries.

b. Only a few African countries have been able to introduce the vaccines to date.

c. In countries where yellow fever poses a risk.

d. In addition, a second opportunity to receive a dose of measles vaccine should be provided for all children.

YF is greater than the JE disease burden. However, a safety issue exists with mouse brain–derived vaccines such as JE.

Oral polio vaccine (OPV) is the vaccine of choice in developing countries, because it is easy to administer and the protective effect spreads to close contacts of vaccinees. It is suitable for mass campaigns, so the vaccine is used in poliomyelitis eradication programs. In 2005, the monovalent type 1 OPV, for which seroconversion rates are substantially higher than for trivalent OPV, has started to be used in areas where only type 1 wild poliovirus remains in circulation.

The selection of the original EPI vaccines was made on programmatic criteria rather than on considerations of disease burden. The need for consistent and standardized regimens determined the strategies selected by EPI. Adaptations over time, as new vaccines came along and local needs changed, were slow, and the uptake of newer vaccines remains a major constraint in most developing countries, although support provided through GAVI has improved the situation.

The term *vaccine gap* is used to describe the phenomenon whereby children in developing countries receive at most eight vaccines, if they are reached by immunization programs at all, whereas children in industrial countries normally receive 10 to 12 antigens, depending on national schedules. Furthermore, two vaccines in the routine schedule in the affluent world are less reactogenic than those given in developing countries: acellular pertussis vaccine (aP) and inactivated polio vaccine (IPV). The combination measles-mumps-rubella (MMR) vaccine is normally given twice, offering long-term protection against measles and rubella, important diseases in the developing world. The vaccine gap therefore consists mainly of three vaccines—aP, IPV, and MMR.

The pneumococcal vaccine, which is currently used in some countries, illustrates an additional aspect of the vaccine gap. Its composition is directed against the most prevalent strains, which cause otitis media in children. At the same time, millions of children die in the developing world from pneumonia caused by other strains of the bacteria, but no vaccine is currently available against those strains.

## PROCUREMENT OF DRUGS

After the drugs have been selected, the next step is to decide how much to order. Usually this decision is based in part on past consumption, but it is also based on treatment guidelines and morbidity patterns. Concentrating on larger quantities of fewer drugs and dosage forms simplifies the process of ordering and reduces the chances of running out of stock. Ordering tablets or capsules rather than syrups or injections saves a great deal of money.

In 1997, when the second edition of *Managing Drug Supply* was published (Quick and others 1997), four methods of

procurement were recommended under different circumstances. These methods were open tender, restricted tender with performance monitoring, negotiated procurement, and direct procurement. At that time, the World Bank was a major funder, and many countries favored the use of open tender. However, a major shift has taken place to restricted tender based on prequalification and direct procurement from non-profit suppliers. The World Bank has produced a number of useful documents and resource materials that can be used for national procurement activities (World Bank 2000).

Another method of procurement that has been more widely used has been procurement from nonprofit suppliers, such as the United Nations Children’s Fund (UNICEF) or the International Dispensary Association (International Dispensary Association 2004; UNICEF 2004). These organizations produce price lists twice yearly, and products can be ordered directly. Management Sciences for Health (2004) publishes an international drug price indicator guide annually that reports these prices and other procurement prices. Interestingly, the trend in drug prices generally has been downward. Prices of some TB drugs fell by more than 90 percent when procurement managers opened intensive negotiations with suppliers. And since 2000, prices of many important first-line antiretroviral drugs have fallen considerably. This trend is attributable to “advocacy, corporate responsiveness, competition from generic manufacturers, sustained public pressure, and the growing political attention paid to the AIDS epidemic. In addition, originator companies began announcing discount offers for the benefit of the poorest countries or those where the HIV/AIDS prevalence is the highest” (WHO 2004d, 5). The influence of economies of scale, in which unit costs have fallen because of the increased consumption of needed pharmaceuticals, might also have played a role.

Generic drugs obtained in bulk are almost always 10 or more times less expensive than brand-name drugs. Bulk purchase of generic drugs is the single best way to make a given budget go farther to satisfy the drug needs of a population. For price comparison, international prices (ex-factory, free-on-board—that is, not including insurance, freight charges, or taxes) are available online from Management Sciences for Health (2004). Local prices must, of course, include transportation and freight, as well as any applicable local taxes. Organizations that procure drugs in bulk but then sell smaller quantities, usually to nonprofit organizations, can help smaller purchasers obtain the advantages of competitive tendering. Examples include the International Dispensary Association, which is based in the Netherlands, and the Copenhagen office of UNICEF, which is able to supply drugs at very low cost to government-supported institutions.

Recent studies have revealed just how much the local component of drug costs can be, particularly in the private sector. A survey of costs in nine countries found an average

markup of 68.6 percent, with retail markups of 16 to 50 percent comprising the largest single component in most cases. In countries that charge a value added tax on drugs, the tax can add 15 to 20 percent to the price of the drug (Levison and Laing 2003). Many of these cost elements are within the control of national policy makers.

Finally, when considering a change of standard therapy, managers of disease control programs need to take into account the long lead time between ordering a particular drug and having it arrive in the country ready for use—which can be a year or more. Time will also be required to prepare, print, and disseminate new guidelines, to train prescribers and dispensers, and to dispose of drugs used in the older therapy (Williams, Durrheim, and Shretta 2004).

## PROCUREMENT OF VACCINES

Countries can be grouped into three categories according to the way they procure vaccines: procurement through United Nations (UN) agencies, direct procurement, and local production. Some countries procure their vaccines from a range of sources and may cut across all three categories. Over the past 25 years, UNICEF has been the main bulk procurer of traditional vaccines for most of the developing world, with the Pan American Health Organization Revolving Fund for Vaccine Procurement serving most Latin American countries. Because the fund takes advantage of large volume purchasing, it obtains prices comparable to those of UNICEF, which are available to all participating countries—regardless of their income level or size. The Gulf Cooperation Council also operates a purchasing program for its member states. That program includes 43 different vaccines and sera.

Some countries, where governments take on an increasing share of vaccine financing, purchase the vaccines directly from the producers or their representatives. Unfortunately, procurement is often being undertaken with little recognition that stringent quality assurance procedures must be in place to oversee the entire process. WHO is organizing workshops specifically targeted at vaccine procurement and has developed a vaccine procurement manual to guide such countries (WHO 2005a).

## QUALITY ASSURANCE FOR PHARMACEUTICALS AND VACCINES

In an ideal world, all products to be imported into a country would be registered by a fully competent national drug regulatory authority to ensure quality. Unfortunately, this situation is not always the case. A study of antimalarial samples from seven African countries found that failures in ingredient content

ranging from 20 percent to 67 percent for chloroquine tablet (CQT) and 5 percent to 38 percent for sulphadoxine/pyrimethamine tablet (SPT) and dissolution failures ranging from 5 percent to 29 percent for CQT, and 75 percent to 100 percent for SPT (WHO 2003c). Good procurement practices of both brand-name and generic drugs require that suppliers be prequalified through the inspection of dossiers and factory inspections for good manufacturing practice (GMP) and that their performance be monitored.

Counterfeit medicines are a particularly difficult problem. Counterfeit medicines “are deliberately and fraudulently mislabeled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products, and counterfeit medicines may include products with the correct ingredients but fake packaging, with the wrong ingredients, without active ingredients, or with insufficient active ingredients” (WHO 2005b, 1). In industrial countries, the newer brand-name medicines are counterfeited most often; Viagra is the frequent subject of counterfeiters. In poorer developing countries, the most commonly used antimalarials, antibiotics, and now antiretrovirals are the targets of the counterfeiters. The U.S. Food and Drug Administration estimates that up to 25 percent of medicines in developing countries are either counterfeit or otherwise substandard and that earnings from counterfeit drugs are more than US\$32 billion per year (WHO 2005b).

## THE WHO PREQUALIFICATION SCHEMES

Because undertaking prequalification tasks may be beyond the capabilities of national authorities, WHO has, on behalf of all UN agencies, started a prequalification scheme (WHO 2004d) covering AIDS, TB, and artemisinin-containing malaria drugs. The prequalification process is rigorous but efficient. WHO provides a positive list of prequalified products and manufacturers that have applied for and received favorable product assessments and manufacturing site inspections. Since January 2005, the Global Fund to Fight AIDS, Tuberculosis, and Malaria has required recipients to use WHO-prequalified products.

Ensuring quality is also an important aspect of any immunization program. For countries receiving their vaccines through UN agencies, WHO advises on the quality, efficacy, and safety of vaccines on the market through a prequalification of vaccines that entails the following steps: (a) reliance on a fully functional national regulatory authority (NRA) in the country of production and (b) verification of compliance with specifications through a thorough process of independent dossier reviews, testing of samples, site visits, ongoing monitoring of quality, and follow-up of complaints.

For a successful prequalification process, the NRA of the country of production must be functional and empowered by

the government. A set of laws and structures must be in place that guarantee the NRA's authority and independence and that the NRA exercises the following functions: licensing, postmarketing surveillance, lot release, laboratory access, GMP inspections, and evaluation of clinical performance. These functions constitute the prerequisite for vaccines of assured quality and are the focus in vaccine regulation.

## LOCAL PRODUCTION OF PHARMACEUTICALS

Large-scale production of pharmaceuticals in the developing world is limited to a few larger countries, most of which export primarily to other developing countries.

Whether local production of pharmaceuticals should be encouraged in low- and middle-income countries is a controversial issue. During the 1980s and early 1990s, the United Nations Industrial Development Organization encouraged the establishment of national production facilities. Recently, the World Bank and the executive board of WHO have reviewed this issue (Kaplan and others 2003; WHO 2004a). The more extensive World Bank report concluded:

In many parts of the world, there is no reason to produce medicines domestically, since it makes little economic sense. In the local pharmaceutical manufacturing sector, local production is often not reliable and, even if reliable, it does not necessarily mean that medicine prices are reduced for the end user. If local production is adopted by many countries, it may lead to less access to medicines, since there are no economies of scale in having a production facility in each country" (Kaplan and others 2003).

Profit margins on bulk generic drugs are low so that public production must be as efficient as private manufacturing. For many countries, technical expertise, raw materials, quality standards, and production and laboratory equipment all need to be imported, so foreign exchange savings may be small or nonexistent. Few developing countries have the capacity to produce active ingredients for pharmaceutical manufacture. Industrial investment to promote local manufacture of pharmaceuticals in most, but not all, developing countries could be better used to improve health infrastructure (Kaplan and others 2003).

In summary, a manager of a disease control program is likely to obtain quality-assured products by procuring them from prequalified suppliers at the lowest prices without considering whether the products are locally produced.

## STORAGE AND DISTRIBUTION OF ESSENTIAL DRUGS AND VACCINES

In the past, essential drugs, vaccines, and contraceptives were for the most part distributed using separate logistics systems. For vaccines and contraceptives, such systems were organized

vertically to some extent, and because they were concerned with a far more limited range of products, the task was somewhat simpler.

A push has been made to integrate the distribution systems for drugs, vaccines, and contraceptives, although in most places separate systems are still operating, at least at the national level and often down to provincial levels. Vian and Bates (2003) noted a number of changes to the distribution systems in the past few years. In many countries, health sector reform programs included efforts to reform central medical stores to allow more autonomy and to introduce commercial incentives and improved management methods. In some cases, this reform has led to higher staff productivity, better performance, and more enforcement of payment policies. However, disruption in supply often occurs during central medical store transition phases. Increased integration of commodities, including contraceptives and vaccines, has also been noted. In some cases, it has decreased the amount and reliability of data collected on logistics, creating problems for needs estimation and for tracking of consumption (Vian and Bates 2003).

Another trend is the increasing use of private transporters and contracting out for transportation management; contracting transport can generate cost savings and improve services. Finally, a trend toward computerized systems exists, particularly involving the use of donor-financed software for improved management of logistics as well as a number of comprehensive assessment tools and indicator sets for evaluating drug supply systems. But the proliferation of software systems, with little coordination and not enough support and maintenance of complex and fragile computer systems, can be counterproductive, especially if paper-based systems that are difficult to reintroduce upon failure of the computer system are abandoned (Vian and Bates 2003).

### Storage and Stocks Management

Drugs require secure storage in controlled climatic conditions and a reliable method of stock rotation. The FEFO rule (first expiry, first out) helps ensure that older stock is used up first. Security is another major consideration: access to the storehouse must be carefully controlled so that theft and embezzlement are minimized, and the persons who control access must themselves be trustworthy. Proper storage conditions, including minimizing exposure to heat, light, and humidity, are important for some drugs, but most drugs have proved remarkably resistant to poor conditions. Notable exceptions are tetracycline products, which become toxic when exposed to heat, and oxytocin and ergometrine, which lose their potency when exposed to light and heat; all should thus be stored in the refrigerator. The same applies to insulin and, of course, most vaccines. Correct FEFO stock rotation will ensure that exposure to harsh conditions is minimized and that potency is

preserved as much as possible. Ensuring good air circulation and preventing direct water contact are most important.

### **Management of Donated Drugs**

Management of donated drugs is a major problem in some areas, particularly if an emergency has precipitated an influx of drug donations. The best strategy is to accept only invited donations of drugs that the facility has specifically asked for (WHO 1999a). Any drug that is neither vital nor essential, that is not labeled clearly with its generic name, that is expired, that is in a package that contains only a few days' dosage, or that is not on the national essential drugs list or on the facility's formulary should be discarded—and the pharmacist should feel no guilt and fear no sanctions about disposing of such materials. They take up space, require tracking like other drugs, and present a risk of being accidentally dispensed to a patient and causing the patient harm—a factor that must also be taken into account. Proper disposal can be a problem. These drugs constitute potential toxic waste, and they should be treated as such and disposed of so that they cannot be retrieved and sold (WHO 1999b).

### **Vaccine Management**

Vaccines are delicate products that are destroyed if handled incorrectly. Vaccine management involves the use and distribution of vaccines, from the manufacturers to the end users. Aspects of vaccine management include inventory and forecasting, stock control, in-country distribution, storage and handling, equipment replacement plans, procedures for the use of the vaccine, monitoring of vaccine storage, transport management, and operational management.

Forecasting of vaccine needs is the first building block of an adequate management system. In 2002, 22 of 82 countries surveyed by UNICEF indicated that they had experienced a vaccine stockout. In addition to lack of resources, the main reasons cited included poor or late forecasting.

In recent years, attention has focused on avoiding heat exposure. The introduction of costly vaccines that are sensitive to freezing has drawn attention to the need to protect vaccines from excessive exposure to cold as well as heat. WHO guidelines for the international transport of vaccines now include specific recommendations for each category of vaccine, including freeze sensitivity. National cold stores are the next critical level of the vaccine management system. A failure there—where vaccines are received, stored, and distributed in bulk—can result in extensive losses. The WHO-UNICEF Effective Cold Store Management Initiative encourages countries to procure equipment and adopt management and training practices that fully protect vaccines in national and intermediate vaccine stores.

At the country level, emphasis is being put on the use of new tools, such as the vaccine vial monitor. This heat-sensitive label is a time-temperature indicator used to ensure that the vaccines have not been damaged by excessive exposure to heat, to identify weaknesses in the cold chain, and to take vaccines beyond the cold chain to children who have no access to fixed health facilities.

Together with the increased use of vaccine vial monitors, the gradual adoption of the multidose vial policy contributes to the reduction of wastage. This policy of using opened multidose vials of vaccine in subsequent immunization sessions applies to all multidose vials of liquid vaccine containing thimerosal (WHO 2000). The policy was formulated in 1996 but its adoption remains limited.

## **PRESCRIPTION AND RATIONAL USE OF DRUGS**

Rational drug use involves the correct drug being given to the correct patient, for the correct indication, in the correct dosage, by the correct route of administration, for the correct duration of treatment. The dispenser must also correctly dispense and label the drug and counsel the patient, and the patient must take the drug correctly or comply with or adhere to treatment. An error at any stage of this complex process can prevent the drug from being effective. Usually, at least half of these errors are attributable to the failure of patients to adhere to treatment, but the other half of the errors occur before the patient actually begins taking the drug. Few of the recommended treatments for common diseases involve more than one or two drugs, yet in actual practice, multiple drugs are often prescribed, even for uncomplicated cases. Such overuse of drugs rapidly consumes stocks, does not add to the quality of care (although patients may believe that more drugs are better), and allows stockpiling by patients.

The use of injections instead of equally effective oral preparations is also common. Not only are risks associated with the injections themselves, but also the cost of these injections is far greater than for the equivalent oral preparations. If all the prescribers at a facility can agree on and adhere to standard treatment guidelines that can be used as the basis for procurement and storage, the problem of overprescription and stockouts can gradually be eliminated. Uncertainties about dosages, particularly pediatric dosages, can also be reduced by the use of standard guidelines by age or weight. Doctors often cite their mistrust or delay of laboratory results as a reason to “cover” the patient for a variety of conditions. Dealing with laboratory efficiency or accuracy issues may be a worthwhile way to improve prescription practices that would also yield great benefits in terms of quality of care. Regularly reviewing a sample of prescriptions or case records and comparing treatments given to the standard treatment guidelines is likely to have a dramatic

effect on the improvement of treatment practices (Laing, Hogerzeil, and Ross-Degnan 2001).

## DISPENSING

Finally, the last step in the chain of the drug supply system is delivery to the patient. Often, dispensing is done by untrained staff members who know little about the drugs they are dispensing and are unable to communicate effectively with the patient. Anecdotal stories about patients receiving a handful of white pills and throwing them on the ground are discouraging to staff members but demonstrate that patients need explanations about the drugs they are getting. Increasing the use of dispensing materials—paper or plastic bags—may be worthwhile if it improves adherence to treatments. Brief training courses for dispensers can substantially improve the quality of dispensing.

Another major problem is the presence of dispensing doctors. A number of studies in both developed and developing countries have demonstrated that dispensing doctors prescribe more by value and not according to national or accepted guidelines (Trap, Hansen, and Hogerzeil 2002). The higher number of prescriptions is strongly associated with symptomatic treatment (that is, a drug was prescribed for every symptom); general overprescribing of antibiotics; overuse of injections; and prescription of medicines with lower clinical value. From a policy and safety perspective, the functions of prescribing and dispensing should be separated whenever possible (Nizami, Khan, and Bhutta 1996).

## ADHERENCE

Delivering the drug to the patient is not the end of the story: the patient must adhere to the therapy. Failure to comply or adhere will result in poorer health outcomes; it may compromise the effectiveness of treatment, decrease the quality of life, increase preventable disability, and lead to premature death. It may also result in increased health care costs, more use of emergency rooms, more and longer hospitalizations, and potentially more use of intensive care units (Sabate 2003).

## FINANCING ISSUES

The share of expenditures on health that goes to pharmaceuticals is presented in table 72.2.

Asking patients to pay part or all of the cost of their drugs can aid in holding down costs, reducing overuse, and replenishing the funds for drugs in the system. Drugs are often targeted for such fees because it is felt that patients will pay for them if they have no other choice. A substantial literature now

exists on the advantages and disadvantages of user fees. On the one hand, they do raise some revenue, but administrative costs have often taken a large proportion of it. Their net contribution has rarely exceeded 5 percent of a government's recurrent expenditure. On the other hand, they often accounted for as high as 100 percent of nonsalary recurrent expenditures. Moreover, where they have been retained at the facility level, they have allowed for improvements in infrastructure and staff income, as well as ensuring a more regular supply of drugs (Xu and others forthcoming).

However, from a public health perspective, the disadvantages are numerous. They are often applied inequitably, with exemptions provided to richer people—such as government workers, the military, and the police—while poorer people must pay. But the main problem is that user fees discourage some people, particularly the poor, from seeking care at all. And among those who do seek care, the resulting costs can be financially crippling, to the extent that households may sacrifice food, education, or other important purchases to pay for drugs. Some are forced into poverty as a direct result of user fees. A related issue of increasing importance with the advent of effective antiretroviral therapy for AIDS is that user fees discourage adherence to long-term treatment, resulting in treatment failure, increased disease transmission, and the development of drug resistance. Fees are, therefore, particularly problematic for transmissible diseases.

On the basis of similar evidence, Creese (1997, 203) concluded, "A range of policy options other than user fees exists for dealing with situations of both under financing and rapid growth in expenditure. As an instrument of health policy, user fees have proved to be blunt and of limited success and to have potentially serious side effects in terms of equity. They should be prescribed only after alternative interventions have been considered." In this respect, WHO is now advocating that fees should be minimized and that countries should be supported in attempts to channel a high proportion of health expenses through taxes or prepayment mechanisms such as forms of insurance.

**Table 72.2** Measured World Pharmaceutical Spending, by per Capita Income Clusters, 1990–2000 (percent)

Income group	Share of world total		Share of expenditure on health	
	1990	2000	1990	2000
High income	80.2	78.7	13.0	13.8
Middle income	17.1	18.8	22.5	24.8
Low income	2.7	2.4	20.8	19.2

Source: WHO 2004f.

Note: Income groups refer to World Bank classifications as of July 2000.

## SUSTAINABLE FINANCING OF VACCINES AND IMMUNIZATIONS

Immunization is now generally accepted as representing one of the “best buys” for the health sector that governments must play a lead role in financing, but sustainable financing mechanisms have been largely absent in poor countries (WHO 2004a). The cost of immunizing a child against the six basic diseases hovers between US\$15 and US\$20 at current levels of coverage, representing no more than US\$0.50 per capita, and on average 0.2 percent of the gross domestic product in most low-income countries. These costs suggest that immunizations are affordable for most developing countries from national budgets. However, immunization programs account for only 5 to 10 percent of total government health expenditures in many countries, which often rely heavily on donor funds.

Although the international community has recognized the important reasons that financing of vaccines cannot be left to individuals or households, donor support has often been quite erratic. The result is volatile financing that is vulnerable to shifts in donor priorities. In addition, recipient governments recognize that donors are more likely to fund vaccines than many other services, so they have taken the opportunity to spend their own resources on activities that are important to them but are less attractive to donors. This phenomenon can be seen in the apparent mismatch between data on disease burden, stated government priorities for health, and the allocation of government funds.

The challenge facing governments in poor countries is how best to finance vaccines, taking into account the variety of other health problems and the possible sources of funds. More funds could probably be raised from firms and households for health in general, but user fees for immunization, as for drugs, discourage people from seeking vaccination for their children. However, helping countries move to a system in which more prepayment exists for health services in general—either through taxes or the various possible forms of health insurance—would provide a pool of domestic funds that could be used for vaccines. If these funds were raised progressively, the rich could subsidize the poor.

A number of new issues relevant to immunization financing have arisen recently, including the evolving nature of the world market for vaccines, the growing divergence in vaccination schedules between developed and developing countries, the increasing diversity of products and presentations available to countries, the emergence of developing country manufacturers, and the importance of new global initiatives such as GAVI and the Vaccine Fund. The Vaccine Fund focuses on helping low-income countries introduce newer vaccines, such as HepB and Hib, which are generally more expensive than the older vaccines. In addition, the technology associated with the production of new combination vaccines has increased prices, with

the cost per fully immunized child now reaching US\$30 if HepB and Hib are included. This increased cost adds to the challenge. Governments in low-income countries and international development partners need to develop long-term strategies to ensure adequate financing for key health programs and interventions, including vaccines.

Since GAVI and the Vaccine Fund were established, renewed attention has been paid to financing issues as they relate to vaccine and immunization financing. GAVI has worked with WHO and countries to consider how much it would require to maintain existing levels of coverage after GAVI funding ends, whereas among the prerequisites for countries to obtain assistance from the Vaccine Fund is preparation of long-term financing plans for immunization programs. However, most low-income countries clearly will be unable to fund even a minimum set of essential interventions in the short to medium term without the assistance of international partners, thereby increasing the need to develop the long-term financing strategies described above. A mix of such strategies would include raising additional domestic funds, ensuring that funds are used effectively and efficiently, moving to greater reliance on prepayment mechanisms, and ensuring increased and stable flows of external funds. Table 72.3 summarizes and compares some recent trends in the financing of essential drugs, vaccines, and contraceptives.

## ISSUES FOR THE FUTURE

As the world's population ages, health systems that formerly focused primarily on infectious disease are being asked to deliver new types of care, mostly for chronic illnesses and increasingly for mental illness. By 2020, the major causes of the burden of disease will shift from pneumonia, diarrhea, and perinatal conditions to heart disease, mental illness (particularly depression), and road traffic accidents. Tobacco will kill more people than any other cause of disease, including HIV. Unlike the United States and the countries of Western Europe, China and India will face the challenges of an aging population before they become high-income countries. Most health systems in the developing world are now prepared to deliver acute care, particularly for infectious disease, rather than chronic care. They are ill suited to long-term chronic care and follow-up; in general they lack recordkeeping, demonstrate little development of personal relationships with caregivers, and have little provision for enhancing patient adherence with medication. In many situations, the irregular and intermittent supply of medications for chronic disease means that the chronically ill suffer many interruptions of their treatment. The changing nature of health care will require changes in drug supply, which are only beginning to become visible. The (perceived) difference between “good” and “bad” care is often the availability of

**Table 72.3** Trends and Developments in Financing and Procurement of Essential Drugs, Vaccines, and Contraceptives

Commodity	Trends and developments	Implications for logistics
Essential drugs	Use of loans and pooled or “basket” financing arrangements is increasing, leading to increased government involvement in procurement.	In the short term, procurement delays, shortages, emergency procurement requests, higher prices, and greater waste will result while governments develop internal capacity to procure. Also, increasing government involvement can mean less predictable results because of politics and governance issues.
	Procurement models adapted for health reforms such as decentralization and privatization proliferate.	Donors are more concerned about how procurement is done, translating into more technical assistance and emphasis on performance benchmarking. Difficulties in evaluating procurement systems are caused by a proliferation of models.
	Countries are moving toward restrictive tender and prequalification of suppliers.	In the longer term, prequalification may shorten the procurement cycle and lower costs. Similar effects from use of NGO suppliers are possible.
	Role of NGO suppliers continues in some countries as well as role of international NGO suppliers.	
	User fees represent a major trend for essential drugs, with many health facilities operating on a cash-and-carry basis.	Fee systems can decrease demand unless mechanisms exist to ensure service for those unable to pay.
	Private sector role is increasing as it becomes more apparent that public sector and NGO services cannot meet all needs.	Policy makers and managers will need to design and implement programs that promote appropriate use of the private sector
Vaccines	Donor contributions have been decreasing starting in 1990s.	Concerns are similar to those with essential drugs.
	Government financing and procurement of vaccines is increasing; a dependence on external resources persists.	GAVI supplies may require logistics changes because of new vaccines and injection equipment.
	Some shift in financing from grants to loans, and more use of basket financing.	Pressure on governments to finance vaccine purchases may lead to less government funding for EPI operating expenses and other Ministry of Health programs.
	Use of pooled procurement mechanisms and revolving funds or other international financial mechanisms, some based on achievement of outcomes, is increasing.	Outcome-based support requires information systems resistant to manipulation.
Contraceptives	New vaccines and vaccine combinations (new with old) are supplied through GAVI.	
	Donor contributions have been flat or have decreased, starting in 1990s.	Concerns are similar to those with essential drugs.
	Despite efforts to increase government contributions, there is still a major dependence on external resources.	Demand is created without supply keeping up.
	Many governments continue to give contraceptives (as compared with drugs) low priority for procurement with their own funds.	Constraints of Mexico City policy (“global gag rule”) have limited funding for contraceptives.
	Financing through loans and basket financing are increasing, and governments are increasingly involved in procurement.	

Source: Adapted from Vian and Bates 2003.

drugs and supplies. Programs and funding agencies that are planning improvements in health care—for example, increasing coverage or case detection rates—often overlook the fact that such improvements will increase drug needs and costs.

### Drug Resistance

Although the burden of chronic and noninfectious disease is increasing rapidly in the developing world, infectious diseases still account for nearly half of deaths in low-income countries. Most of these deaths are caused by six diseases: acute respira-

tory infections (mainly pneumonia), diarrheal disease, HIV and AIDS, tuberculosis, malaria, and measles. Drug resistance complicates the effective treatment for nearly all of these acute infections. Furthermore, this trend is expected to accelerate in the coming decades. In the treatment of HIV and AIDS, the increase of retroviral drug resistance is becoming a serious problem, especially in view of the limited number of treatment regimens available to date.

Drug-resistant malaria is now widespread. Chloroquine—once a cheap and reliable first-line treatment for malaria—is

no longer effective in most countries. Newer drugs are significantly more expensive. Most recently, the trend has been toward multidrug combinations of products, and the addition of more than one drug is often to “protect” the component drugs from developing resistance as well as to improve the therapeutic effect (WHO 2002a).

Drug resistance in tuberculosis control—in particular, multidrug resistance—is a growing problem. Multidrug-resistant TB has now appeared around the world, and in many places more than 20 percent of resistant new tuberculosis cases are resistant to several drugs. Furthermore, the emergence of multidrug-resistant bacilli means that medication that once cost US\$20 must now be replaced with drugs that are significantly more expensive and more difficult to use (WHO 2002a). Another major concern is the use of antimicrobials in farming, because about half of the antimicrobials produced each year are used in farm animals. Some of the new resistant bacteria are transmitted from food of animal origin or through direct contact with farm animals. Some reports indicate that as much as 50 percent of human antimicrobial resistance is caused by growth promoters in livestock, which are added to feed in subtherapeutic antibiotic doses (WHO 2002a).

### **HIV and AIDS**

The HIV epidemic has had a tremendous impact on the pharmaceutical supply situation. First, it has highlighted weaknesses of drug supply and access around the world; the arrival of highly active antiretroviral therapy for the treatment of HIV/AIDS (HAART) means that HIV is to a large extent now a treatable condition, yet treatment is not available to the majority of those who suffer from HIV. Second, it has drawn the world’s attention to the growing gap between rich and poor in terms of pharmaceutical provision. Unlike many other highly prevalent illnesses in the developing world, HIV and AIDS are also of major concern in the wealthier countries, and thus significant research has been undertaken and has yielded effective new medications (HAART, in particular).

A recent WHO report highlights the issue of the affordability of medications, pointing out that of the 23 countries that are estimated to make up 80 percent of the 2003 global need for HIV and AIDS treatment—estimated at about US\$300 per annum per patient—only 8 have pharmaceutical expenditure levels above US\$5 per capita, far short of the level of expenditure needed (WHO 2004c). Prices have fallen dramatically; WHO has continued to monitor the quality of AIDS drugs available on the world market for sale in developing countries and has removed substandard drugs from its list when necessary (WHO 2004e). Many high-profile initiatives to solve this problem have been started, most notably the WHO’s “3 × 5” program; the Global Fund to Fight AIDS, Tuberculosis, and Malaria; the Clinton Foundation’s efforts to lower prices for

HAART; and President George W. Bush’s Emergency Plan for AIDS Relief. A number of issues are raised by the delivery of a complex, lifelong, costly treatment to poorer communities, especially in rural areas, one of which will be how to ensure adequate adherence to treatment in different clinical settings, ranging from district hospitals to health centers or even home settings, for HAART delivery.

### **Aging and Chronic Diseases**

One of the important results of the exercise to estimate the global burden of disease was to highlight the growing importance of chronic disease, particularly in the developing world. A large percentage of chronic illnesses are related to smoking and lifestyle, and thus attempts to reduce smoking—or the lethality of smoking—would have an important effect on the need for medication for chronic disease.

Although many cancers are not yet curable, many are treatable with the goal either of slowing the spread or of palliating the symptoms of the disease. As the burden of cancer increases, palliative care, which involves the treatment of the symptoms and especially the pain that accompanies most cancers, needs to be given much higher priority. At present, the vast majority of the millions of cancer patients in the developing world receive totally inadequate pain control and suffer needless agony, in part because of antiquated laws governing the use of opioid analgesics (particularly morphine) and attitudes of medical and nursing personnel toward pain control (as well as attitudes of family members in some settings). The myths about morphine need to be dispelled. When used appropriately, especially in oral form, morphine does not lead to addiction, tolerance, respiratory depression, cognitive impairment, or premature death. In fact, people live longer when their pain is controlled, and they can eat, sleep, and live normal lives (Merriman and others 2002).

In countries where palliative care is fairly well developed and available, the consumption of morphine per capita averages over 20 milligrams, but in most developing countries it is negligible, and most of the needs for pain relief are unmet (Joranson, Rajagopal, and Gilson 2002). The World Bank recognized the importance of alleviating pain, which it included in its package of “essential clinical services” (World Bank 1993). As the population ages, the ability of the health care system to provide palliative care must grow along with it.

The trend toward more sedentary lifestyles and toward consumption of diets with higher fat and sugar content is leading to a steep increase in the burden of diabetes, with 150 percent increases in prevalence predicted for many countries by 2030; the absolute numbers will grow from 171 million in 2000 to about 366 million in 2030. The greatest increases in diabetes prevalence are predicted for the Middle East, Sub-Saharan Africa, and India (Wild and others 2004). Most of these

**Table 72.4** New Vaccines Needed

Priority vaccines	Close to licensure vaccines	Vaccines for neglected diseases	Other vaccines of importance	Vaccines for new threats
HIV, TB, malaria	Meningococcus, streptococcus pneumoniae, rotavirus	Shigella, dengue, Japanese encephalitis, leishmaniasis, schistosomiasis, cholera	Human papilloma virus, respiratory syncytial virus, herpes simplex, enterotoxigenic, <i>Escherichia coli</i>	SARS, anthrax, smallpox, pandemic influenza

Source: Authors.

SARS = Severe acute respiratory syndrome.

new cases will be type 2 and, thus, most will not be insulin dependent, but they will require oral diabetic medications. For those who do require insulin, given the current state of technology, the main barrier (other than cost) is the need for storage of the insulin in a cold or cool location and for sterile injection equipment. In either case, to meet the predicted rise in cases and to treat them with current drugs, a major expansion of drug supply for diabetes must be anticipated. Many diabetics currently do not receive adequate treatment. The pressure to provide adequate treatment will increase as the population ages and begins to demand treatment of its chronic afflictions—and in that case the increase in demand for diabetes medications would potentially be much more than 150 percent.

Another important finding of the global burden-of-disease exercise was the high number of DALYs lost to mental illness, depression in particular. In 2020, unipolar depression is projected to be the leading cause of morbidity and disability among females worldwide and in developing countries. Whereas in the industrial countries a pharmacological solution is often used, this approach may not be feasible in the developing world, at least not at present price levels. Recent research in the developing world has shown good results with weekly group interpersonal therapy, without the use of antidepressants. Trained laypersons ran the therapy sessions, not psychiatrists or medical personnel (Bolton and others 2003).

## VACCINE RESEARCH PRIORITIES

In the past two decades new advances in biotechnology have resulted in the licensure of new vaccines, such as Hib, acellular pertussis, HepB, and attenuated varicella. Research institutions in the public sector have generated most of the basic scientific breakthroughs, whereas the large pharmaceutical companies have borne the cost for clinical development. Because such development requires heavy investments that need to be recouped from profits, new vaccines are expensive and therefore out of reach for poor populations.

Of all the vaccines currently under development, the three most needed today are vaccines to prevent the three big diseases—AIDS, TB, and malaria—which jointly account for

more than 5 million deaths per year, or about 50 percent of all infectious disease deaths (see table 72.4). The total investment in vaccine against these diseases is not impressive, and it will probably take at least 5 to 10 years before a vaccine against any of them is available.

GAVI has selected three vaccines for accelerated development: meningococcal meningitis, rotavirus, and pneumococcal vaccines. They have been selected because they are considered close to licensure, or “near term.” Other important diseases are considered neglected in terms of vaccine development, among them shigella dysentery and dengue fever.

New diseases emerge and old ones reemerge, influencing priorities in vaccine research. The severe acute respiratory syndrome (SARS) epidemic, the outbreak of avian influenza, and the emergence of bioterrorism threats such as anthrax have led to a new search for vaccines against these infections. The threat of a pandemic of a reassorted influenza virus strain has recently highlighted the need for much greater resources and attention to be devoted to the development and distribution of effective flu vaccines.

## New Vaccine Technologies

Alternative routes of administration would improve program safety, avoiding needle transmission of bloodborne pathogens. The ability of nonprofessionals to administer vaccines would also ease vaccine delivery strategies. New administration routes, such as oral, nasal, and transcutaneous routes, are being explored. An interesting project concentrates on the development of a nasal measles vaccine that would greatly enhance the feasibility of eliminating this disease by facilitating the administration during mass campaigns.

The concept of using plant-derived or edible vaccines involves encoding protective antigens from pathogens into transgenic plants. The plants are processed so that they can deliver a uniform dose of vaccines. Human clinical trials have been conducted with, for example, bananas and raw potatoes, which have shown encouraging antibody responses. The potential advantages of this technology could include thermostability, low investment needs, multivalency, and oral administration.

## New Immunization Technologies

Priority is given to new delivery technologies that will expand access, improve safety, and cut the cost of immunization programs. They include the following technologies:

- The reuse of disposable syringes and needles is widespread and contributes significantly to the transmission of hepatitis B and C and HIV. The autodisable syringe prevents reuse, and disposal in safety boxes reduces the risk to health staff and the general public from contaminated syringes and needles.
- Four different technologies are being explored to minimize the risk of infection from accidental exposure to sharps: corrosive disinfectants, thermoprocessing, needle destruction, and plastic melting. However, none of these options will soon be put into use in the field.
- Although the adoption of the multidose vial policy will contribute to the reduction of wastage, the ultimate aim is to provide all immunizations as monodose preparations. Injection devices prefilled with a monodose increase quality and safety at the point of use. Uniject is one such device that has been tested with HepB and tetanus toxoid. Village health workers or traditional birth attendants can use such devices. Currently, the cost of the device and the need for additional cold storage space when multidose presentation is exchanged for monodose pose obstacles to implementation.
- Needle-free injection devices deliver vaccine at high velocity into the skin without penetration of a needle, reducing the risk of transmission of bloodborne pathogens. Technologies are being developed for both mono- and multidose presentations. Available multidose injectors have not been found safe, and new models are under development. However, regulatory obstacles and high cost have rendered the monodose injector models that are currently available infeasible for large-scale programs.
- Vaccine distribution and storage without a cold chain would considerably simplify the delivery system, reduce cost, and allow for an integrated supplies mechanism. Development of vaccines that do not need a cold chain should be the highest priority for technology research. Sugar glass drying is one such technology that has shown great promise. It can be used to produce multivalent vaccines that are completely heat stable except under extreme climatic conditions. The high cost of regulation and licensing and the uncertainty about market prospects in industrial countries have so far impeded the development and use of this technology.

## Obstacles to Vaccine Research

A host of obstacles confront vaccine research, the most important being the low level of investment for vaccine development when there are limited market prospects in the industrial

world. Only a limited number of research centers have the capacity and experience required to conduct phase 2 and especially phase 3 trials of new vaccines, and they are mainly located in industrial countries. The capacity to conduct phase 3 trials in developing countries needs to be strengthened; the current situation impedes further development of vaccines needed in those countries.

Pilot lot production of vaccines is required for all phases of clinical trials. The global capacity to produce pilot lots is, however, inadequate to meet demand. Close public-private partnerships are necessary to ensure that the production capacity is available.

Manufacturers need markets to provide some assurance that the development cost for new products can be recouped. Such incentives require realistic forecasts of demands. Various mechanisms have recently been put in place to try to guarantee future markets, most notably the Vaccine Fund.

Last, disease burden data are needed for both selections of vaccines for national programs and for estimations of vaccine requirements, including market projections. However, such data are lacking in many countries and regions. Existing data are especially weak for respiratory disease of both bacterial and viral origin.

## PRIORITIES FOR PHARMACEUTICAL RESEARCH

The WHO Priority Medicines Project, a recent exercise that used evidence-based methods to outline the priorities for public funding of pharmaceutical research, has recently been published (WHO 2004b). It incorporated data from the burden-of-disease rankings and from the Cochrane Database of Systematic Reviews of data on clinical efficacy. It also incorporated the use of criteria of social justice, social solidarity, and equity, so that neglected diseases and the needs of special patient groups (the elderly, women, and children) were also taken into account. The research identified 20 major diseases that account for 60 percent of the total DALY burden both in Europe and in the rest of the world—diseases that are common to both groups included unipolar depression, ischemic heart disease, cerebrovascular disease, chronic obstructive pulmonary disease, and digestive diseases (excluding diarrheal diseases).

The authors also mention the important contributions of various cancers, lower respiratory tract infections, and diabetes to the burden of disease, which is common to both developed European countries and to the developing world (WHO 2004b). Smoking is clearly a major contributing risk factor, and the authors caution that expenditure on pharmaceuticals for smoking cessation must not divert resources from other efforts to reduce smoking. The priority areas identified by this exercise are presented in table 72.5.

**Table 72.5** Preliminary List of 16 Priority Areas for Pharmaceutical Research

Rank	Condition
1	Infections caused by antibacterial resistance
2	Pandemic influenza
3	Cardiovascular disease
4	Diabetes (types 1 and 2)
5	Cancer
6	Acute stroke
7	HIV/AIDS
8	Tuberculosis
9	Neglected diseases <sup>a</sup>
10	Malaria
11	Alzheimer's disease
12	Osteoarthritis
13	Chronic obstructive pulmonary disease
14	Alcohol use disorders: alcoholic liver disease and alcohol dependency
15	Depression in the elderly and adolescents
16	Postpartum hemorrhage

Source: WHO 2004b.

a. Neglected diseases include, but are not limited to, trypanosomiasis (sleeping sickness), Buruli ulcer, leishmaniasis, and Chagas disease.

## CONCLUSION

Ensuring that needed essential medicines and vaccines are available is critical for the success of any disease control program. A great deal is known about what works and what does not work. Careful selection, procurement from prequalified suppliers, proper storage and distribution using secure reliable channels, and assurance of rational use and correct dispensing are all critical components of any drug and vaccine supply system. Ensuring that adequate funds are available to pay for the procurement, distribution, and quality assurance of all medicines and vaccines is equally critical. Depending on the circumstances, either the public or the private sector or a combination of both can efficiently deliver quality-assured medicines and vaccines. The experience of a number of countries and programs has demonstrated that essential medicines and vaccines can be reliably delivered to poor people using the approaches described in this chapter.

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