The World Medicines Situation

World Health Organization

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THE WORLD MEDICINES SITUATION

WORLD HEALTH ORGANIZATION

CONTENTS

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INTRODUCTION

This second review of the world medicines situation (first published in 1988 as *The World Drug Situation)* presents the available evidence on global production, research and development, international trade and consumption of pharmaceuticals. In addition, it draws on the most recent surveys and studies in WHO Member States to examine the state of national medicines policy. The aim is to provide an easily accessible source of information on the pharmaceutical situation at global and national levels.

Although the text is based on and around the available data, these data pose several challenges. For example, reliable data on the large pharmaceutical markets in the world's most populous countries, the People's Republic of China and India, are in short supply. Trade, production, expenditure and consumption data all come from different sources. In addition, the use of monetary values, rather than an indicator of volume, gives a distorted picture of production and consumption since it fails to reflect the scale of global consumption of traditional medicines and low-priced generics (both branded and non-branded).

Another problem is that certain key terms, such as "generic" medicines, are used differently by different parties, and usage is also changing. While 10 years ago the term "drugs" was widely used by WHO and other agencies, in today's usage this seems too vague and inclusive, and is increasingly understood to refer to illicit substances. As a result, the term "pharmaceuticals" is now increasingly used (meaning both medicines and vaccines) or alternatively "medicines". All three terms are used in this report, with explanations given when needed, and this is reflected in the change in title from the 1988 report.

Meanwhile, the pharmaceutical industry itself is difficult to define. Its products extend from first aid and cough remedies which are on sale to all, to highly specialized medicines for use only by hospital specialists. Some definitions bundle veterinary medicines and vaccines, bulk ingredients, medical devices and diagnostic products with finished pharmaceutical products. The Standard International Trade Classification (SITC Rev 3) distinguishes pharmaceuticals from medicaments and itemizes 57 four- and five-digit sub-items of these two commodities. Within these classifications the main focus of this report is medicines for human consumption, including those available only on prescription and those which can be purchased over the counter. However, in Chapters 1 and 3, the broader industrial and trade classifications are used.

The manufacturers of pharmaceuticals are numerous and diverse. At one end of the spectrum are the many firms of all sizes which collect and process herbs and medicinal plants for use in traditional medicine. No data are available on the volume of products involved. At the other end of the spectrum are large, "integrated" transnational corporations, with the capacity to develop new molecular entities and to manufacture, market and distribute medicines to most parts of the globe. Situated in between is a wide range of manufacturers differing in size, the kind of pharmaceuticals produced and in manufacturing and marketing techniques. In India, for example, 20 000 pharmaceutical manufacturers have been inventoried, but only 250 of these are in the "organized" sector, and they account for 70% of the country's total output of branded generics. Elsewhere, China's

rapidly growing pharmaceutical industry has an estimated 7500 manufacturers but, according to one source, only 87 of these have internationally accepted Good Manufacturing Practice certification.[1]

Finally, the pharmaceutical markets of the high-income countries differ widely from those in developing countries. Not only is per capita spending on health and medicines many times higher in high-income countries, but a much greater share of the medicines bill is publicly subsidized. In the lowest-income countries, spending on medicines comes largely from household resources and has to be paid for out of pocket at the time the person is ill. Markets also differ in the extent and effectiveness of regulation in areas such as medicine prices and safety. This report therefore covers a wide range of different products from multiple and varied sources, prescribed, purchased and consumed in very different domestic contexts.

The report does not attempt to deal in a comprehensive way with a number of key policy issues in medicines policy, such as parallel trade, intellectual property rights, counterfeiting, or corporate pricing strategy, around which vigorous debate continues at both the national and international level. Whilst WHO's concerns and policy positions are made clear at relevant points in the text, our primary aim is to provide an up-to-date set of basic information on the global medicines situation and on the current status of national medicines policies. It is hoped that these data will serve as a useful set of reference material for analysts, researchers and others concerned with the global pharmaceutical situation.

REFERENCE

1 *Patents, pills and public health. Can TRIPS deliver?* PANOS Report No.46. London, PANOS Institute, 2002.

1

WORLD MEDICINE PRODUCTION

SUMMARY

- Trends from 1985 to 1999 indicate that the value of medicine production has grown four times more rapidly than the world's income.
- Medicine production is highly concentrated in the industrialized countries, where just five countries – the USA, Japan, Germany, France and the UK – account for two-thirds of the value of all medicines produced.
- Large volume markets of lower-price medicines exist in the highly competitive domestic markets of China and India.
- A small number of transnational companies dominate the global production, trade and sales of medicines. Ten of these companies now account for almost half of all sales. This concentration has increased considerably since 1987.
- The 10 best-selling drugs account for 12% of the value of all medicine production.

1.1 INTRODUCTION

This chapter summarizes available data on the pattern of global pharmaceutical production.[i] Production means the value added at each stage of the manufacturing process, whether it is the manufacturing of active ingredients in bulk from basic chemicals, the preparation of finished new medical entities, or the repackaging of imported generic ingredients to make finished branded or unbranded generic products. When measured in monetary terms, global production is geographically a highly concentrated activity, with over 90% of world production located in a few high-income countries. The relative market share of major producing countries has been fairly stable over the past decade.

Two-thirds of the value of medicines produced globally is accounted for by firms with headquarters in just five countries — the USA, Japan, Germany, France and the UK. Production is also concentrated in a few key products and in a relatively small number of companies, which often have factories and offices in many countries.

Since monetary values are the most easily available and convenient measures of production, trade and sales of medicines, they are widely used in this report. However, they give a misleading measure of the therapeutic value of medicines.[ii] Some of the expensive drugs

[i] As used in the major different industrial and trade classifications the term "pharmaceuticals" often includes more than medicines for human use. Vaccines and other biological products, blood and blood derivatives, diagnostic products, and all of the preceding intended for veterinary use, are frequently bundled together in economic statistics, though finished pharmaceutical products for human use usually constitute by far the largest single component of this set. While the concern of this book is with medicines for human use, the industrial production and international trade data in this and the next chapter should be understood to include these other products.

[ii] Therapeutic value can be measured in different ways. Simple measures of clinical improvement, such as fever reduction or recovery times, are widely used. For comparisons across different conditions and interventions, composite assessments such as "healthy life years gained" or "disability-adjusted life years" gained are increasingly used.

available today have only modest therapeutic benefits, while many inexpensive medicines are highly effective and safe. Most of the medicines on WHO's Model List are in this second category. Manufacturers provide a stream of new products for the medicines market place, usually at higher prices than existing products. New medicines with patent protection, which may have resulted from costly research and development processes (R&D), and where large markets are anticipated, tend to be particularly expensive. Yet price and therapeutic gain are not necessarily related. Large quantities of traditional and generic medicines are manufactured and consumed, particularly in low-income countries, and the therapeutic value of these is not reflected in available monetary measures. For India and China in particular, the dollar value of medicine transactions bears little relation to the health value of these products. Where available, volume measures such as weight or the number of prescriptions can change the global perspective on production and consumption dramatically. However, they still cannot measure the health value of medicines. India, for example, accounts for about 1% of the world's production by value, but 8% by volume (weight). The country ranks thirteenth in world production by value but ranks fourth in the volume of pharmaceuticals produced.[3] However, these measures are still no closer to an index of therapeutic value, and the available data are too limited to allow international comparison or analysis of trends.

The total value of global pharmaceutical production in 1999 was just over 320 billion US dollars.[i] This corresponded to 1.12% of global gross domestic product (GDP). **Table 1.1** shows trends in global production for the period 1985–1999. The average annual growth rate of pharmaceutical production over this period was just under 10.5% at current prices, in comparison with an average annual growth rate of global gross national product (GNP) of under 7.5%. The value of manufactured pharmaceuticals has thus grown substantially faster than the total value of goods and services. When these figures are converted into constant prices to adjust for inflation, the rate at which pharmaceutical production has outstripped GDP growth increases substantially. The average real growth rate of GDP was 3.6% per annum and the average real growth rate of pharmaceutical production was 14.9% per annum.

TABLE 1.1 **Estimated global value of pharmaceutical production 1985–1999, in current and constant US$ billion**

Year	1985	1990	1999
Pharmaceutical production current prices	82,1	175,9	327,2
Global GNP current prices	10,766	22,299	29,232
Pharmaceutical production constant (1995) prices	46,2	140,5	370,1
Global GNP constant (1995) prices	20,302	24,555	33,672

Source: WHO estimates from database of UNIDO, OECD Health Data, World Development Indicators 1987, 1992, 2001, International Financial Statistics Yearbook, 2002

Note: List of countries from which data were available is given in Annex 1. 1999 values for many countries are projections, estimated from data from 1981 to the most recent year available.

[i] This estimation corroborates with that of the European Federation of Pharmaceutical Industries and Associations (EFPIA) which found a value of US$ 350 billion in 2000.

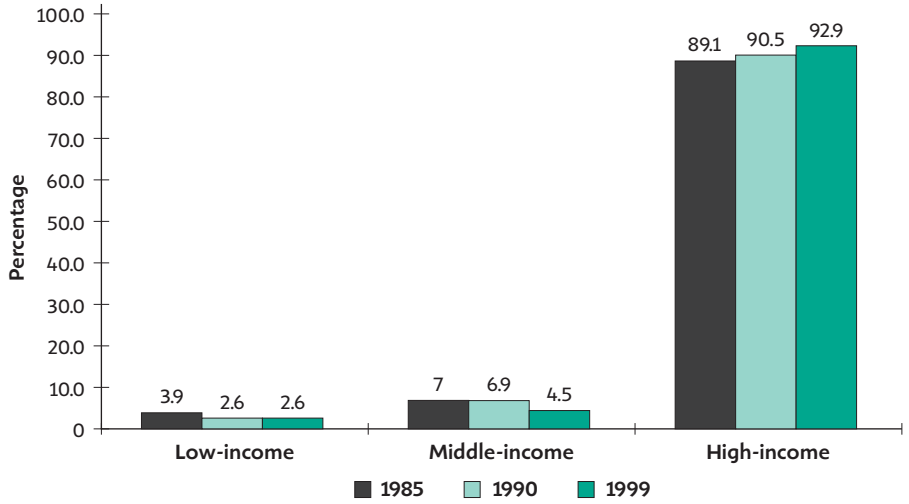
Figure 1.1 shows how total production was distributed among countries according to their level of economic development, using the World Bank classification of countries, which groups them according to the level of income as follows:[2]

High-income:	GNP per capita of US$ 9361 or more in 1999
Middle-income:	GNP per capita of US$ 761 –US$ 9360 in 1999
Low-income:	GNP per capita of US$ 760 or less in 1999

Figure 1.1 shows that the high-income countries dominate in world pharmaceutical production (by value). These countries' share of production increased from 89.1% in 1985 to 92.9% in 1999. The combined share of middle- and low-income countries decreased from 10.9% to 7.1% over the same period.

FIGURE **1.1**

Share of low-, middle- and high-income countries in world pharmaceutical production



Source: WHO estimates based on data reported by UNIDO, OECD

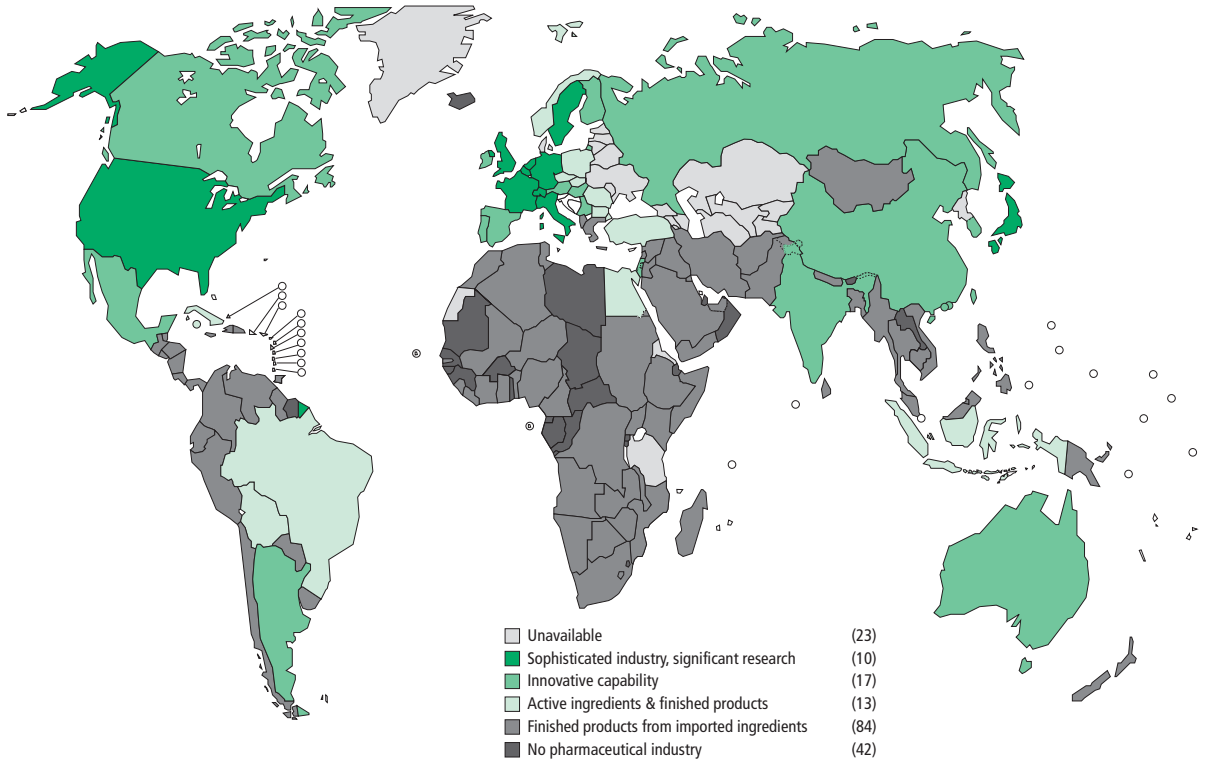
1.2 LEADING COUNTRIES IN GLOBAL PHARMACEUTICAL PRODUCTION

In **Figure 1.2**, 188 countries are classified according to their medicines production capability, updating a typology first used in 1992.[3] Ten countries are classed as having a "sophisticated industry with significant research". Manufacturing in these countries is done by all three types of classified producer: transnational corporations, innovators and reproducers. Very large transnational corporations develop, manufacture and distribute medicines.[i] These 10 countries, through the 10 companies headquartered in them and, in some cases, through large amounts of publicly funded research, are the principal sources of new medicines discovery. Numerous smaller companies are also innovators but lack the fully integrated capability of the big transnational corporations. This group has grown dramatically with the growth of biotechnology over the past decade. Unlike the two previous

[i] In 2000, nine of the top 100 transnational corporations (ranked by foreign asset value) were pharmaceutical companies. World Investment Report, 2002, UNCTAD, Geneva.

FIGURE 1.2

Local pharmaceutical production capacity varies greatly among countries



groups, reproducer firms manufacture medicines which are not protected by patent (unless under licence). These firms may be public or privately owned and are typically small- to medium-sized.

A further 16 countries, including India and China, have "innovative capability", meaning that at least one new molecular entity was discovered and marketed by these countries in the period 1961–1990. Over the past decade, important changes have occurred in this group, which includes some of the world's biggest exporting countries. India, for example, has a rapidly growing pharmaceuticals biotechnology market currently estimated to be worth over US$ 1 billion, and in 1999–2000 spent some US$ 66 million on medicines R&D, up from US$ 2.2 million in 1976–77.[1]

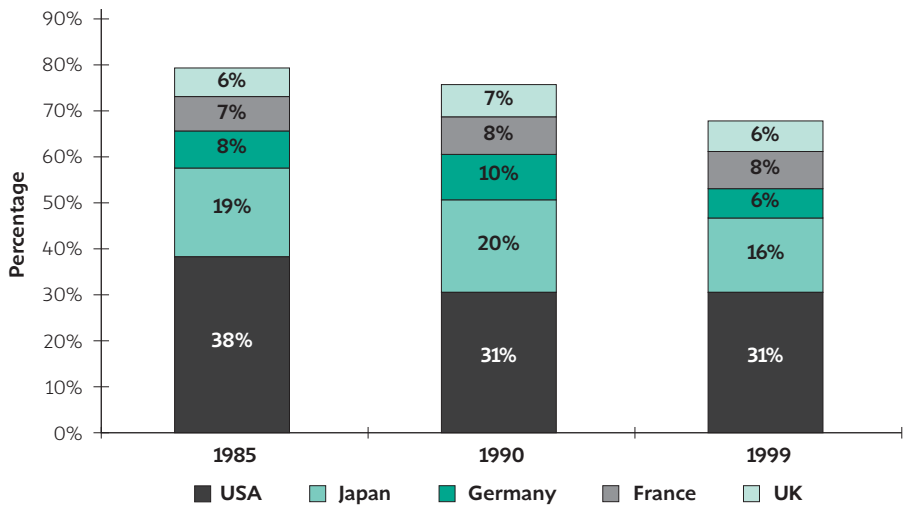
Elsewhere, 97 countries have a domestic medicines industry based on reproducer firms, manufacturing branded or commodity generics. While the majority (84) of these manufacture finished products from imported ingredients, 13 countries (including Brazil, Egypt, Norway, Turkey and Indonesia) are considered to have industries which make both active ingredients and finished products.

Figure 1.3 shows the share of total pharmaceutical production in each of the five top producing countries from 1985 to 1999. The combined share of these countries fell from 78% of total pharmaceutical production in 1985 to about 67% in 1999 while both Switzerland and Italy increased their output to about 4.5% each, just behind Germany and the UK, and just outside the top five. Since 1985, the top 10 medicines producing countries have accounted for 84%–88% of world production. The USA remains the biggest single producer (by value), accounting for almost one-third of total production, and Japan the second biggest. Together, these two countries produced 57% of the world's pharmaceuticals in 1985 and 47% in 1999. The USA lost some of its market share to Japan and

Germany between 1985 and 1990. During the period 1985 to 1999, the market share of the UK was 6%–7%, while that of France remained at 7%–8%.

FIGURE 1.3

Share of the top five countries in world pharmaceutical production, by value

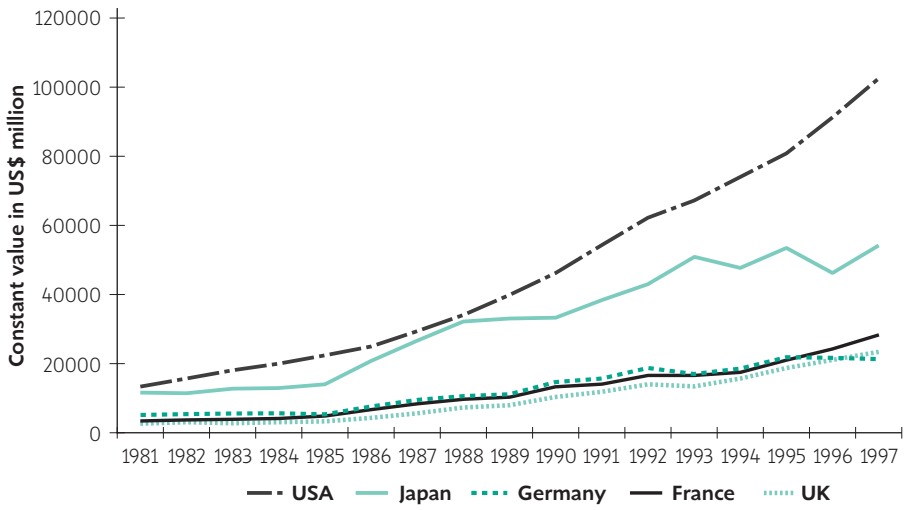


Source: WHO estimates based on data reported by UNIDO, OECD

Figure 1.4 shows pharmaceutical production in constant value terms (to base 1995) in each of the five major producing countries from 1981 to 1997. Production in the USA increased in each year throughout the period, while growth in the other four major producing countries was somewhat less regular.

FIGURE 1.4

Pharmaceutical production trends (constant US$ million), top five countries 1981–1997



Source: WHO estimates based on data reported by UNIDO, OECD

The concentration of value in industrialized countries occurs because the parent company headquarters of major transnational medicines corporations are located there. The parent enterprises control the assets of parts of the company elsewhere in the world, usually by

equity ownership. The top 10 companies by value of sales accounted for almost half of estimated world sales for 2001: US$ 175.3 billion out of a total of US$ 364 billion.[5] This figure is consistent with time-series data which show growing concentration in the share of these top companies, as **Table 1.2** shows. Further data on medicines sales and consumption is presented in **Chapter 4**.

TABLE 1.2 **Industry concentration: changing percentage shares by value in the world pharmaceutical market**

	1987	1990	1994	1997	2000
Number 1 manufacturer	3.42	3.99	4.9	4.6	7.3
Top 10 manufacturers	27.50	28.70	31.8	36.2	45.7

Source: IMS data, cited in J.Morris: Pharmaceuticals Global Insights, February 2002

Concentration is also apparent when the medicines market is analysed by therapeutic class and individual medicines or products. Sales of medicines in the top 10 therapeutic classes (**Table 1.3**) account for over 30% of global sales, and sales of the 10 best-selling medicines account for US$ 40.2 billion or 13% of global market share.[6]

TABLE 1.3 **Sales of medicines in the top 10 therapeutic classes, 2001**

Class	Total sales (US$ billion)	Percentage share in global sales	Percentage growth 2000–2001
Anti-ulcers	19.5	6	14
Cholesterol & triglyceride reducers	18.9	5	22
Antidepressants	15.9	5	20
Non-steroidal anti-inflammatory drugs (NSAIDs)	10.9	5	16
Antihypertensive drugs (Ca antagonists)	9.9	3	4
Antipsychotics	7.7	2	30
Oral antidiabetics	7.6	2	30
ACE inhibitors (plain)	7.5	2	5
Antibiotics (cephalosporins and combinations)	6.7	2	0
Systematic antihistamines	6.7	2	22
All 10	111.3	34	16

Source: SCRIP 2747, 17 May 2002, based on IMS World Review data

In value terms, therefore, 10 countries account for 85% of all pharmaceutical production and 10 companies for about half of all sales. The medicines in the top 10 therapeutic classes account for one-third of all sales and the 10 best-selling medicines for one-eighth of the world pharmaceutical market.

REFERENCES

1 Joshi RD. *The pharmaceutical industry in India - emerging trends.* Business Briefing, PharmaTech, 2001.

2 *Human development report, 2000.* New York, United Nations Development Programme, 2000.

3 Balance R, Pogany J, Forster H. *The world's pharmaceutical industries: an international perspective on innovation, competition and policy.* Report prepared for the United Nations Industrial Development Organization. Aldershot, UK, Edward Elgar, 1992.

4 *Financial Times,* 24 July 2002, *SCRIP* 2747, 17 May 2002.

5 IMS data, cited in *SCRIP* 2747, 17 May 2002.

2

RESEARCH AND DEVELOPMENT

SUMMARY

- Governments and pharmaceutical manufacturers are the main funders of the R&D of new medicines and other health products.
- Investment in health R&D is concentrated in the industrialized economies.
- In the second half of the 20th century, rapid progress was made in developing powerful new medicines. More recently, new developments in molecular biology and genetics hold great promise for the discovery of new medicines. Yet the number of new molecular entities being brought to market has slowed in recent years.
- Manufacturers attribute the high prices of new medicines to R&D costs and the risks of new product development. However, critics query the actual cost of new medicines development and point to the neglect of disease problems affecting poor populations.
- The pattern of new medicines R&D reflects market opportunities rather than global public health priorities. Only 10% of R&D spending is directed to the health problems that account for 90% of the global disease burden — the so-called 10/90 Gap.
- Redeployment of a small portion of current public and private R&D funds and/or private medicines marketing funds could make a major contribution to the development of new medicines for neglected diseases. New incentives are needed for such a shift to occur.

2.1 INTRODUCTION

Knowledge about the causes and treatment of illness expanded rapidly during the last century and research into new medicines played an important part in this growth. At the beginning of the twentieth century, aspirin was the only widely available modern medicine. In the 1940s, the first antibiotic, the first mass-produced antimalarial and the first antitubercular medicine were introduced. In the 1950s and 1960s, oral contraceptives were introduced, as well as medicines for diabetes, mental illness, many infectious diseases, cardiovascular disease and cancer. "By the 1970s effective medicines — though not always ideal — existed for nearly every major illness we know".[i] This progress continued throughout the 1980s and 1990s with the development of new drugs against HIV/AIDS.

Since the publication of *The World Drug Situation* in 1988, the development of medicines has undergone a major transformation — moving from a chemistry-based R&D process to molecular biology-based processes. Advances in the analysis of DNA have opened up the possibility of understanding the genetic causes of disease. As a result, many new

[i] Dr Gro Harlem Brundtland. Access to essential medicines as a global necessity: Seminar to mark the 25th Anniversary of the WHO Model List of Essential Medicines. Geneva, 21 October 2002.

genomics-based companies have emerged, recognizing the commercial potential of this knowledge for medicines development. Some of these are owned or partnered by major transnational pharmaceutical corporations, whose initial response to these new research opportunities was often slow.[1,2] The full implications for major pharmaceutical manufacturers of the potential use of advances in genetic science are not yet clear. One possibility is that discovery of new mechanisms of biological action could lead to the development of multipurpose medicines to treat several disease pathologies. Another is that "targeted" medicines may be developed, tailored exclusively to the treatment of population groups with the same genetic characteristics. The R&D and marketing implications of these alternatives are obviously very different. Data presented later in this chapter indicate that the recent shift in the medicines research and discovery process has not yet had an impact on the number of medicines entering clinical development.

New pharmaceutical products are a key component of improved knowledge in health, though several other components are also important. The Global Forum for Health Research,[3] in its comprehensive analysis of global funding for health research, identifies five principal content areas and resource flows:

1. Basic research
2. Research into health conditions, diseases or injuries
3. Exposures or other risk factors that impact on health (determinants)
4. Health systems research
5. Research capacity building.

This framework helps to put the R&D of new medicines into the wider context of new medical, or health improving knowledge. While content area number 5 (capacity building) may be seen as an input into the previous four, new knowledge in any of the first four areas can contribute to improvements in the health of individuals and populations. Research on the development of new medicines is most likely to fall into category 2 of this list.

2.2 TRENDS IN RESEARCH AND DEVELOPMENT

Table 2.1 gives estimates of the sources and amounts of global health research and development funding in 1998, totalling some US$ 73.5 billion. Private funding for R&D by the pharmaceutical industry is estimated to account for 42% of this total, slightly less than total public funding of health R&D by the high-income and transition countries. Private not-for-profit funding sources also make a measurable contribution to health R&D. In 1998, the two biggest were the Wellcome Trust (UK) and the Howard Hughes Medical Institute (USA). In 2000, the Bill and Melinda Gates Foundation was established in the USA, and has rapidly become a major source of global health research funds, spending over US$ 500 million on global health in 2002.

The 1998 estimates show a substantial increase from previous estimates for 1992 (US$ 55.8 billion), using a broadly similar approach. Some of this US$ 17.7 billion increase is from improved reporting. About one-third of the remainder is estimated to be a genuine increase.

TABLE 2.1 **Estimated global health R&D funding, current US$, 1998**

Source	Total in US$ billion	% of total
Public funding: high-income and transition countries	34.5	47
Public funding: low- and middle-income countries	2.5	3
Private funding: pharmaceutical industry	30.5 *	42
Private not-for-profit funding	6.0	8
Total	**73.5**	**100**

** A global estimate by PhRMA for 2000 gives a figure of US$ 35.4 billion*
Source: Global Forum for Health Research, 2002

The notion of a broad perspective on health R&D is relatively recent and so data are scarce. Country-specific data are generally limited to OECD member countries, and even these are not always collected in a consistent way.[4] **Table 2.2** uses OECD data to estimate overall spending (public and private) on health R&D in selected countries, and the proportion of this accounted for by the private sector pharmaceutical industry.

TABLE 2.2

Share of pharmaceutical industry R&D in total health R&D in selected countries, current US$ billions, 1988 and 1997

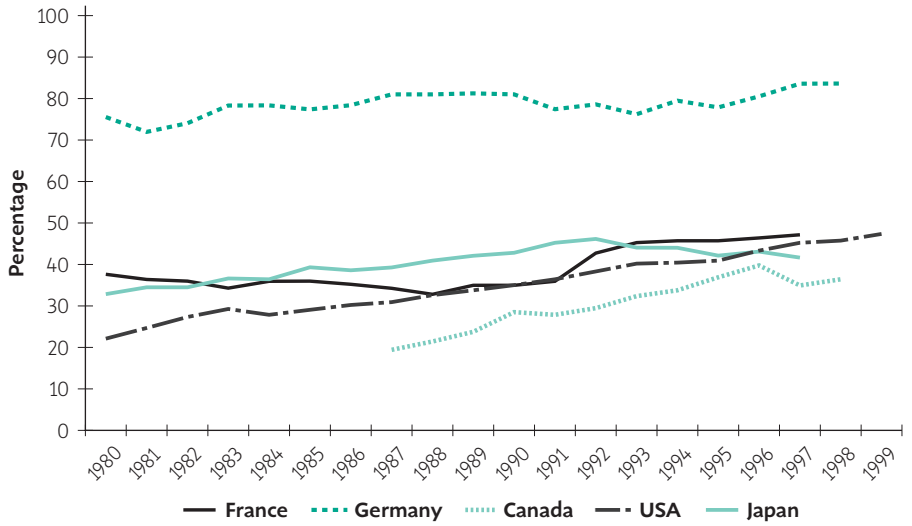
Country	Health R&D 1988	Pharmaceutical industry R&D 1988	Pharm. ind. as % total 1988	Health R&D 1997	Pharmaceutical industry R&D 1997	Pharm. ind. as % total R&D 1997
USA	16.0	5.2	32.6	34.2	15.5	45.3
Japan	7.9	3.2	41.0	12.7	5.3	41.6
France	2.7	0.9	32.9	5.1	2.4	47.2
Germany	1.6	1.3	80.9	2.5	2.1	83.5
Canada	0.5	0.1	21.5	1.1	0.4	34.9

Source: OECD Health database 2001

These data show that combined non-industry sources of health R&D remain dominant in the USA, Japan, France, Germany and Canada. However, in all five countries, industry-funded R&D in medicines has grown faster over the decade than total health R&D, with the growth in the industry R&D share being particularly fast in the USA, France and Canada. **Figure 2.1** shows longer-term trend data on industry spending on pharmaceuticals R&D, as a percentage of total health R&D, for these countries over the period 1980 to 1999. The gradual increase in the role of private pharmaceutical R&D in total health R&D in all countries is apparent. Most conspicuous is Germany, where private pharmaceutical R&D is 72%–84% of total health R&D. In the other countries, public and private funding are more evenly balanced.

FIGURE 2.1

Private expenditure on pharmaceuticals R&D as a percentage of total health R&D, selected countries, 1980–1999

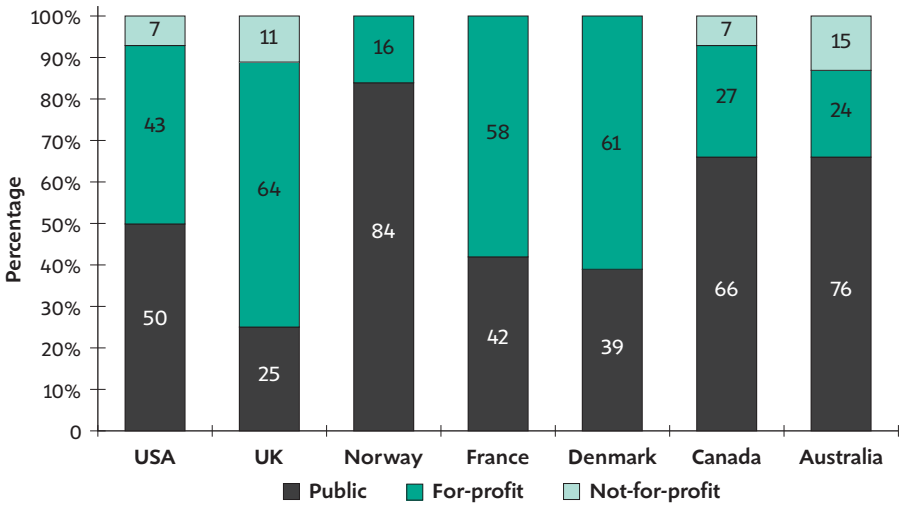


Source: OECD Health database 2001

An OECD study on health R&D broadly confirms the above results and shows much variety in funding patterns for health R&D in industrialized countries. Different public and private bodies contribute significantly to total health R&D. However, data sources on public funding are often fragmented and are seldom organized into the five categories of health R&D set out above. **Figure 2.2** groups the results of in-depth analyses undertaken in several countries on health R&D and are probably more accurate than the data in **Table 2.2**. The figure shows the relative importance of R&D funds from the public sector, industry and the not-for-profit sector in these countries in 1997.

FIGURE 2.2

Public, private for-profit and private not-for-profit shares in health R&D, selected OECD countries, 1997



Source: Measuring expenditure on health-related R&D, OECD, 2001

Among these seven countries, the UK's health R&D spending in 1997 is the most heavily dominated by private sector pharmaceutical research and Norway's the most dominated

by public spending. The presence of funding by not-for-profit agencies is visible in the USA, UK, Canada and Australia. The share of GDP allocated to health R&D in these countries in 1997 varied from a high of 0.4% in France and the UK, to 0.2% in the USA and Denmark, and 0.1% in Australia and Canada (1997 data are not available from the same source for Norway).

Table 2.3 shows the estimated value of health R&D spending and its percentage of GDP for six countries in economic transition (1998). All six countries allocate less than 0.25% of GDP.

TABLE 2.3 **Health R&D 1998, selected countries in transition**

Country	Health R&D, US$ million	Percentage of GDP for health R&D
Czech Republic	84.2	0.06
Hungary	165.5	0.16
Poland	267.2	0.08
Russia	188.2	0.02
Slovak Republic	43.0	0.08
Slovenia	56.3	0.24

Source: Global Forum for Health Research, 2001

Data on health R&D from some developing countries suggest that, as income levels fall, an even lower proportion of national income is devoted to this type of investment. **Table 2.4** shows that Thailand, the Philippines and Malaysia together spent some US$ 30 million in 1998 on health R&D. But the proportion of GDP (0.01%–0.049%) allocated for health R&D is generally much lower than in countries in transition, or in high-income market economies.

TABLE 2.4 **Health R&D, selected Asian developing countries, 1998**

Country	Health R&D, US$ million	Percentage of GDP for health R&D
Malaysia	6.9	0.01
Philippines	7.4	0.049
Thailand	15.7	0.012

Source: Global Forum for Health Research, 2001

2.3 R&D SPENDING BY THE PHARMACEUTICAL INDUSTRY

Innovation is an essential part of the identity of the major transnational pharmaceutical companies, which distinguish themselves as the "research-based industry" in contrast to the manufacturers of generic medicines. Innovative capability conveys scientific prestige, a competitive advantage over other manufacturers and, when a new product or process is sufficiently important, protection under national patent (intellectual property) law. This is of special importance as it allows the patent-holding company exclusive rights over the product for a defined period so that it is protected from competition, except where independent therapeutic advances are made in the same area by competitors using a

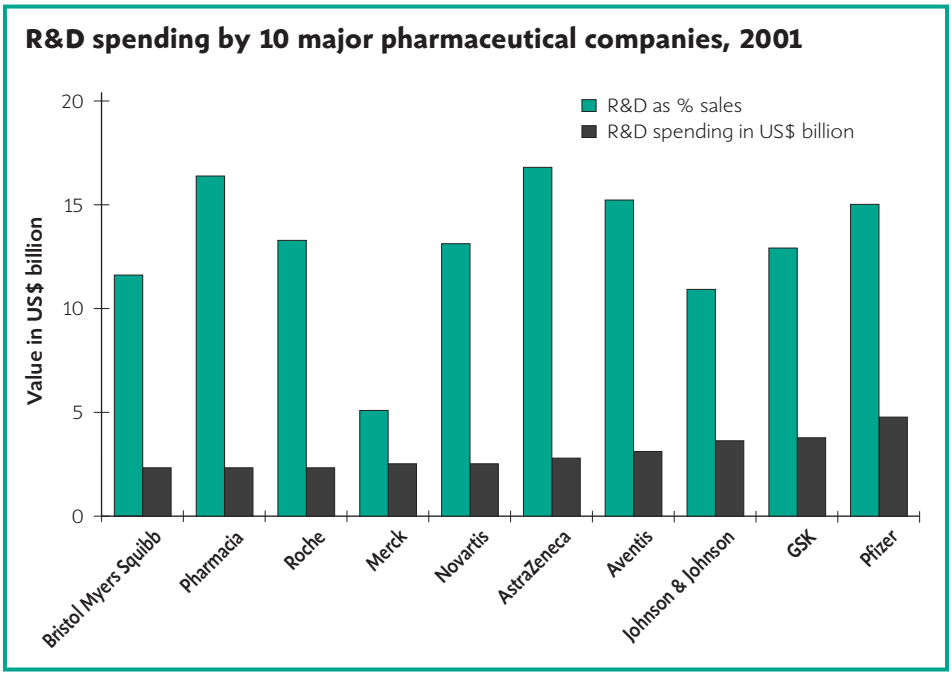
different technology. Patent protection allows the manufacturer to set prices according to what the market will bear, which is likely to be well above production cost for break-through medicines that are effective in tackling widespread and severe illnesses in high-income markets. The temporary monopolies which patents create are said to be necessary to reward firms for taking expensive risks in new medicines development. These can be extremely valuable to companies, as their efforts to prolong patent life beyond the original period show. However, critics query the actual costs of new medicines development and point to the neglect of disease problems affecting poor populations.[5]

The role of medicine patents in an era of increasingly global trade rules is a key issue in arguments over access to essential medicines, as demonstrated by the conflict over access to antiretroviral medicines for people with HIV/AIDS in low-income countries. Possible routes to achieving lower prices for essential medicines in low-income countries are discussed in **Chapter 7**. Patent protection is also a contentious issue in high-income countries, wherever access to effective treatment is impeded by high medicine prices.[6]

Following several years of rapid innovation from 1980 to the mid-1990s (measured by new drug approvals in the USA) there is increasing evidence of a recent fall in the output of global R&D into new medicines.[7,8] While R&D spending tripled between 1990 and 2000, the annual number of new medicines approved fell from its peak of over 50 in 1996 to 32 in 2000, the lowest output for over 20 years. Only one in about 5000 early drug candidates survive to reach market approval. It is considered likely that over the period to 2006, major companies will launch an average of 1.3 new active substances each per year. A forecast published in October 2002 indicated that only four companies were likely to have more than two new medicine launches in 2003.[9] According to an annual review of the industry in 2000, "Pipeline sizes remain static, the number of submissions is decreasing, and the output of new molecular entities has fallen to a 20-year low".[10]

After marketing costs, R&D is typically the second biggest item in the spending profile of large pharmaceutical companies. However, significant differences exist among the major companies in this respect, as **Figure 2.3** illustrates.

FIGURE 2.3



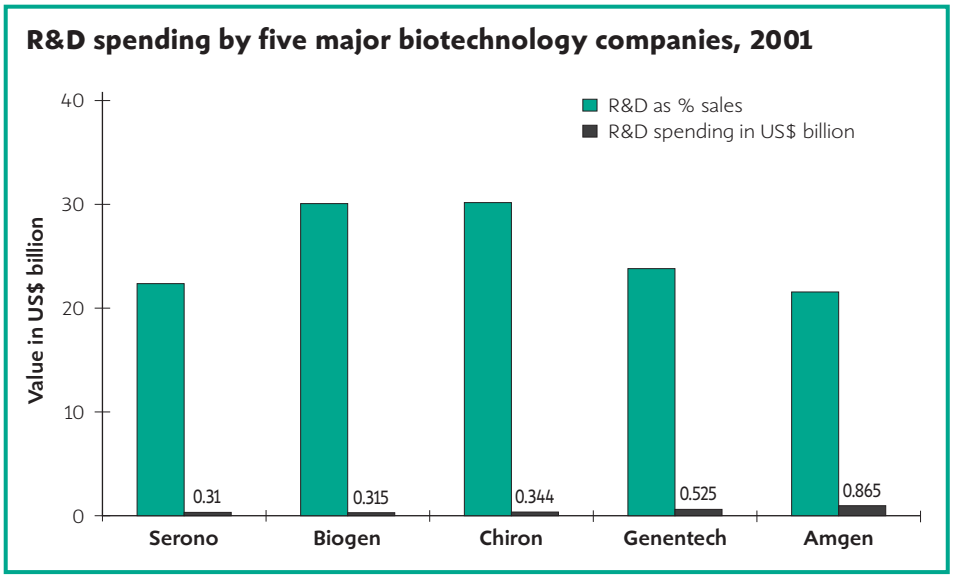
Source: Moses Z. The Pharmaceutical Industry Paradox. Reuters Business Insight, 2002

Pharmacia (merger with Pfizer completed in April 2003), AstraZeneca, Aventis and Pfizer all spend at least 15% of their sales revenue on R&D, whereas Merck spends about 5%, though the actual R&D budgets of these 10 big companies vary less than these percentage differences.

Many companies involved in the R&D of new medicines, particularly those specializing in biotechnology, are relatively small and some of these spend far higher proportions of sales revenue on R&D than the established major companies. Data for 1998 indicate that several biotechnology firms with sales of between US$ 4 million and US$ 140 million were spending more on R&D than they were receiving in sales revenue in that year, in one case 2.4 times more.[11] Although annual sales figures are volatile in this sector, such patterns are clearly not sustainable in the longer run unless companies have significant non-sales sources of revenue such as research grants or licence revenue. Such data indicate the levels of both risk and opportunity associated with new medicines discovery.

Figure 2.4 shows R&D spending as a percentage of sales in the five biotechnology companies with the largest research budgets for 2001. In these companies, the size of the R&D budget in relation to sales more closely resembles that of some major pharmaceutical companies.

FIGURE **2.4**



Source: Moses Z. The Pharmaceutical Industry Paradox. Reuters Business Insight, 2002

2.4 PHARMACEUTICAL INDUSTRY R&D INVESTMENT: WHERE THE MONEY GOES

Most of the R&D budget of the major companies goes on the different stages of clinical evaluation of new products. Pharmaceutical Research and Manufacturers of America (PhRMA) data for the USA in 1998 indicate the breakdown as:

Clinical evaluation:	40%
Basic research:	27%
Development of production process:	19%
Implementing regulatory requirements:	7%
Other:	7%

The increasing costs of R&D and recent falls in productivity have been factors in encouraging mergers. Much of the analysis of merger prospects is conducted in terms of companies' product pipeline size and complementarity. Rising R&D costs are also prompting manufacturers to develop strategic alliances with small research companies, particularly biotechnology companies, with partial equity, financing and commitments to buy products. Over 700 such alliances were consolidated in 1997 and 1998, compared with 319 in 1990 and 428 in 1992.[1] Contractual outsourcing of some research and product testing is also being used. In addition, companies are increasingly trying to implement rational drug design strategies to guide their R&D efforts.

In terms of product development, the diseases and conditions that affect people in the world's major markets largely determine where the pharmaceutical industry's investments go. The Global Forum for Health Research highlights the fact that only 10% of R&D spending is directed to the health problems that account for 90% of the global disease burden — the so-called 10/90 Gap.[3]

In 1998, over 60% of total R&D investment was allocated for the development of medicines for the central nervous and sense organs, cancers, endocrine and metabolic diseases and cardiovascular diseases. **Table 2.5** shows that in the period 1981–1996 there was some growth in investments in anti-infective and antiparasitic diseases, as indicated by the number of new compounds. This probably reflects the HIV/AIDS epidemic and the spread of antimicrobial resistance. However, no new class of antituberculosis medicine has been developed in almost 20 years despite the high burden of this disease. In 2003 Médecins Sans Frontières, with the support of several ministries of health and research institutes, and assistance from some pharmaceutical manufacturers, launched the Drugs for Neglected Diseases Initiative. Initially focussed on drugs for sleeping sickness, leishmaniasis and Chagas disease, this not-for-profit research organization is specifically concerned with developing new knowledge in areas with little profit-making potential.[12]

TABLE 2.5 **Compounds under R&D by therapeutic class, 1981, 1986 and 1996**

	Number of compounds per year		
Therapeutic class	**1981**	**1986**	**1996**
Anticancer	378	909	1394
Neurological	582	967	1314
Anti-infective	514	955	1167
Musculoskeletal	221	422	780
Diabetic	250	480	777
Cardiovascular	469	962	766
Respiratory	166	352	442
Gynaecological/urological (including sex hormones)	104	173	438
Blood and clotting	196	451	405
Dermatological	81	217	357
Hormones (excluding sex hormones)	124	204	154
Antiparasites	46	87	48

Source: SCRIP Yearbook 1999, World Drug Situation Report 1988

In 1999, 6046 products were in development worldwide and 10 companies accounted for over 15% of all new pharmaceutical products under development.[13] **Table 2.6** shows which companies had most R&D products in development in 1999.

TABLE 2.6 **Total number of products in R&D, top 10 companies, 1999**

Company	Total products in R&D 1999
Roche	122
SmithKlineBeecham	114
American Home Products	93
Glaxo Wellcome	92
Merck	89
Novartis	89
Hoechst Marion Roussel	84
Warner Lambert	84
Pharmacia & Upjohn	80
Eli Lilly	74

Source: SCRIP Yearbook 2000

However, many of the products under R&D may not be new molecules. Only 40 new molecular entities were launched in 1999.

Seen in the wider context as part of total health R&D, pharmaceutical companies and governments are the two major players in the development of new knowledge. Four decades of rapid advance in the second part of the twentieth century have been followed by a recent plateau, as the potential of new scientific approaches to aid medicine development slowly unfolds. A small number of national and corporate entities continue to be the major locomotives in new health and medicine knowledge, though this may change rapidly in the decades ahead.

The relevance of today's medicine product mix to the world's health problems could be greatly improved. Some initiatives are already working to this end. In the vaccines area, the Global Alliance for Vaccines and Immunization (GAVI) aims to enhance the commercial attractiveness of the market by stimulating demand in developing country markets, strengthening infrastructure and guaranteeing some purchasing of products. The idea is that a firm advance commitment to purchase safe and effective vaccines will reduce the risks faced by private sector manufacturers and help redirect research towards the vaccines that are a priority for low-income countries.[14] The Medicines for Malaria Venture (MMV), founded in 1999, is a public and private partnership concerned with the discovery, development and registration of new medicines for the treatment and prevention of malaria.[15] A Global Alliance for TB Drug Development[16] was begun in 2000, committed to delivering a new anti-tuberculosis medicine in a decade. And, as mentioned above, in 2003 the Drugs for Neglected Diseases Initiative[17] was launched, driven by public sector stakeholders, to develop or adapt drugs for patients suffering from important diseases with little apparent commercial market, such as sleeping sickness and Chagas disease. These mechanisms fill some important gaps between the opportunities which face commercial medicine manufacturers on the one hand, and the global burden of disease on the other.

In the meantime, the medicines market continues to be dominated by lifestyle-related and convenience medicines for richer populations at the expense of the medicine needs of the poor. This will not change without more extensive management of the global medicines market. Redeployment of a small portion of current public and private R&D funds and/or private medicines marketing funds could make a major contribution to the development of new medicines for neglected diseases. New incentives are needed for such a shift to occur.

REFERENCES

1 Moses Z. The pharmaceutical industry paradox: a strategic analysis of the countertrends of consolidation and fragmentation. *Reuters Business Insight,* Datamonitor, 2002.

2 Dyer G. A risky therapy. *Financial Times,* 24 July 2002.

3 *The 10/90 Report on health research 2001–2002.* Geneva, Global Forum for Health Research, 2002.

4 OECD health data, 2001.

5 Trouiller P et al. Drug development for neglected diseases: a deficient market and a public health policy failure. *Lancet* 2002 June 22;359:2188–94.

6 Mallaby S. Cadillacs for rickshaw riders. *Washington Post,* 7 October 2002.

7 Pollack A. Drug research yields a decreasing return. *New York Times,* 19 April 2002.

8 Taylor D. Fewer new drugs from the pharmaceutical industry. *British Medical Journal* 326 (7386) 408 26 February 2003.

9 Eli Lilly: bloom and blight. *The Economist,* 26 October 2002.

10 Ogg MS, van den Haak MA, Halliday RG. *Pharmaceutical investment and output.* CMR International, 2000.

11 SCRIP phamaceutical company league tables, 1991.

12 Médecins Sans Frontières, Press release 3 July 2003, (http://www.msf.org/countries/).

13 *SCRIP yearbook 2000. Vol.1: Industry and companies.*

14 *State of the world's vaccines and immunization.* Geneva, World Health Organization, 2002.

15 Medicines for Malaria Venture, (http://www.mmv.org).

16 Global Alliance for TB Drug Development, (http://www.tballiance.org).

17 Drugs for Neglected Diseases Initiative, (http://www.accessmed-msf.org/dnd/dndi.asp).

3

MEDICINES IN INTERNATIONAL TRADE

SUMMARY

- International trade in medicines grew rapidly between 1980 and 1999, from around US$ 5 billion in 1980 to almost US$ 120 billion in constant price terms.
- Trade is dominated by imports and exports among high-income countries. Industrialized countries are both the biggest individual exporters and the biggest importers of medicines. The biggest 10 exporting countries accounted for 80% of world exports, and the biggest 10 importers accounted for over 60% of all imports in 1999.
- This concentration grew between 1980 and 1999, with low- and middle-income countries losing their combined share of both exports and imports. However, several individual low-income countries, including India, Pakistan and Indonesia, expanded their export share during this period. Low-income countries manufacturing medicines produce predominantly for the home market.
- Major exporters among low- and middle-income countries export to other low- and middle-income countries. However China's exports are mainly to industrialized countries. Imports by low- and middle-income countries come mainly from industrialized countries.
- Many countries both import and export medicines. The USA and Japan, the world's two biggest producers, were also the biggest net importers in 1999.
- WHO recommends that medicines on a country's essential medicines list should not be subject to tariffs. However, in the 10 developing countries with the highest tariffs on imported medicines, the average tariff adds almost 23% to the price of active ingredients and over 12% to the price of finished medicaments.

3.1 INTRODUCTION

In 1999, international trade in pharmaceuticals represented about 1.8% of global exports and imports.[i] Total exports and imports were each worth some US$ 104 billion (**Table 3.1**). During the 1990s, trade in pharmaceuticals grew substantially faster than production. **Table 3.1** shows that, in constant price terms, the international trade in pharmaceuticals has expanded dramatically since 1980, growing three times faster than current prices indicate.

International trade in pharmaceuticals is dominated by the high-income industrialized countries. In 1999, they accounted for 93% of global exports and 80% of global imports,

[i] Pharmaceuticals or medicines in this chapter are defined in accordance with Standard International Trade Classification (Revision3) code 54, which comprises medicinal and pharmaceutical products (541) and medicaments, including veterinary medicaments (542). This definition includes active ingredients, intermediate products, bulk products and finished items. Fuller details may be found on the United Nations Statistical Office website at: http://unstats.un.org/unsd/cr/registry.

by value. This concentration in trade has increased since 1980. Between 1980 and 1999, middle-income countries' share of world exports fell, and the shares of both low- and middle-income countries in world imports dropped significantly.

TABLE 3.1 **Global trade in pharmaceuticals, US$ billion, 1980 to 1999**

Direction of trade	1980	1990	1999
Exports (current prices)	14.53	36.04	104.22
Exports (constant 1995 prices)	5.35	28.79	117.86
Imports (current prices)	13.54	34.64	104.80
Imports (constant 1995 prices)	4.98	27.67	118.53

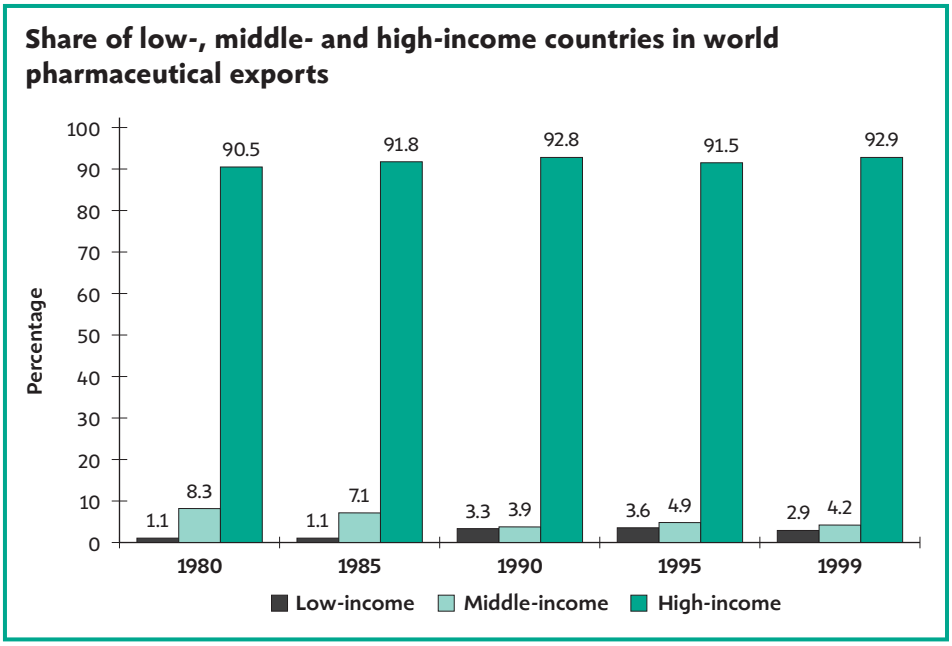
Source: Commodity Trade Statistics Section, ITSB, United Nation Statistics Division, New York, US Pharmaceutical Price Index

With the notable exception of Japan, the countries which contribute most to world trade – both in exports and imports – are also the world's major producers: the USA, UK, Germany and France. Japan, the world's second largest producer, continues to produce primarily for the domestic market and since 1980 has reduced its share of the world's pharmaceutical imports.

3.2 PHARMACEUTICAL EXPORT PATTERNS

Figure 3.1 shows the shares of countries by income level in world pharmaceutical exports from 1980 to 1999. The share of high-income countries rose from 90.5% to 92.9% of the world total while that of middle-income countries dropped from 8.3% to 4.2%. The export share of some low-income countries, such as India, Pakistan and Indonesia, more than doubled, from 1.1% to 2.9%.

FIGURE 3.1

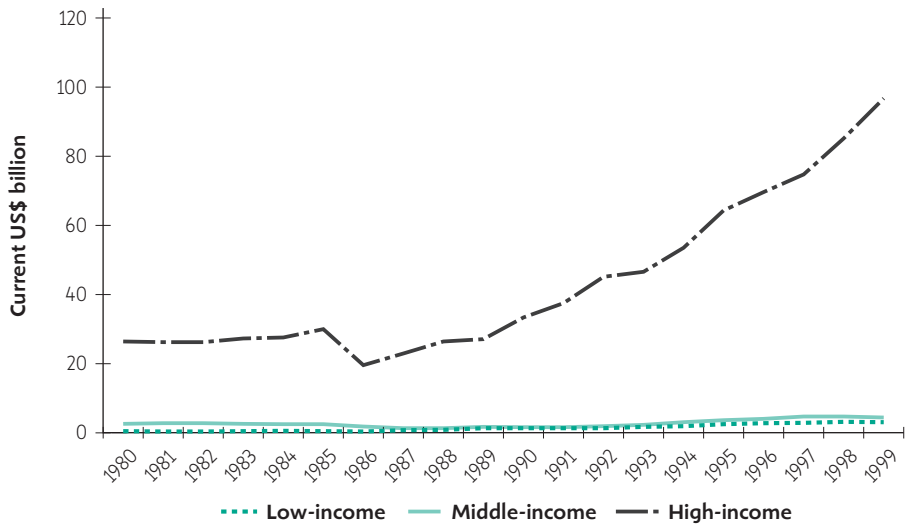


Source: WHO estimates based on data from Commodity Trade Statistics Section, ITSB, United Nations Statistics Division, New York

Figure 3.2 shows that the value of exports from high-income countries was relatively stable in the early 1980s, but began to increase steadily from 1986 onwards and rose steadily throughout the 1990s.

FIGURE 3.2

Pharmaceutical export trends in low-, middle- and high-income countries, current US$ billion 1980–1999



Source: WHO estimates based on UN Commodity Trade Statistics database

3.2.1 Leading pharmaceutical exporting countries

Table 3.2 shows that from 1980 onwards, over 70% of the world's pharmaceutical exports originated in just eight countries. By 1999 this figure was 79.7%. Four of these countries are also among the top five pharmaceutical producers; only Japan is missing from the major exporter group. **Figure 3.3** shows that Germany contributed the largest share of world pharmaceutical exports in 1980 and in subsequent years.

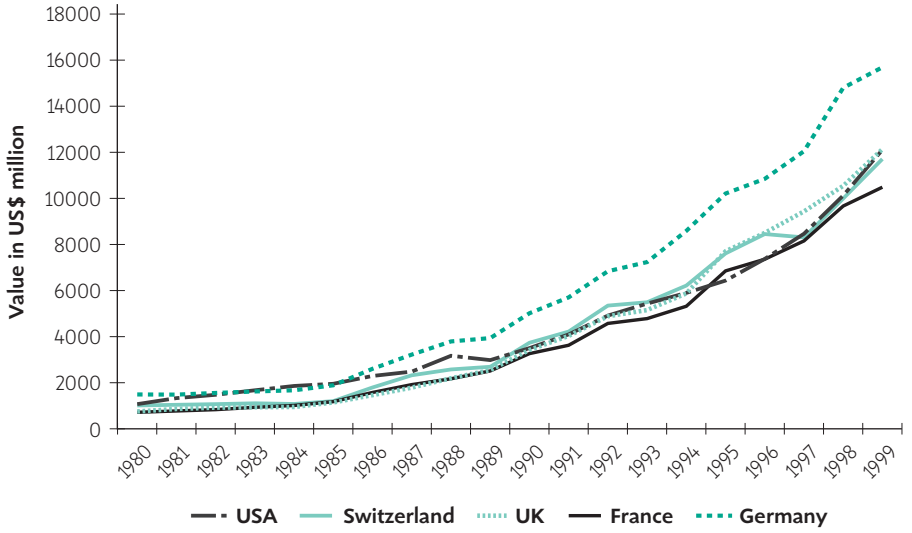
TABLE 3.2 **Top exporting countries, current US$ billion, 1980 to 1999**

Country (in 1999 rank order)	1980		1990		1999		
	Value	% world	Value	% world	Rank	Value	% world
Germany	2.272	15.6	5.8612	16.3	1	14.978	14.5
Switzerland	1.615	11.1	4.3595	12.1	2	11.452	11.1
USA	2.020	13.9	4.1032	11.4	3	11.071	10.7
United Kingdom	1.732	11.9	4.0404	11.2	4	10.053	9.7
France	1.497	10.3	3.6652	10.2	5	10.043	9.7
Belgium	0.670	4.6	1.6329	4.5	6	6.438	6.2
Italy	0.688	4.7	1.5169	4.2	7	5.607	5.4
Ireland					8	5.122	4.9
Sweden					9	4.010	3.9
Netherlands	0.619	4.3	1.3771	3.8	10	3.852	3.7
Top countries	11.113	76.4	26.554	73.7		82.626	79.8
World export	14.526	100	36.037	100		103.619	100

Source: WHO estimates based on database from Commodity Trade Statistics Section, ITSB, United Nations Statistics Division, New York

FIGURE 3.3

Trends in value of pharmaceutical exports in the top five countries, US$ billion, 1980–1999



Source: WHO estimates based on database from Commodity Trade Statistics Section, ITSB, United Nations Statistics Division, New York

Japan's situation shows that a big producer is not necessarily a big exporter. Countries with a manufacturing base differ widely in their propensity to export pharmaceuticals. Japan exported only 2% of local production in 1985, 3% in 1991 and 4% in 1997.

The low-income manufacturing countries produce predominantly for the local market. Even in India, with over 20 000 pharmaceutical manufacturers, where the export share of local production has tripled since 1985, less than 20% of total production enters international trade.

Major pharmaceutical exports from low- and middle-income countries in 1998 have been analysed according to their destination, with the results shown in **Table 3.3**. China is the only country in this group to export most of its pharmaceuticals to industrialized countries; all the other exporters supply mainly developing country markets.

TABLE 3.3

Pharmaceutical exports from low- and middle-income countries, US$ million, 1998

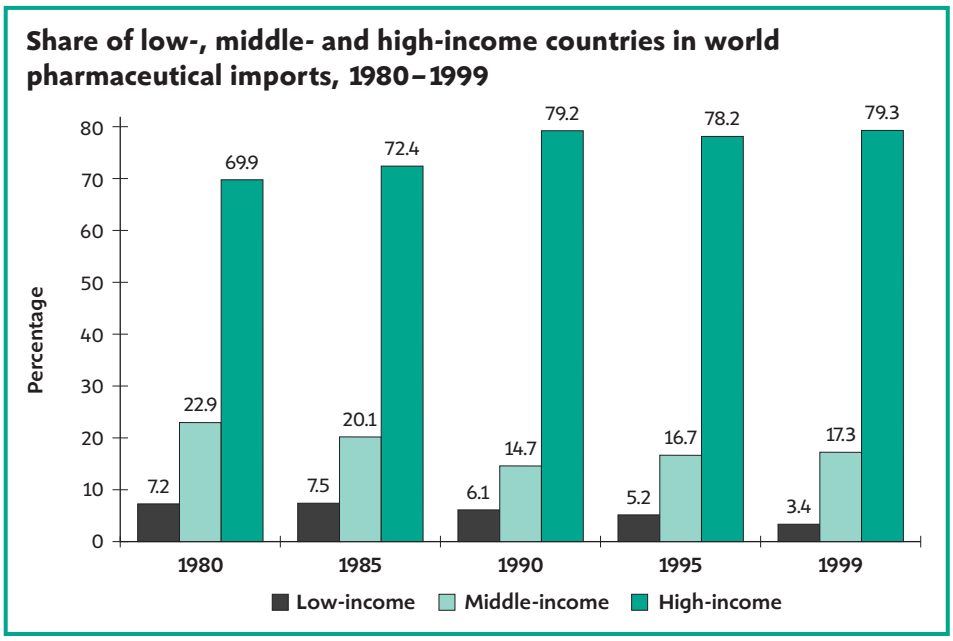
Exporter	Exports to industrialized countries	Exports to developing countries	Exports to developing countries as % of total
China	1079	592	35.4
India	288	576	66.7
Mexico	304	410	57.4
Argentina	25	277	91.7
Korea, Republic of	85	204	70.6
Brazil	64	183	74.1
Colombia	10	173	94.5

Source: Adapted from H. Bale: Consumption and trade in off-patented medicines. Commission on Macroeconomics and Health, Working Paper WG4:3, May 2001. http://www.cmhealth.org/cmh_papers &reports.htm#Working Group 4.

3.3 PHARMACEUTICAL IMPORT PATTERNS

Figure 3.4 shows the shares of countries, by income level, in world pharmaceutical imports from 1980 to 1999. The share of high-income countries rose from 69.9% of total imports to 79.3%. The shares of both low- and middle-income countries fell over the same period from a combined 30.1% of the world market to 20.7%. As with exports, trade became increasingly concentrated among the high-income countries in these two decades.

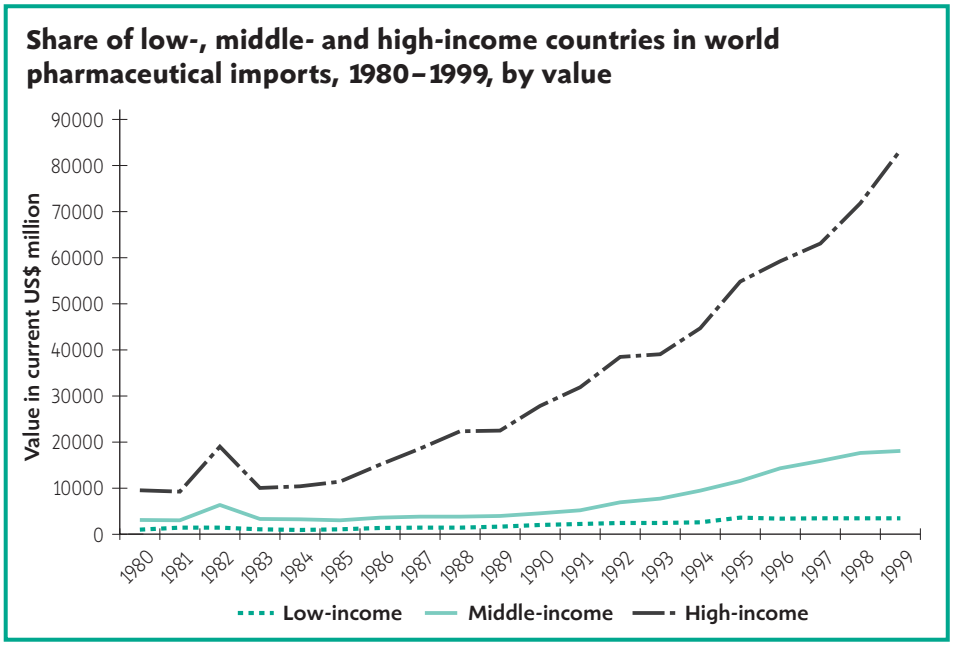
FIGURE 3.4



Source: WHO estimates based on database from Commodity Trade Statistics Section, ITSB, United Nations Statistics Division, New York

Figure 3.5 shows the value (in current prices) of pharmaceutical imports in each year, confirming the relatively weak growth of middle-income and particularly low-income country imports.

FIGURE 3.5



Source: WHO estimates based on database from Commodity Trade Statistics Section, ITSB, United Nations Statistics Division, New York

Table 3.4 identifies the principal importing countries, which include the five principal producers. The combined imports of these 11 industrialized countries accounted for 54% of world imports in 1980 and 66% in 1999. Germany was the world's leading importer in 1980 and 1990. Japan's position as an importer has fallen since 1990.

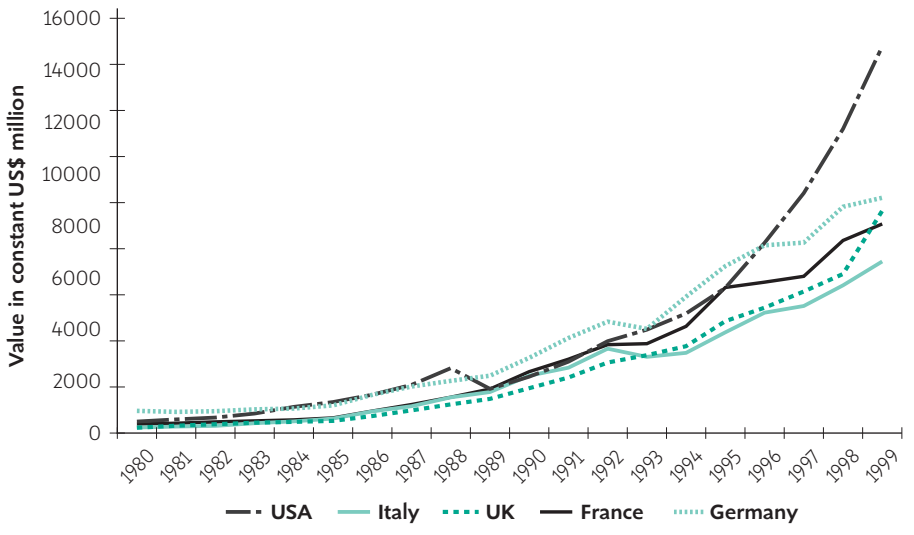
TABLE 3.4 **Leading pharmaceutical importing countries, current US$ million 1980–1999**

Country (in order of 1999 ranking)	1980		1990		1999		
	Value	% world	Value	% world	Rank	Value	% world
USA	803.1	5.9	2540	7.3	1	13649	13.0
Germany	1291.0	9.5	3396	9.8	2	8669.6	8.3
France	700.8	5.2	2646	7.6	3	7748.7	7.4
United Kingdom	516.9	3.8	2064	6.0	4	7746.6	7.4
Italy	652.6	4.8	2817	8.1	5	6195.8	5.9
Switzerland	411.0	3.0	1193	3.4	6	5050.5	4.8
Belgium	654.9	4.8	1510	4.4	7	5023.6	4.8
Japan	1074.2	7.9	2836	8.2	8	4593.4	4.4
Netherlands	568.9	4.2	1447	4.2	9	4174.6	4.0
Spain	245.2	1.8	975.7	2.8	10	3509.0	3.3
Canada	356.2	2.6	860.3	2.5	11	3237.6	3.1
11 top pharmaceutical importing countries	7274.8	53.5	22286	64.3		69599	66.4
World imports	13543.2	100	34636	100		104801	100

Source: WHO estimates based on database from Commodity Trade Statistics Section, ITSB, United Nations Statistics Division, New York

Figure 3.6 shows that, in addition to being the world's main exporter, Germany was the most important importer until 1996, when it was overtaken by the USA.

FIGURE 3.6 **Import trends, top five pharmaceutical importing countries, 1980–1999**



Source: WHO estimates based on database from Commodity Trade Statistics Section, ITSB, United Nations Statistics Division, New York

Bale (source for **Table 3.3**) also identifies the leading developing country importers of pharmaceuticals and the origin of these, summarized in **Table 3.5**. Pharmaceutical imports from other low- or middle-income countries account for a minority share in each of these countries. Import data from the 10 leading African countries (**Table 3.6**) show that Uganda and Tanzania were the only two countries which imported more from other developing countries than from industrialized countries in 1998. A possible explanation for this is the presence of strong essential medicines policies favouring generic imports in both countries. However, other factors, such as import prices and the marketing policies of manufacturers, may also contribute.

TABLE 3.5 **Pharmaceutical imports by low- and middle-income countries, in US$ million, 1998**

Importer	Industrialized country sources	Developing country sources	Imports from developing countries as % of total
Brazil	1325	263	16.6
Mexico	955	109	10.2
Argentina	638	139	17.9
Korea, Republic of	463	92	16.6
China	423	103	19.6
Colombia	294	202	40.7

Source: H. Bale, op. cit.

TABLE 3.6 **Top 10 pharmaceutical importing countries in Africa, in US$ million, 1998**

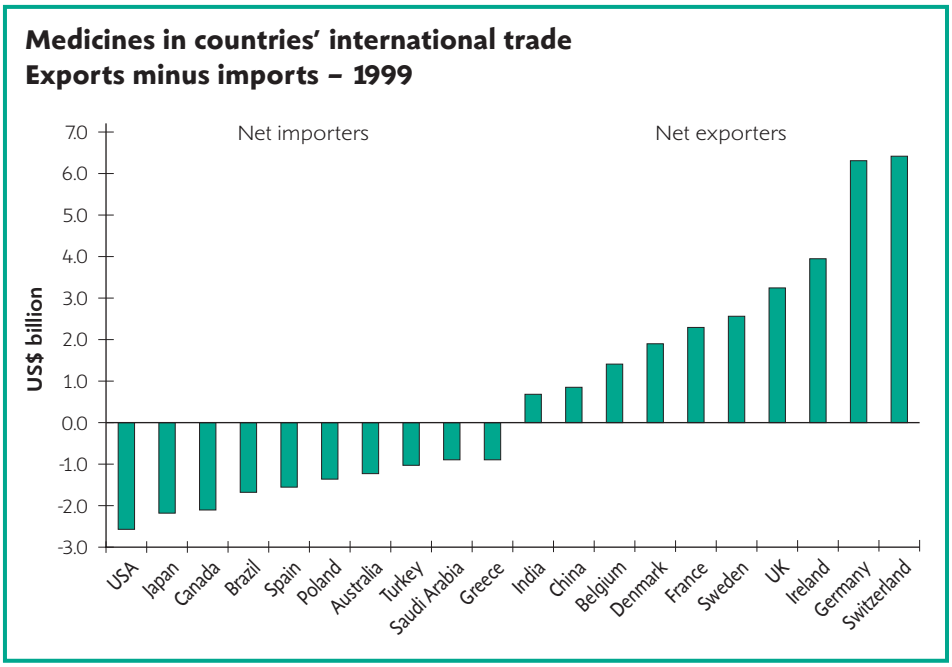
Importer	Industrialized country sources	Developing country sources	Imports from developing countries as % total
South Africa	565	36	6.0
Tunisia	164	8	4.7
Nigeria	79	39	33.1
Kenya	78	27	25.7
Uganda	20	34	63.0
Senegal	49	2	3.9
Tanzania	19	22	53.7
Mauritius	32	6	15.8
Madagascar	13	3	18.8
Togo	13	1	7.1

Source: H. Bale, op. cit.

3.3.1 Net pharmaceutical exporting countries

Many countries are both importers and exporters. **Figure 3.7** shows the principal net exporter countries (exports minus imports) in 1999. Switzerland and Germany were the biggest net exporters, and India and China both appear in the top 10 net exporter group. The USA and Japan, the world's two biggest producers, were also the biggest net importers in 1999.

FIGURE **3.7**



Source: ITC database

3.4 TARIFFS AND OTHER CHARGES ON IMPORTED MEDICINES

WHO recommends that medicines on a country's essential medicines list (EML) should not be subject to tariffs,[1] and many countries comply with this. While a source of revenue for governments, tariffs are also a barrier to trade. Governments may also use tariffs to protect a domestically-owned manufacturer against foreign competition. Whatever their purpose, tariffs raise the retail price of imported medicines and are therefore a potential barrier to access. Other aspects of fiscal policy, such as corporate taxation, can also affect the price to consumers, thus reinforcing the need for a risk-pooling approach to medicines financing as part of an overall health system strategy.[2]

In his review of consumption and trade in off-patent medicines, Bale assembled data up to 1999 on tariffs on active ingredients and on finished medicaments for highest and lowest tariff developing countries.[3] In the top 10 developing countries in the highest tariff group, the average tariff was 22.67% for active ingredients and 12.34% for finished medicaments. In the lowest tariff countries, the corresponding rates were less than 1% or zero.

The highest tariff rates observed may have a measurable influence on the final price to the consumer, and are clearly a potential threat to public health objectives. However, many countries exempt medicines from this form of trade tax. Other forms of domestic price "add-on", such as import, wholesale and retail margins, are likely to be more substantial components of final price — often adding 50%–80% to the factory gate or landed import price. **Table 3.7** summarizes data for 10 countries on mark-ups, margins and other charges on pharmaceuticals.

TABLE **3.7**

Percentage additions to manufacturers' CIF price on pharmaceuticals in 10 countries

	Sri Lanka 2000	Kenya 2000	Tanzania 2000	South Africa 2000	Brazil 2000	Armenia	Kosovo	Pune, India	Nepal	Mauritius
Import tariff	0%	0%	10%		11.7%	0%	1%	0%	4%	5%
Port charges	4%	8%	1%				4%	0%		
Clearance and freight		1%	2%						1.5%	5%
Pre-shipment inspection		2.75%	1.2%							
Pharmacy board fee			2%							
Importer's margins	25%						15%	25%	10%	
VAT				14%	18%	20%	0%			
Central govt tax								4%		
State govt tax					6%			9%		
Local town duty								1.5%		
Wholesaler	8.5%	15%	0%	21.2%	7%	25%	15%	10%	10%	14%
Retail	16.25%	20%	50%	50%	22%	25%	25%	15%	16%	27%
Total cumulative mark-up	64%	54%	74%	74%	82%	87.5%	74%	82%	48%	59%

Data refer to 2002 except where indicated. Source: Levison[4]

REFERENCES

1 *How to develop and implement a national drug policy.* 2nd ed. Geneva, World Health Organization, 2001.

2 *World health report 2000: health systems - measuring performance.* Geneva, World Health Organization, 2000.

3 Bale H. *Consumption and trade in off-patented medicines.* Commission on Macroeconomics and Health, Working Paper WG4, 2001. Http://www.cmhealth.org/cmh_papers&reports.htm#Working Group 4

4 Levison, L. *Policy and programming options for reducing the procurement costs of essential medicines in developing countries.* Http://dcc2.bumc.bu.edu/richard/IH820/Resource_materialsWeb_Resources/Levison-hiddencosts.pdf

4

WORLD PHARMACEUTICAL SALES AND CONSUMPTION

SUMMARY

- In 1999, the 15% of the world's population who live in high-income countries purchased and consumed about 90% of total medicines, by value. This concentration in the pattern of global sales and consumption has increased over the past 15 years, with the share of the low-income countries falling and that of the high-income countries growing. The market share of the USA alone rose from 18.4% of the world total in 1976 to over 52% in 2000.
- In low-income countries, the share of pharmaceuticals consumed fell from 3.9% of the total in 1985 to 2.9% in 1999, and their share of sales fell from 0.98% in 1990 to 0.64% in 2000.
- The global generic medicines market is worth over US$ 80 billion, about 30% of total sales, and is much larger than the commonly reported market in unbranded generics alone.
- Patterns of medicines consumption differ between high- and low-income countries. In high-income countries, "originator" (patented) pharmaceuticals account for two-thirds of sales and the share of these in total sales grew substantially from 1990 to 2000. In low-income countries, these pharmaceuticals account for only about one-third of total sales.
- Generic pharmaceuticals represent almost two-thirds of total sales in low-income countries and about 60% of sales in middle-income countries. Branded generics are much more important than unbranded generics in sales.
- Some countries in transition have experienced a rapid change in the composition of their pharmaceutical sales, with generics rapidly being replaced by originator brands or by pharmaceuticals made under licence from originators.
- Better data on many developing countries, and on China and India in particular, are urgently needed to improve knowledge about consumption patterns.

4.1 GLOBAL PHARMACEUTICAL CONSUMPTION

The preceding chapter has shown that international trade in pharmaceuticals means that many medicines are not consumed in the country where they are produced. In order to estimate the amount of medicines a particular country consumes, two approaches are used in this chapter: estimates of consumption and analysis of sales data.

Consumption (see Annex tables) is estimated by using the production and trade data presented previously. A country's consumption is measured as the value of its production plus the value of its imports and minus the value of its exports. For the sake of simplicity, zero stock and stock fluctuation are assumed. **Table 4.1** shows world pharmaceutical consumption from available data according to countries' level of income for the years 1985, 1990 and 1999.

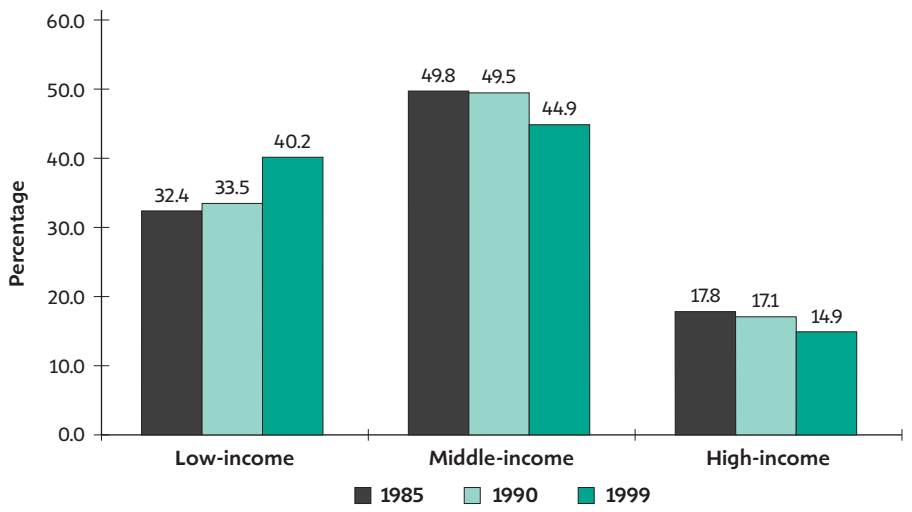
TABLE 4.1 **Global pharmaceutical consumption by countries' level of income, in US$ billion,* 1985–1999**

Country income level	1985			1990			1999		
	No.	Value	%	No.	Value	%	No.	Value	%
Low	8	3,512	3.9	8	4,675	2.7	8	9,222	2.9
Middle	14	5,884	6.6	19	13,121	7.5	18	18,614	5.9
High	22	79,006	88.9	20	156,578	89.8	22	289,822	91.2
Total	44	88,402	100[1]	47	174,374	100	48	317,658	100

*Differences due to rounding

Data for high-income countries is again much more complete than for low-income countries. Although the global picture is incomplete, it is clear that high-income countries dominate, consuming over 90% of the world's medicines in 1999. The data suggest that this dominance has even increased since 1985, with low- and middle-income countries' consumption accounting for a slightly smaller share of the total in 1999 than in 1985. When population is added to the picture, the pattern of consumption becomes even more skewed. **Figure 4.1** shows the distribution of population by countries' level of income in the same three years.

FIGURE 4.1 **Share of low-, middle- and high-income countries in world population**



Source: WHO estimates based on statistics of the UNDP Human Development Report (2001)

In 1985, the 18% of the world population living in the high-income countries consumed 89% of the world's pharmaceuticals: by 1999, the population share of these countries had fallen to 15% but their pharmaceutical consumption had grown to 91% of the total.

4.2 WORLD SALES OF MEDICINES

Information on sales provides an additional measure of the consumption of pharmaceuticals. **Production** measures the output of all manufacturers. We have defined **consumption** to be domestic production plus imports and minus exports. Globally, production and consumption totals should be similar, with only inventories accounting for differences.

The sales data reported here are provided by IMS Health, and are based on manufacturers' sales to wholesalers and hospitals as well as retail sales of prescription medicines.

TABLE 4.2 **Global sales of prescription medicines by countries' level of income, in current US$ billion, 1990 and 2000**

Country income group	1990 Value US $ billion	1990 %	2000 Value US $ billion	2000 %
Low (n=4)	1.25	1.0	1.81	0.6
Middle (n=23)	13.21	10.3	29.38	10.4
High (n=25)	113.28	88.7	251.30	89.0
Total (n=52)	127.74	100	282.49	100

Source: IMS Health, IMS MIDAS Customized Insights (October 2001)
The information contained in this study is a guide to sales and not a guide to consumption.

Non-prescription medicines, of which the great majority are over-the-counter sales for self-medication, accounted for an additional US$ 33.9 billion of sales in 2000. Adding together the prescription and non-prescription sales gives a global medicines total of just over US$ 316 billion in 2000, which compares reasonably with the calculated 1999 consumption total of US$ 317.6 billion in **Table 4.1**.

Available data on global medicine sales show a similar pattern of skewness towards high-income countries as do production and consumption data. In 1999, 15% of the world's population lived in high-income countries, 49% in middle-income and 36% in low-income countries. Once again, the disparity between sales and population is dramatic: at the top end, approximately 15% of the world's population bought almost 90% of the world's medicines; at the bottom end, over one-third of the world's population bought less than 1% of the world's pharmaceuticals. For the half of the world's population who live in middle-income countries, their share in total sales accounted for a little over 10% in 2000. **Table 4.3** shows a remarkable concentrating trend in the global shares of both individual countries, such as the USA and Japan, and of the top 10 markets as a group, which accounted for 62.4% of global sales in 1976 and 98.7% in 2000. **Table 4.3** also shows strong concentration even within the high-income countries. In 2000, over 95% of global sales were concentrated in the top 10 pharmaceutical markets: USA, Japan, France, Germany, UK, Italy, Spain, Canada, Brazil and Mexico. In India, which was in the top 10 in 1985 but not in 2000, sales were estimated to be US$ 3.4 billion in 2000.

TABLE 4.3

Top 10 pharmaceutical markets in the world, in current US$ billion

Country	1976		Country	1985		Country	2000	
	Value	% world		Value	% world		Value	% world
USA	7.90	18.4	USA	26.45	28.1	USA	149.5	52.9
Japan	4.02	9.3	Japan	14.04	14.9	Japan	51.5	18.2
Germany	3.41	7.9	Germany	6.00	6.4	France	16.7	5.9
France	2.70	6.3	China	4.70	5.0	Germany	16.2	5.7
China	2.60	6.0	France	4.47	4.8	UK	11.1	3.9
Italy	1.90	4.4	Italy	3.67	3.9	Italy	10.9	3.9
Spain	1.32	3.1	UK	2.35	2.5	Spain	7.1	2.5
Brazil	1.21	2.8	India	1.78	1.9	Canada	6.2	2.2
UK	1.03	2.4	Canada	1.69	1.8	Brazil	5.2	1.8
Mexico	0.77	1.8	Brazil	1.41	1.5	Mexico	4.9	1.7
Top 10	26.86	62.4	Top 10	66.56	70.8	Top 10	279.3	98.7
World sales	43.05	100	World sales	94.10	100	World sales	282.5	100

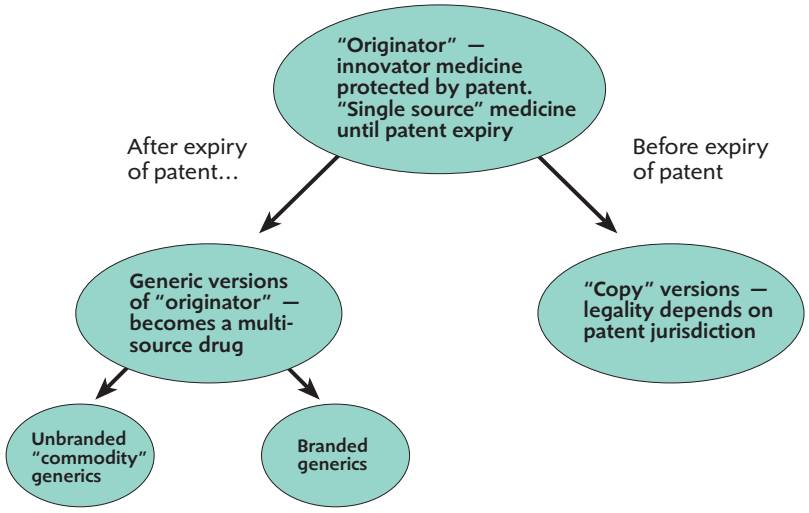
Source: World Drug Situation 1988 and IMS Health, IMS MIDAS Customized Insights (October 2001)
The information contained in this study is a guide to sales and not a guide to consumption.

4.3 THE SHARE OF ORIGINAL BRANDS, OTHER BRANDS AND UNBRANDED GENERICS IN TOTAL SALES

The pharmaceutical market consists of several distinct sub-markets, characterized by very different degrees of competitiveness. **Figure 4.2** indicates schematically some of the major components of the pharmaceutical market.

FIGURE 4.2

Major components of the medicines market



Innovative pharmaceutical products with patent protection (hereafter referred to as "original brands") are protected from competition in the jurisdiction of the patent for the life of the patent. Legal competition in this sub-market is limited to competition by "therapeutic equivalent" medicines with either a different composition or manufacturing

process from the original brand. At the other end of the spectrum are some generic pharmaceuticals known as "commodity generics". Generics in general are pharmaceutical products usually intended to be interchangeable with the originator product, marketed after the expiry of patent or other exclusivity rights and usually manufactured without a licence from the innovator company. This large category includes pharmaceuticals that were formerly patent protected, but whose patent has expired. It also includes pharmaceuticals that have never been patented, as well as copies of patented pharmaceuticals in countries without such a patent. Whether such copies are legal or illegal depends on the patent jurisdiction in which such pharmaceuticals are manufactured.

A valuable sub-sector of the generics market is generic medicines with their own brand names, each manufactured by a single company and hereafter referred to as "other brands". Yet other generic medicines (commodity generics) are sold under the generic name and may be manufactured and marketed by many companies. This is a highly price-competitive sub-market, as buyers can choose among several sources of supply of chemically identical medicines. Many developing countries also have important markets in counterfeit medicines. A counterfeit medicine is defined as "one which is deliberately and fraudulently mislabelled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct ingredients, wrong ingredients, without active ingredients, with incorrect quantity of active ingredient or with fake packaging."[1] Though no precise figures exist on the scale of the counterfeit problem, it affects countries at all income levels and appears to be most widespread where the manufacture, importation, distribution, supply and sale of medicines are less effectively regulated and where enforcement is weak.

On the manufacturing side, the distinction between "research-based" (i.e. originator) companies and generic manufacturers is frequently blurred. Novartis and Merck, for example, both major innovator companies, have generics subsidiaries which account for important shares of the world's generics.

Recent changes in international trade law to strengthen the protection of intellectual property (patent) rights[2] have coincided with national policy changes in many countries to promote opportunities for competitive pricing of generic medicines. By 2005, patent rights on new medicines must be respected in all World Trade Organization member countries except those classified as "least developed", which have the possibility to negotiate extensions.

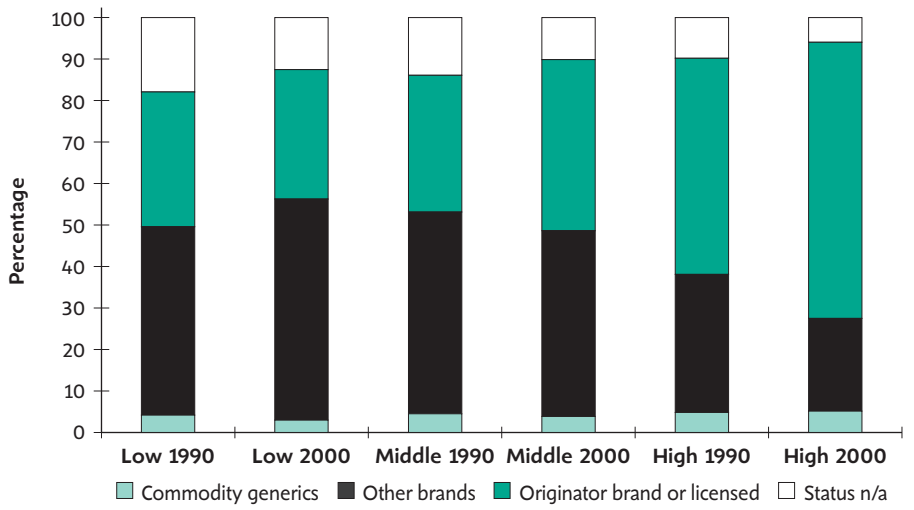
The complexity of the definition of generic medicines has led to considerable understatement of their importance in the global market. A recent study puts the size of the global generics market at about US$ 20 billion. However, like several other studies, it restricts the definition of generic to unbranded (commodity) medicines (SCRIP Global Generic Pharmaceuticals 2002). Using IMS's definition of "other brands" (branded generics and other copy drugs, both legal and "pirated") in addition to unbranded generics considerably expands this market to some US$ 87 billion in 2000, about 30% by value of total world sales. **Figure 4.3** shows generic market shares for 52 high-, middle- and low-income markets for which comparable data are available for 1990 and 2000.

Comparing sales data for 2000 across country income groups clearly shows a larger share of originator/licensed medicines in the total sales of high-income countries — about two-thirds in the latter compared with less than one-third in low-income countries and around 40% in the middle-income group. Comparing 1990 with 2000 sales, the data also show that the share of "other brand" generic medicines in total sales grew in low-income

markets but fell in middle- and high-income markets. Over the same period, the share of commodity generics in high-income markets grew slightly.

FIGURE 4.3

Originator and generic (unbranded plus other brands) shares in total sales, high-, middle- and low-income markets, 1990 and 2000



Source: IMS Health, IMS MIDAS Customized Insights (October 2001)
The information contained in this study is a guide to sales and not a guide to consumption.

In countries at all income levels, the period saw a growth in clarity regarding the legal status of medicines, probably a reflection of the strengthening of intellectual property rights referred to above. The share of the market for which patent status information was not available fell from 18% to 13% in low-income markets, from 14% to 10% in middle-income countries, and from 10% to 6% in high-income markets.

Comprehensive and reliable data for the decade from 1990 are unfortunately not available for some major markets, such as Russia, China and India. The rate of growth of "originator and licensed" medicines in some of the countries in transition to mixed economies has been far greater than the averages in **Figure 4.3**. In the Czech Republic, for example, "originator brand and licensed" medicines grew from 15.5% of the total market to nearly 45% from 1990 to 2000. Hungary, the Slovak Republic and the Republic of Korea also experienced faster than average growth in this category of medicines. In contrast, Pakistan's market showed the largest recorded shift away from originator and licensed medicines, and towards "other brands" over the decade.

Table 4.4 indicates that in 1997 the leading seven generic markets (unbranded plus branded) were all in high-income countries. The biggest of these, in absolute value, are the USA, Japan and Germany. Yet these major generics markets are in countries with very different health financing arrangements. In the USA, the incentive to keep medicine costs to patients at a low level derives from two pressures: a large population (64.5 million people, almost a quarter of the total population) who lack any insurance cover for medicine costs[3], plus increasingly cost-conscious insurers and providers for the insured majority. In Germany and Japan, by contrast, where most people have been covered by social insurance for a long time, pressure for cost-containment has come from insurers and government.

TABLE 4.4 **Leading generics markets by sales value, 2000**

Country	Value of generic market, US$ billion, 2000[1]	Generic share as % of total market (value)[2]	Generic share as % of total prescriptions volume (year)[2]
USA	31.7	11.0 (1997)	44.6 (1998)[3]
Germany	5.7	17.0 (1997)	40 (1988) www.inpharm.com[4]
France	4.4	2.0	3.0 (1996)[5]
UK	4.5	21.7 (1997)	47 (1998) www.inpharm.com[4]
Italy	3.0	27.9	
Brazil	2.4	47.5	
Spain	2.2	31.2	
Argentina	2.0	58.6	
Mexico	2.0	40.0	
Canada	1.9	15.0 (1997)	40 (1997)

Sources:
[1] *IMS customized study (value and generic share in total value)*
[2] *de Joncheere et al,* Drugs and money. *Amsterdam, IOS Press, 2003*
[3] *Scott-Levin. Source prescription audit (SPA), December 1999*
[4] *Reuters Business Insights*
[5] *SCRIP complete guide to the world generic drugs market, 1999*

TABLE 4.5 **Top six generics markets by share of total sales, 2000**

Country	Share of generic medicines in total sales
Bangladesh	70.9%
Dominican Republic	63.0%
Uruguay	61.5%
Republic of Korea	58.7%
Argentina	58.6%

Source: IMS customized study

For unbranded generics, the USA and the UK represent the major markets where generics are traded at very low prices as commodity items. In this relatively underdeveloped market, sales efforts are generally focused on pharmacists. In the branded generics markets, by contrast, marketing is oriented towards doctors to promote branded generics such as branded products, even if the emphasis is still on lower prices. IMS data for the USA gave the average price of an (unbranded) generic prescription medicine as US$ 14.70 in 2002, in contrast to the price of brand name drugs (both patent and branded generics) of US$ 77.02.[4]

Growth in the generics market is encouraged by the needs of governments and insurers to contain spending, and also by the time-limited nature of intellectual property protection. Public policy to encourage such prescribing and dispensing in the UK, for example, led to the level of generic prescriptions written increasing from 43% in 1992 to about 50% in 1996.

The expiry of patents also creates opportunities for more competition in the manufacture of commercially successful medicines. **Table 4.6** shows expected patent expiry dates for

16 products, together worth US$ 27 billion in sales (1999) and due to become off-patent before 2005.

TABLE 4.6 **Pharmaceutical products due to lose patent protection by 2005**

Product	Manufacturer	Patent expiry	1999 sales US$ billion
Clarithromycin	Abbott	2002	1.25
Lisinopril	AstraZeneca	2001	1.22
Omeprazole	AstraZeneca	2001	5.91
Ciprofloxacin	Bayer	2003/4	1.69
Pravastatin	Bristol-Myers Squibb	2005	1.8
Cefuroxime axetil	GlaxoSmithKline	2000/3	0.42
Nabumetone	GlaxoSmithKline	2002	0.45
Ondansetron	GlaxoSmithKline	2005	0.42
Fluoxetine	Eli Lilly	2001/3	2.61
Nizatidine	Eli Lilly	2002	0.35
Lisinopril	Merck	2001	0.81
Lovastatin	Merck	2001	0.6
Simvastatin	Merck	2005	4.49
Azithromycin	Pfizer	2002/5	1.3
Fluconazole	Pfizer	2004	1.0
Loratidine	Schering-Plough	2002/4	2.7

Source: Global Generic Pharmaceuticals, SCRIP Report BS1140, 2002

Considerable countervailing pressure is maintained by the manufacturers to promote sales of medicines with patent protection, as these typically command prices well above manufacturing cost. These include actions to prolong patent life, particularly in the most lucrative markets, as well as intensive marketing of patented medicines to prescribers and directly to patients, where this is allowed. The rapid fall in generic medicine shares in countries such as Hungary and the Czech Republic over the past decade (see above) is a partial indication of how powerful these pressures can be in markets with rising incomes and liberalizing policies.

4.4 THE WORLD'S LEADING PHARMACEUTICAL COMPANIES

The profile of the world's leading pharmaceutical companies changes rapidly. Mergers among major companies averaged almost three per year during the 1990s. As a result, some companies which were previously in the top league, such as Hoechst and Sandoz, had lost their separate identity by 2001.

Table 4.7 shows, however, that over 20 years, eight companies (six of them American) have consistently been among the 15 leading pharmaceutical companies in the world: Merck, Bayer, Pfizer, Bristol-Myers Squibb, Eli Lilly, Roche, American Home Products and Warner-Lambert. In 1998, nine out of the 15 leading world companies were American, compared with two Swiss, one German, one French-German, one Swedish-British, one Japanese, and one British-American.

TABLE 4.7 **The world's top 16 pharmaceutical companies by value of sales, 1977–2001**

Company (2001 rank order)	Country	Rank 1977	Rank 1985	Rank 1998	Rank 2001
Pfizer (incl Warner Lambert)	USA	8	6	5	1
GlaxoSmithKline	UK/USA	–	12	12	2
Merck	USA	2	1	1	3
Astra/Zeneca	Sweden/UK	–	–	4	4
Aventis (Incl Hoechst)	France/Germany	–	–	2	5
Bristol-Myers Squibb	USA	14–13	10	6	6
Johnson & Johnson	USA	–	–	9	7
Novartis (incl Ciba Geigy)	Switzerland	–	–	7	8
Upjohn/Pharmacia	USA	11	13	–	9
Wyeth/American Home Products	USA	6	2	11	10
Eli Lilly	USA	10	9	8	11
Roche	Switzerland	5	15	10	12
Bayer	Germany	3	5	3	13
Schering-Plough	USA	–	–	14	14
Abbott	USA	–	8	13	15
Takeda	Japan	15	–	–	16

Source: World Drug Situation 1988, SCRIP 2000, Company reports

Table 4.8 shows that in 1997 the Swiss company Novartis had captured the largest share of the world's generic drugs market, by value of sales. A year later, Novartis was ranked the seventh leading pharmaceutical company in the world on the basis of the total value of the company's sales of both branded and generic medicines. **Table 4.8** also reveals that American companies largely predominate among the world's leading generic medicines producers. In 1997, almost half of the top 15 generic medicine manufacturers were from the USA, the biggest generic market.

TABLE 4.8 **World's leading generic companies, 1997**

Rank	Company	Country	Sales (US$ million)
1	Novartis	Switzerland	981
2	Teva	Israel	875
3	ICN	USA	752
4	Merck	USA	651
5	Ivax (IVX Bioscience)	USA	602
6	Mylan	USA	555*
7	Apotex	Canada	500**
8	Schein	Germany	490
9	Ranbaxy	India	433**
10	Ratiopharm	Germany	430**
11	Hexal	Germany	420**
12	Novopharm	Denmark	400**
13	Barr	USA	377***
14	Alpharma	USA	329
15	Watson	USA	324

*Note: * year ending 31 March 1998; **estimated; *** year ending 30 June 1998*
Source: Hay and Atkinson: SCRIP's complete guide to the world generic drugs market, volume 2, 1999

Table 4.9 identifies the world's major biotechnology companies in 2001, a league table which has changed even more rapidly than that of pharmaceutical manufacturers.

TABLE 4.9 **World's leading biotechnology companies, 2001**

(total product sales in US$ millions)

1	Amgen	4015
2	Genentech	2202
3	Serono	1376
4	Genzyme	1224
5	Chiron	1141
6	Biogen	1043
7	Immunex	987
8	MedImmune	619
9	Celltech	437
10	IDEC	273

Source: Company reports

REFERENCES

1 *Counterfeit drugs: report of a joint WHO/IFPMA workshop.* Geneva, World Health Organization, 1992 (unpublished document WHO/DMP/CFD/92).

2 *Globalization, TRIPS and access to pharmaceuticals.* WHO Policy Perspectives on Medicines No.3. Geneva, World Health Organization, 2001.

3 Kreling DH et al. *Prescription drug trends: a chartbook*. Menlo Park, Calif., Kaiser Family Foundation, 2002.

4 As drug patents end, costs for generic drugs surge. *New York Times,* 27 December 2002.

5

GLOBAL TRENDS IN PHARMACEUTICAL SPENDING AND FINANCING

SUMMARY

- In a quarter of WHO's 192 Member States medicines spending was less than US$ 5 per person in 2000. Adequate and sustainable financing of medicines remains a remote prospect for almost half of the world's population.
- WHO's National Health Accounts (NHA) data, which provide a more comprehensive measure of pharmaceuticals financing than other available sources of data, suggest that actual global spending on pharmaceuticals is at least one-third higher than the figures reported in preceding chapters.
- Pharmaceuticals account for over 15% of measured global spending on health.
- In 2000, average per capita spending on pharmaceuticals in high-income countries was almost 100 times more than in low-income countries — nearly US$ 400 compared with slightly over US$ 4. At opposite ends of the spectrum, there is a thousandfold difference between what the highest spending and lowest spending countries spend on pharmaceuticals per capita.
- Private spending by households is today the principal source of pharmaceutical spending worldwide. This trend increased during the 1990s. Governments' share in pharmaceutical spending has fallen faster than their share in total health spending.
- While external assistance has boosted pharmaceutical spending in a small number of countries, most countries with high HIV/AIDS mortality are still spending less than US$ 5 per capita on medicines overall.
- A much greater role for public finance of medicines is needed to counterbalance market demand. Both low-income country governments and external funders have roles to play.

5.1 TOTAL SPENDING ON PHARMACEUTICALS: A NEW ASSESSMENT

The data reported in preceding chapters on pharmaceutical production, trade and sales offer an incomplete picture of total spending on medicines by households, governments and other sources of funding. In particular, the data in preceding chapters exclude most spending on traditional and alternative medicinal products, which are part of the pharmacopoeia in many countries and a sizeable share of medicines consumption in Asia and other parts of the world. The available data on production, trade and sales also exclude many of the mark-ups and price additions identified in the preceding chapter, and exclude medicines transactions which occur in informal markets, through unregistered and unlicensed suppliers. In many countries, these are also an important component of the overall medicines market.

As part of its work in assembling systematic evidence of health system expenditures through supporting the preparation of National Health Accounts (NHA)[i] in Member

[i] NHA provide a quantitative, systematic, consistent and comprehensive model of resource flows in health systems.

States, WHO is now able to make a first attempt at a comprehensive estimate of pharmaceutical outlays. The methodology is still under development and subject to some risks of double counting and omissions. However, these new figures are believed to be more reliable estimates of spending on pharmaceuticals. A finely tuned statistical system is not required to identify the imbalances in world spending on pharmaceuticals. The evidence gathered for this report, which embraces 90% of the world's countries and over 99% of world outlays on pharmaceuticals, lends additional rigour to the measurement of these inequalities. Moreover, anecdotal evidence suggests that the spending levels presented in this chapter are more likely to underestimate than to overstate the total level of pharmaceutical spending.

Initial results suggest that the value of resources allocated to medicines in 2000 is US$ 440 billion – at least one-third higher than the total production, trade and sales figures reported above. It should be remembered that this estimate is not a global aggregate, but is based on individual country health accounting estimates for 180 of 192 WHO Member States in 2000. Pharmaceutical expenditure estimates for a large sample of countries are contained in the statistical annex.

Table 5.1 summarizes WHO's estimates of measured pharmaceutical spending for all Member States, and by countries' level of per capita income in three clusters for 1990, 1995 and 2000.

TABLE 5.1 **Measured world pharmaceutical spending, by per capita income clusters, 1990–2000**

Income cluster	Measured expenditure level		Share of world total		Share of expenditure on health	
	US$ million at exchange rate		%		%	
	1990	2000	1990	2000	1990	2000
WHO Member States	245,000	440,300	100	100	14.2	15.2
High-income	196,019	345,758	80.2	78.7	13.0	13.8
Middle-income	41,916	82,740	17.1	18.8	22.5	24.8
Low-income	6,568	10,675	2.7	2.4	20.8	19.2

Source: WHO National Health Accounts (NHA) datafiles
Notes:
1. *Pharmaceuticals refers to medicines for human consumption.*
2. *The details do not add up exactly to 100% because the WHO total comprises 180 countries whereas the World Bank classification (see Note 3) includes only 161 countries. Data for an additional 11 WHO Member States were not available at the time this report was collated. Timor-Leste was not a Member State until 2002.*
3. *High-income countries refers to a World Bank classification of 33 countries (of which 23 from the OECD) with a per capita income (at average exchange rate in 1999) higher than US$ 9265. Among these, only the SAR Hong Kong is not monitored as a State entity in the WHO NHA files.*
   Middle-income countries refers to a World Bank classification of 70 countries with a per capita income (at average exchange rate in 1999) of between US$ 756 and US$ 9265.
   Low-income countries refers to the same World Bank classification of 58 countries with a per capita income (at average exchange rate in 1999) lower than US$ 756.

The data on total pharmaceutical spending in **Table 5.1** indicates that, at 15.2% of total expenditure on health in 2000, pharmaceuticals account for an important share of all health resources. According to the WHO *World Health Report 2003*, expenditure on medical goods and services constituted 8.1% of the combined GDP for the WHO Member States in

2000. Therefore, expenditure on pharmaceuticals for human consumption represents about 1.4% of world GDP.[i]

Table 5.1 suggests a slightly different balance in the distribution of pharmaceutical resources among countries than the sales estimates in **Chapter 4** (**Figure 4.1**). According to National Health Accounts (NHA) data, the high-income countries account for slightly under 80% (rather than 90%) of global pharmaceutical spending, the middle-income countries for about 19% (rather than 6%) and the low-income countries for 2.4% (rather than 2.9%). This reflects a better capture by NHA data of the character of both low-income country markets and the many more middle-income country markets with a large informal medicine branch in which traditional remedies have an important role. The inequitable overall pattern of spending emerges clearly.

Table 5.1 also indicates that the share of high-income countries has fallen slightly, mainly due to a recent growth in the share of middle-income countries. The share of medicines in total health spending is lowest in high-income countries but is higher in middle-income countries than in the low-income group.

Table 5.1 also shows that global pharmaceutical spending grew in nominal terms 7% per annum from 1990 to 2000. The increase was faster in the middle-income countries, about 8% per year compared with about a 6.5% increase over the same period in the high-income countries;[ii] the increase was slower in the low-income countries. Absolute figures provide a more balanced perspective of change. The increase in expenditure on pharmaceuticals has been heavily concentrated in the high-income cluster, an estimated US$ 150 billion against US$ 36 billion for the middle-income cluster and US$ 4 billion for the low-income cluster during the 1990s.

5.2 PER CAPITA EXPENDITURE ON PHARMACEUTICALS

Table 5.1 shows that, in 2000, the high-income countries (which comprised 14% of world population) accounted for 79% of the *measured* value of pharmaceutical outlays.[iii] A per capita analysis (**Table 5.2**) makes the contrasts between high- and low-income countries clearer. The 40% of the world's population living in low-income countries spent on average US$ 4.40 a year per capita on medicines, a figure which did not change significantly between 1990 and 2000. Elsewhere, the 14% of the world's population in high-income countries spent on average US$ 396 per capita in 2000 — almost 100 times more than those in low-income countries.

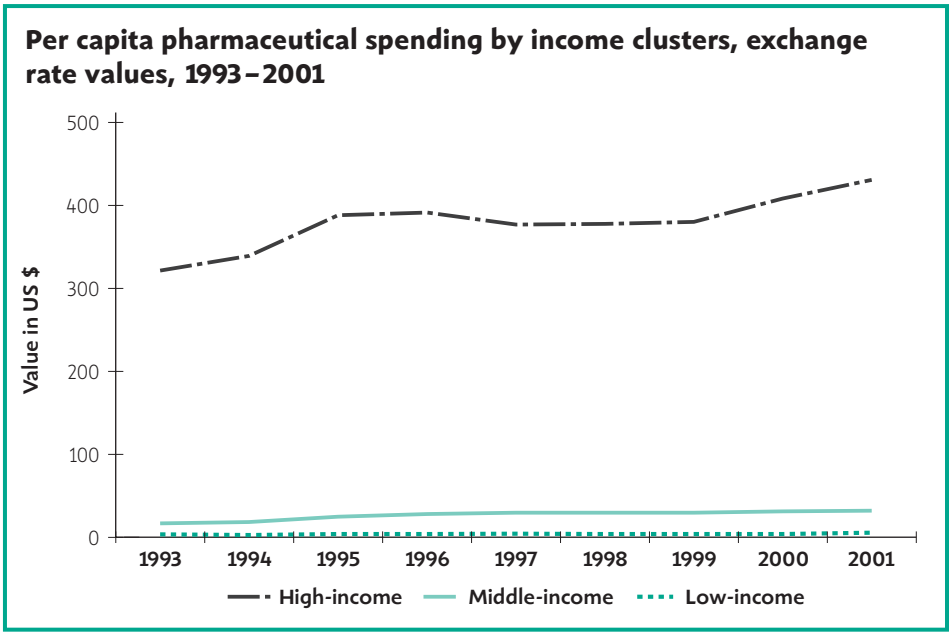
[i] This figure compares with the figure of 1.12% in Chapter 1, estimated by different procedures, for 1999. The ratios cited in the WHR 2003 are measured in *international dollars*, a *numeraire* that emulates economy-wide or GDP purchasing power parity values. At conventional average exchange rate, the health spending to GDP and the pharmaceutical spending to GDP ratios are 9.2% and 1.4% respectively. This report uses mainly exchange rate values, which are more relevant than international dollars to analyse pharmaceutical expenditure trends as these are widely traded at their actual exchange rate value. However, international dollars are more relevant to compare GDP and real health spending.

[ii] These averages mask large differences within each grouping, including within the OECD group, in which the United States experienced an above trend expansion of its pharmaceutical consumption offset by restraint in several other countries of that group.

[iii] This chapter relies on what countries disclose and on data collated from hundreds of official statistical sources, as well as private analyses of the health systems of the world and pharmaceutical usage. That measurement will evolve as more sources become accessible and greater comparability is possible. As of mid-2004, the data used are the most comprehensive set constructed.

Economic growth has been good overall in a number of middle-income countries. **Figure 5.1** shows trends in per capita spending on pharmaceuticals for 1993–2001. It confirms the widening gap between high- and low-income countries, and illustrates that average spending in the middle-income countries is far closer to that in low-income countries than in high-income countries.

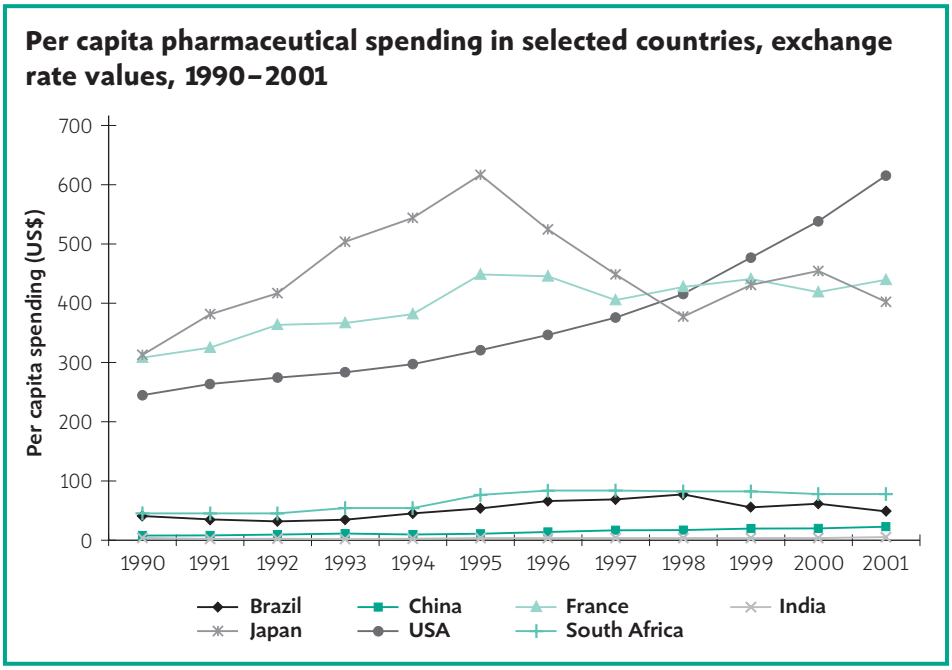
FIGURE 5.1



Source: WHO NHA datafiles

Figure 5.2 shows trends in a selection of large countries from 1990 to 2001, measured at exchange rates.

FIGURE 5.2



Source: WHO NHA datafiles

Expenditure on pharmaceuticals ranges from 10%–20% of expenditure on health in the richest countries and 20%–60% in the poorer countries. Using an illustrative benchmark of US$ 5 per capita in 2000 and based on the expenditure estimates currently available, one-quarter of WHO's 192 Member States had not attained that low threshold. Finding adequate financing for medicines remains a major public health challenge.

Global per capita average consumption of pharmaceuticals, estimated at US$ 74 in 2000, is well above the minimum figure suggested by the 1993 World Bank Report *Investing in Health*. That publication suggested US$ 12 a year per person for all medical goods and services in 1990, of which one-quarter (US$ 3 or about US$ 5 at 2000 prices) was suggested for spending on medicines.[i] The global average also exceeds the recommendation of the WHO Commission on Macroeconomics and Health (2002), which identified a minimum US$ 12–US$ 23 (based on 1997–1998 data adjusted for inflation). However, as **Table 5.2** shows, the global average masks huge differences in spending on medicines.

TABLE 5.2 **Dispersion in per capita pharmaceutical spending, by income clusters, 1990–2000** (US$ per capita at exchange rate)

Income cluster	Measured minimum		Measured maximum		Average expenditure	
	1990	2000	1990	2000	1990	2000
WHO Member States	< 0.5	0.6	330	549	49	74
High-income	50	84	330	549	240	396
Middle-income	2	4	79	198	18	31
Low-income	< 0.5	0.6	19	26	3.6	4.4

Source: WHO NHA datafiles
Notes:
1. *The observed values for individual countries are, paradoxically, subject to more vagaries than the averages for different groupings used in the other tables and graphs as they include outliers, some of which are known to be statistical flukes.*
2. *For a definition of the income clusters, see Table 5.1 note 3.*

5.3 GOVERNMENT AND PRIVATE ROLES IN PHARMACEUTICAL FINANCING

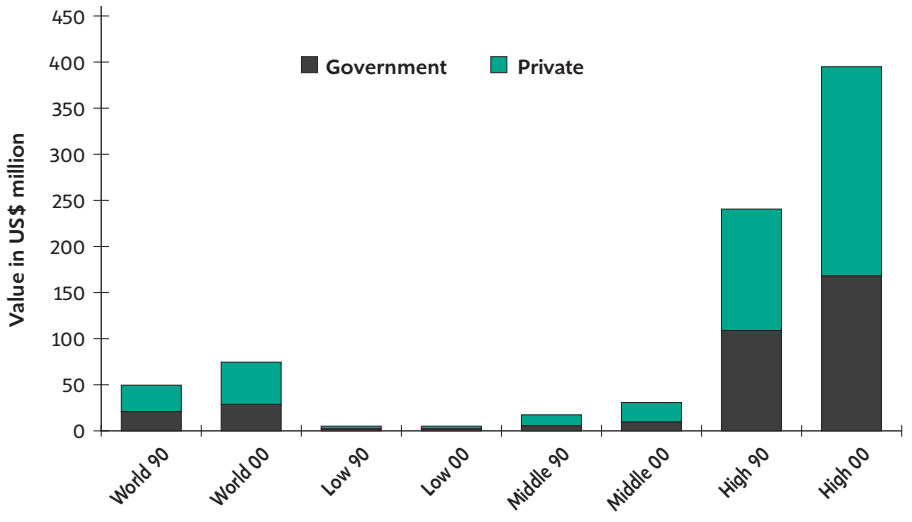
Figure 5.3 summarizes the relative size of government (public) and private per capita spending on pharmaceuticals in 1990 and 2000. It shows that, at the global level, the government share in pharmaceutical spending fell while the private component increased. The level of government spending on pharmaceuticals fell in both low- and high-income countries but increased slightly in middle-income countries overall.

Table 5.3 shows that, both globally and in all income groups, private spending by households is today the principal source of pharmaceutical expenditure, at 57.8% in high-income, 70.9% in middle-income, and 71.6% in low-income countries.

[i] Straight proportions in the strict sense are not applicable. In the wealthier countries, the range is from 9.2% to 35% of health expenditure whereas in the poorer countries it is from 5% to 70%. In dollar terms, in the countries with higher per capita expenditure on pharmaceuticals, the range is from US$ 84 to US$ 549 (as indicated in Table 5.3), while in the poorer countries it is from less than US$ 0.6 to US$ 26.

FIGURE 5.3

Average per capita US$ spending on pharmaceuticals by main financing entities, 1990 and 2000, by income clusters



Source: WHO NHA datafiles

TABLE 5.3

Private and government-funded expenditure on pharmaceuticals, 1990–2000 (% of total expenditure on pharmaceuticals)

Income clusters	1990		2000	
	Private	Public	Private	Public
WHO Member States	57.8	42.2	60.6	39.4
High-income	54.2	45.8	57.8	42.2
Middle-income	72.6	27.4	70.9	29.1
Low-income	71.4	28.6	71.6	28.4

Source: WHO NHA datafiles
Note: For a definition of the income clusters, see table 5.1 note 3.

Though high-income countries finance a larger percentage of pharmaceuticals from government sources than do low- and middle-income countries, the share of pharmaceutical financing falling directly on households has increased overall during the 1990s. This shift has occurred most sharply in high-income countries.

Table 5.4 shows government and private financing of pharmaceuticals in per capita terms for 1990 and 2000, using some of the data in **Figures 5.1** and **5.3**. The biggest per capita increase occurred in middle-income countries over the period. Several countries in this group experienced strong economic growth. Some, such as Egypt, expanded their publicly supported health insurance to include medicines coverage. The global average of US$ 74 per capita spending on pharmaceuticals represented 15.6% of total expenditure on health in 2000. Of that, 60.6% was financed by households and, marginally, by other private sources (health insurers, businesses and NGOs). Worldwide, the measured privately funded share was 57.8% in 1990. The dispersion between and within each income or geopolitical cluster is considerable and has been widening, as shown in **Tables 5.5** and **5.6**.

Government commitment to health care financing varies widely (*World Health Report 2002*, annex 5). High-income countries intervene considerably more in the delivery, financing and regulation of the health care market than is the case in low-income countries.

For countries in all income clusters, the government's share in total pharmaceutical spending (**Table 5.4**) has fallen — from 42.9% to 39.2%.

TABLE 5.4 **Private and government per capita expenditure on pharmaceuticals, 1990–2000** (US$ at exchange rate)

Income clusters	1990			2000		
	Private	Govt.	Total	Private	Govt.	Total
WHO Member States	28	21	49	45	29	74
High-income	130	110	240	229	167	396
Middle-income	13	5	18	22	8	30
Low-income	2.6	1	3.6	3.2	1.1	4.4

Source: WHO NHA datafiles
Note: For a definition of the income clusters, see Table 5.1 Note 3

In part, this may have occurred because, unlike "catastrophic" costs for an episode of inpatient care, medicine costs are a long string of smaller, recurrent bills. This makes them a more avoidable expense for insurers, including public insurers. Another reason may be that pharmaceutical access through pharmacies involves a wider range of both medicines and retail suppliers than through hospital-based (particularly surgical) activity. As a result, it is a less manageable object for public subsidy and regulation than hospital-based care where it is easier for governments to control spending. However, increased private funding of a wider range of pharmaceutical products does not necessarily equate with access to better medical care.

Behavioural patterns also have a key bearing on the consumption of medicines. Although pharmacies are scarce in most rural areas and in some suburban areas, they are the main source of non-prescription medicines for most people, provided the shelves are well-stocked. As a result, a great deal of self-diagnosis, self-medication and re-use of prescriptions occurs — often reinforced by pharmacists on the basis of very poor information about the properties of the medicines they sell.[i]

As **Table 5.3** shows, in each of the income clusters, households account for the majority of pharmaceutical spending. However, the impact of this varies greatly. While in the high-income countries, a prominent concern is lengthy waiting lists for elective surgery, the poor in low-income countries are more likely to be preoccupied with how many items on a prescription they can afford to buy with the little money they have.

During the 1990s, public finance constraints prevented most low-income countries from substantively improving their pharmaceutical benefits. Although some middle-income countries have succeeded in making modest improvements in health insurance cover, household disbursements for health overall have increased in nominal terms by 30% against a 2.8% increase in real income per head during that period.[ii]

[i] While pharmaceutical retailing is a quasi public service involving medical advice, it is also a retail trade in which a retailer addresses an uninformed client, often on the basis of poor knowledge about the objectives of medicines or their appropriate use. In therapeutic as well as in economic terms, the shift towards a greater reliance on private finance cannot necessarily be equated — as some textbooks may suggest — with improved allocation of resources, greater efficiency, greater effectiveness, greater empowerment of the stakeholders. When the functions of prescribing and dispensing are combined, as with "dispensing doctors" or "prescribing pharmacists", overprescribing is likely.

[ii] Measured in purchasing power parity/international dollars GDP per capita has increased substantially more than in figures at exchange rate US dollars: an estimated 22%.

5.4 POSSIBLE IMPLICATIONS OF THE GROWTH IN PRIVATE PHARMACEUTICAL FINANCING

Unregulated pharmaceutical markets are unlikely to lead to the safe use of medicines. Regulation of pharmaceutical production and distribution in high-income countries was strengthened in the 1960s, following a number of medicines-related accidents such as the thalidomide scandal. High-income countries generally have stronger regulatory control of their pharmaceutical and distribution industries, as **Chapter 9** highlights. Elsewhere, in low-income countries and in some middle-income countries, greater reliance on under-regulated suppliers of medicines poses a potential threat to safe, appropriate and effective use of medicines.

The growth in the share of private financing of medicines has meant a reduction in the role of governments in funding pharmaceuticals, except in middle-income countries. Although the available documentation offers only limited information on the breakdown of pharmaceutical spending, there does appear to be a public health focus in the share of pharmaceuticals financed by governments. In particular, there has been greater emphasis on vaccination, a focus on a list of essential drugs, access to medicines for "catastrophic" illnesses and widespread campaigns to improve the health status of populations worst affected by malaria, tuberculosis, onchocerciasis and a range of other infectious diseases.

TABLE 5.5 **Trends in government financing of pharmaceuticals, 1990–2000**

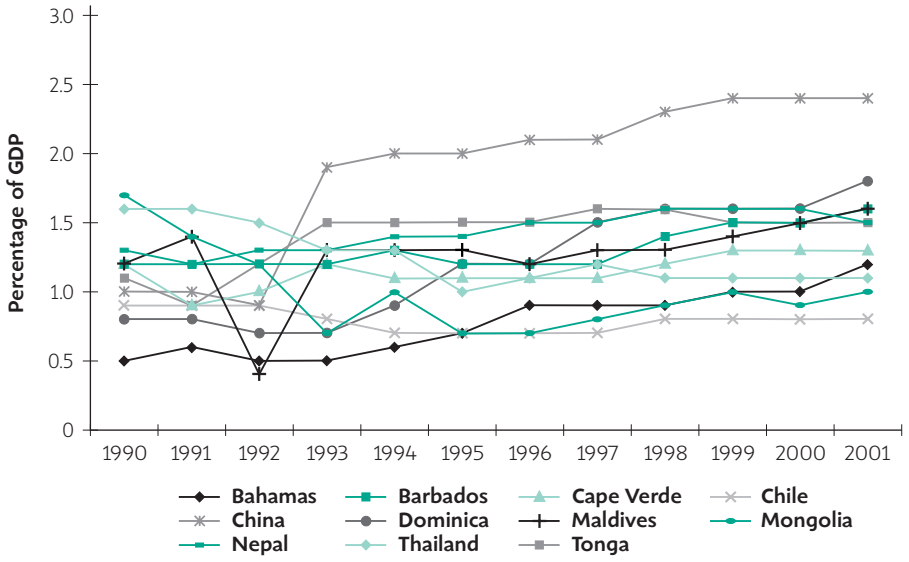
Income clusters	Medicines share in government spending on health (%)		Medicines share in total government spending (%)		Per capita expenditure at average exchange rate (US$)	
	1990	2000	1990	2000	1990	2000
WHO Member States	10.2	10.2	3.0	3.9	21	29
High-income	9.9	9.8	2.8	3.6	110	396
Middle-income	11.9	13.1	4.5	5.6	5	8
Low-income	21.5	16	3.5	3.6	1	1.1

Source: WHO NHA datafiles
Notes:
1. *General government comprises territorial authorities (central/federal, provincial/regional/state, local/municipal authorities) and autonomous / extra-budgetary funds (social security schemes, health boards and similar entities).*
2. *For a definition of income clusters, see Table 5.1 note 3.*

The recent reduction in public commitment towards medicines in total health financing reflects a public finance constraint not limited to health, but shared by all public programmes. In the low- and middle-income countries, the share of medicines in total government spending has been inching slightly upwards (**Table 5.5**), from 3.5% to 3.6% and from 4.5% to 5.6% respectively. However, in low-income countries government spending priorities in the health system have clearly emphasized other inputs, as the share of medicines in government health spending fell dramatically from 21.5% to 16%. This downturn has occurred in countries which have been more severely affected by heavy debt burden and/or major epidemics of diseases such as HIV/AIDS. **Figures 5.4** and **5.5** show pharmaceutical spending trends in GDP.

FIGURE 5.4

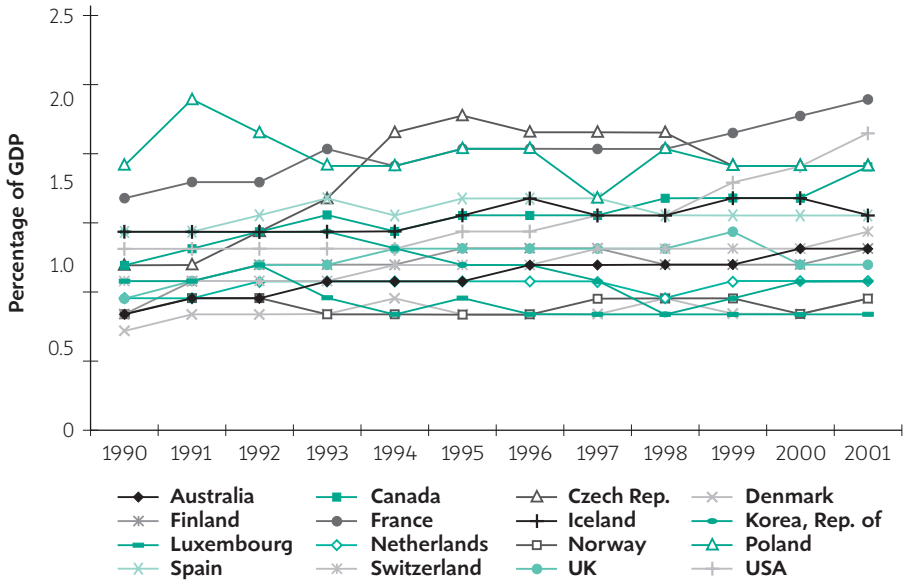
Pharmaceutical spending trends in selected middle-income countries 1990–2001 (percentage share in GDP)



Source: WHO NHA datafiles

FIGURE 5.5

Pharmaceutical spending in selected OECD countries, 1990–2001 (percentage share in GDP)



Source: WHO NHA datafiles

5.5 PHARMACEUTICAL CONSUMPTION: A GREATER ROLE FOR EXTERNAL FINANCING?

A number of low-income countries have been cushioned from the direct consequences of low economic growth on pharmaceutical spending by an increase in the level of transfers from high-income countries. These have been in the form of development loans and

grants for the supply of vaccines and some essential drugs, as well as for other targeted programmes.

However, important though it is, the impact of health funding by external agencies should not be overstated. Greater international solidarity has certainly helped to increase the supply of pharmaceuticals in some of the poorest countries. In Mozambique, for instance, in 1987 only 10.1% of recurrent expenditure on pharmaceuticals came out of budgetary sources and 89.9% out of external funding; in 2000, these ratios were correspondingly 18.9% and 81.1%.[i] Yet, in average per capita expenditure terms, the total outlay on pharmaceuticals in both years was only US$ 1 per head.

In only seven heavily aid-dependent countries (i.e. in which the share of external resources in total expenditure on health is over 20% of the resources available to the government) has external assistance raised per capita expenditure on pharmaceuticals above US$ 5 dollars per head: Belize, Djibouti, Equatorial Guinea, Kenya, Kyrgyzstan, Papua New Guinea and Zimbabwe.[ii]

TABLE 5.6 **HIV/AIDS treatment needs in relation to pharmaceuticals spending**

Country	Estimated treatment need 2003 (US$ thousands)	Percent of global treatment need	Total per capita pharmaceuticals expenditure 2000 (US$)
South Africa	934	15.8	31
India	616	10.4	3
Kenya	378	6.4	7
Zimbabwe	366	6.2	9
Nigeria	362	6.1	2
Ethiopia	299	5.0	1
United Republic of Tanzania	242	4.1	1
China	207	3.5	20
Zambia	196	3.3	5
Democratic Rep. of Congo	191	3.2	2
Malawi	136	2.3	3
Côte d'Ivoire	127	2.1	7
Cameroon	124	2.1	9
Mozambique	123	2.1	2
Thailand	107	1.8	21
Uganda	97	1.6	2
Rwanda	78	1.3	3
Burkina Faso	71	1.2	3
Sudan	62	1.1	4
Burundi	60	1.0	2
Ghana	58	1.0	4
Haiti	56	1.0	3
Guinea	56	1.0	3
Total	4946	83.6	

Sources: WHO NHA datafiles; WHO/HIV/AIDS 3 x 5 Strategic Framework

i Departamento Farmaceutico-MISAU Report. Maputo, 2001.

ii Unpublished details of the WHO National Health Accounts database, as reported in the World Health Report 2003.

A great deal of attention has been given to recent price arrangements that dramatically lower the cost of HIV/AIDS treatment in low-income countries. The costs of treatment for HIV/AIDS and accompanying opportunistic infections nevertheless remain relatively expensive, in excess of US$ 300 per annum in 2003. Yet, in only eight of the 23 countries which make up 80% of the global treatment need, was the average measured spending on pharmaceuticals above US$ 5 per head in 2000 (**Table 5.6**).

Pharmaceutical financing reveals the same patterns of gross imbalance observed in other aspects of the global medicines market place. Falling public support by governments for medicines has pushed the financial burden on to households in both high- and low-income countries, with attendant risks to public health objectives. While external support made a difference in some settings, adequate and sustainable financing of medicines remains a remote prospect for almost half of the world's population.

As experience with responses to the HIV/AIDS epidemic shows, the programmes developed to supply medicines at discounted prices have so far made little more than a dent in the accessibility problems faced by people in the low-income countries. A much greater role for public finance is needed to counterbalance the consequences of market income distribution. Both developing country governments and external funding agencies have roles to play.

6

NATIONAL MEDICINES POLICIES

SUMMARY

- Medicines are important both to a country's economy and to the health of its people, but these two interests can conflict.
- A clear medicines policy supported by credible institutions can ensure that all stakeholders know their roles, rights and obligations in relation to medicines, and that these are supported by monitoring and effective regulation.
- Putting policy into practice entails a three-part process: formulation, implementation, and monitoring and evaluation.
- WHO's World Medicines Situation survey of Member States shows that the number of countries with a national policy on medicines increased from only five in 1985 to 108 in 1999.
- Progress in this period in developing national medicines policies was most rapid in low-income countries (up from 4 to 54) and in middle-income countries (up from 1 to 43).
- However, almost two-thirds of the countries with a medicines policy document (official or draft) had failed to establish an implementation plan by 1999.
- International comparisons suggest that medicines policy is more difficult to implement in circumstances of economic stagnation or decline, and in countries where: the pharmaceutical market is mostly private; prices are unregulated; and where a local pharmaceutical industry exists.
- Poor selection of medicines and inefficient procurement systems invariably lead to shortages.

6.1 INTRODUCTION

Pharmaceutical markets are both complex and important and require careful stewardship. Medicines are important both to a country's economy and to the health of its people, but these two interests can conflict. National laws and regulations relating to medicine are often inconsistent and incomplete and, without an integrated framework, can frustrate the objectives of overall health policy. A clear medicines policy supported by credible institutions can ensure that all stakeholders know their roles, rights and obligations in relation to medicines, and that these are supported by monitoring and effective regulation.

WHO's guidance on national medicines policy is fully set out in a publication that outlines the policy process and the necessary supporting legislation, and identifies the principal components of a national policy.[1] A medicines policy document is important as it reflects formally the decisions, aims and commitments of government and others. A national policy on medicines outlines a country's goals and provides a framework for achieving them, setting out the roles and responsibilities of the main actors in both public and private sectors. Since 1990, many countries have shown their willingness to improve

people's access to essential medicines by formulating a national medicines policy, clearly setting out the country's objectives. Experience shows that such documents are most valuable when developed through a consultative process involving all interested parties. While recognizing that each country's situation may require specific goals, WHO proposes that the general objectives of medicines policy should be to ensure:

- The equitable availability and affordability of essential medicines
- The quality, safety and efficacy of all medicines
- Therapeutically sound and cost-effective use of medicines by health professionals and consumers.[2]

Box 6.1 summarizes the main stages in the process of medicines policy formulation.

BOX 6.1

Medicines policy formulation process: a checklist for policy-makers

- organize the policy process
- identify the main problems and stakeholders
- make a detailed situation analysis
- set goals and objectives
- draft text of policy
- consult on and revise draft text
- secure formal endorsement of the policy
- launch the national medicines policy

6.2 NATIONAL MEDICINES POLICIES: THE GLOBAL SITUATION

Table 6.1 shows that in 1999, out of 152 countries which responded to the survey question on national medicines policy, the majority (71%) had a national medicines policy supported by an official document: 44% had a document published within the last 10 years; 24% had a draft document; and 3% had an official document that was over 10 years old. The remaining respondents (29%) had no official medicines policy document.

TABLE 6.1 **Formulation of national medicines policies, 1999**

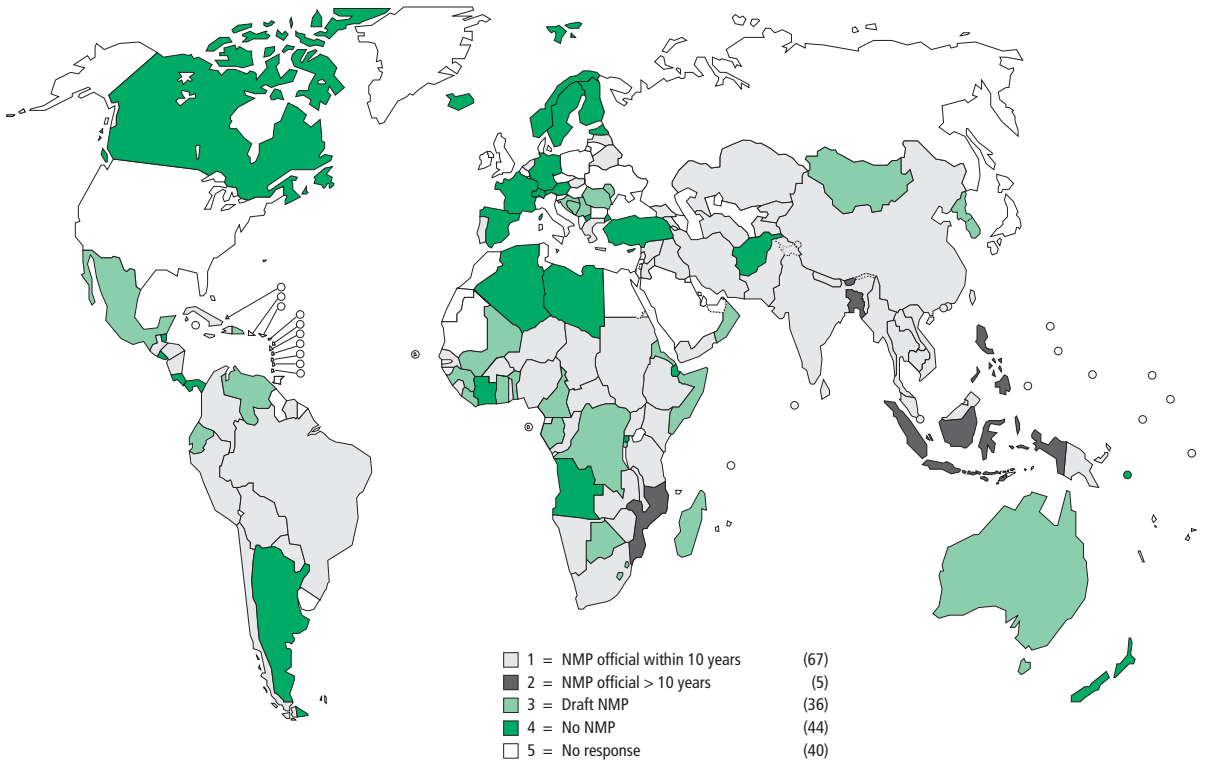
Policy formulation indicator	Number of countries	Percentage of countries (%)
Official national medicines policy document published within last 10 years	67	44.1
Official national medicines policy document more than 10 years old	5	3.3
National medicines policy document in draft	36	23.7
No document	44	28.9
Total	152	100.0

Source: World Drug Situation Survey (1999)

Figure 6.1 shows the geographical distribution of countries with a national medicines policy.

FIGURE 6.1

Formulation of national medicines policies worldwide, 1999



6.3 NATIONAL MEDICINES POLICIES AND INCOME LEVEL

Table 6.2 shows the state of national medicines policy formulation by countries grouped according to income level.

TABLE 6.2 **Formulation of national medicines policies in low-, middle- and high-income countries in 1999**

Status of national medicines policy document	Low-income		Middle-income		High-income		Total
	Number of countries	%	Number of countries	%	Number of countries	%	No.
Official document within 10 years	35	56	29	41	3	17	67
Official document > 10 years	4	6	1	1	0	0	5
Draft document	18	29	17	24	1	6	36
No document	6	9	24	34	14	77	44
Total	63	100	71	100	18	100	152

Source: World Drug Situation Survey (1999)

Table 6.2 shows a substantial correlation between the existence of national medicines policies and a country's level of income. The lower the level of a country's income the greater the percentage of countries with a national medicines policy document. Among

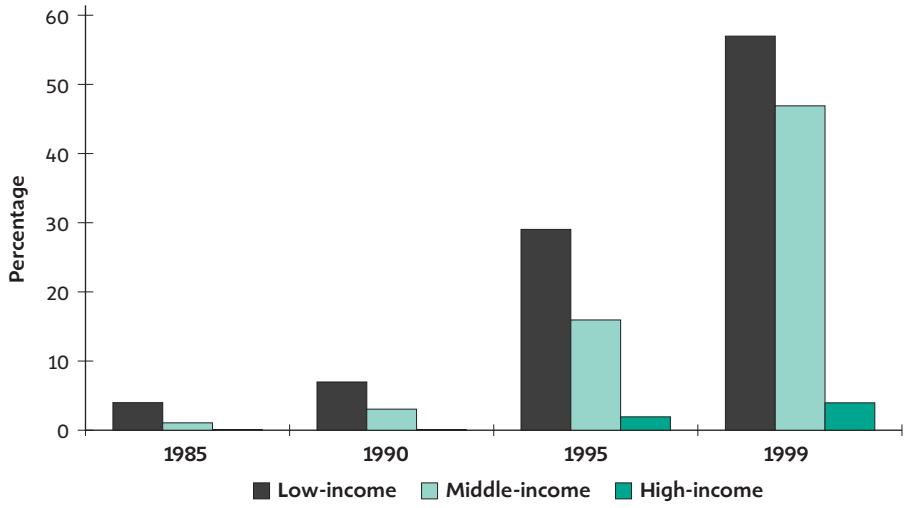
low-income countries, 90% of responding countries had official national medicines policy documents in 1999 compared with 66% for middle-income countries and only 22% for high-income countries.

WHO guidelines on national medicines policies were first published in 1988. **Figure 6.2** shows trends in the formulation of national policies from 1985 to 1999, by income level. It reveals that in the low-income group of countries, the number of countries with a national medicines policy grew from four in 1985 to seven in 1990, 29 in 1995 and 57 in 1999. In the middle-income group, the number went up from one in 1985 to three in 1990, 16 in 1995 and 47 in 1999.

In high-income countries, the formulation of national medicines policies began more recently, particularly in Europe, where only two countries reported having such policies in 1995 and four countries in 1999. However, many high-income countries have extensive laws, regulations and institutions corresponding to much of the implementation machinery of a national policy, without having the overall framework in the form of a written policy. For example, in the 1990s, the government of Australia began implementing several components of a national medicines policy, such as the development of a pharmaceutical benefits system to promote equitable and widespread access to care, the development and promotion of treatment guidelines and prescriber training. Steps were also taken to ensure the viability of a competitive national pharmaceutical industry. Only in 2000, these actions were integrated and amplified to form a national medicines policy, thus making Australia one of the pioneer high-income countries to implement a comprehensive approach to medicines.

FIGURE 6.2

Trends in the formulation of national medicines policies, by countries' level of income, 1985–1999



Source: World Drug Situation Survey (1999)

6.4 IMPLEMENTATION OF NATIONAL MEDICINES POLICIES

When a national medicines policy document has been drafted and approved, setting out key objectives, an implementation plan is needed to identify strategies and actions to attain these objectives. Steps in implementation planning involve:

- Defining priorities for implementation
- Developing an implementation plan which details
  - What is to be done
  - Who is responsible
  - What resources are required and available
  - Timing for start and completion of principal activities.

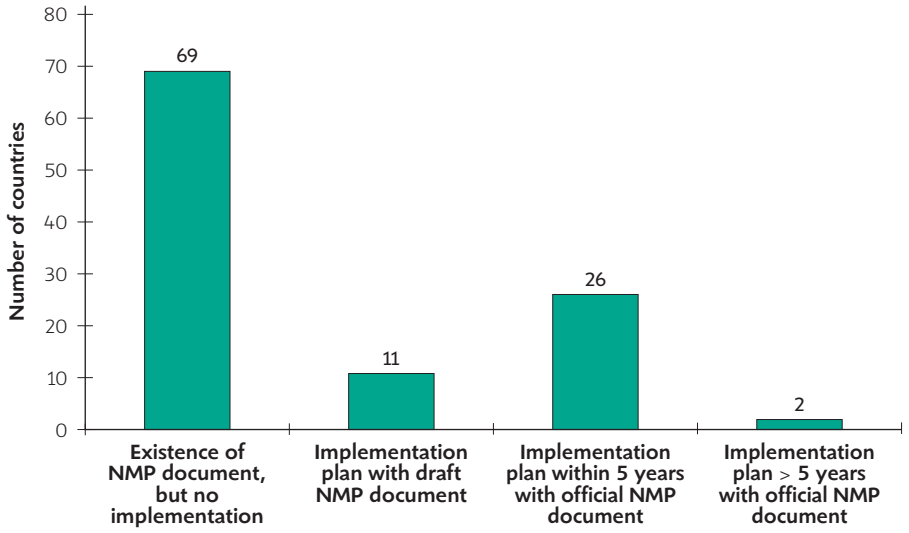
However, in some countries, national medicines policies are implemented without such a plan.

Figure 6.3 shows the status of implementation plans for national medicines policies in countries with a policy document. It shows that:

- In 1999, almost two-thirds of the 108 countries with a national medicines policy document (official or draft) had not yet established a plan to implement their national medicines policy.
- Almost one-quarter of the countries with a national medicines policy document had established a plan of the action within five years of formulating the policy, and 2% took longer than five years to establish their implementation plan.
- Only 10% of countries with a draft policy document also had a plan to implement the policy.

FIGURE 6.3

Countries with implementation plans for national medicines policies, 1999



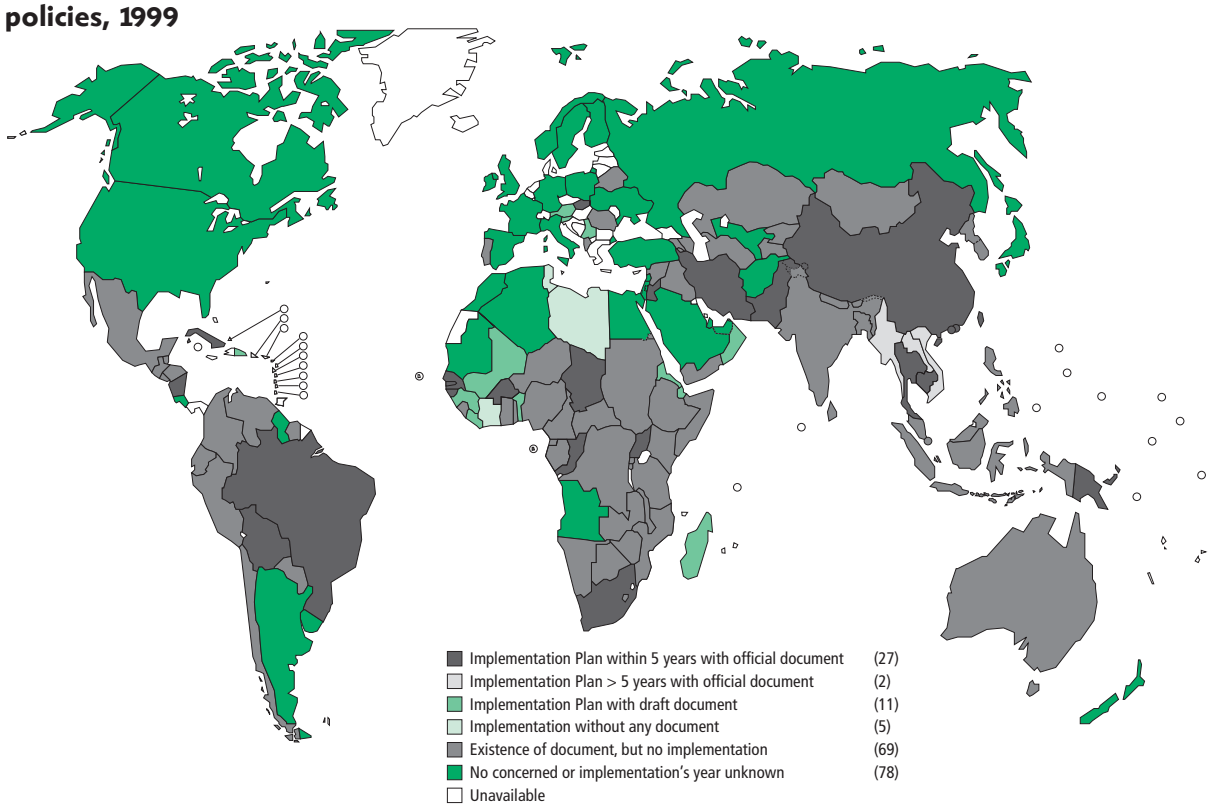
Source: World Drug Situation Survey (1999) datafile implementation-policy.xls
NMP = national medicines policy

Figure 6.4 shows the geographical distribution of countries with implementation plans.

An additional four countries had implementation without a framework national medicines policy: two low-income countries (Côte d'Ivoire, Rwanda) and two middle-income countries (Libyan Arab Jamahiriya, Tunisia).

FIGURE 6.4

Geographical distribution of countries with implementation plans for national medicines policies, 1999



6.5 IMPLEMENTATION OF NATIONAL MEDICINES POLICIES IN COUNTRIES AT DIFFERENT INCOME LEVELS

There is no significant correlation between the status of the implementation plan and a country's level of income. In all groups of countries (low-, middle- or high-income), the percentage of countries which had national medicines policy documents but no implementation plan is quite high: 60% for low-income countries, 59% for middle-income countries and 75% for high-income countries (**Table 6.3**).

TABLE 6.3 **Implementation of national medicines policies in low-, middle- and high-income countries, 1999**

Status of implementation plan	Low-income		Middle-income		High-income	
	Number of countries	%	Number of countries	%	Number of countries	%
Implementation plan within 5 years with official document	13	23	12	26	1	25
Implementation plan over 5 years with official document	2	3.5	0	0	0	0
Implementation plan with draft document	6	10	5	11	0	0
Implementation without plan document	2	3.5	2	4	0	
Existence of document, but no Implementation plan	34	60	28	59	3	75
Total	57	100	47	100	4	100

REFERENCES

1 *How to develop and implement a national drug policy*. 2nd ed. Geneva, World Health Organization, 2001.

2 *How to develop and implement a national drug policy*. WHO Policy Perspectives on Medicines No.6. Geneva, World Health Organization, 2002.

7

ACCESS TO ESSENTIAL MEDICINES

SUMMARY

- Although the percentage of the world's population without access to essential medicines has fallen from an estimated 37% in 1987 to around 30% in 1999, the total number of people without access remains between 1.3 and 2.1 billion people.
- Lack of access is particularly concentrated in Africa and India.
- Access to essential medicines appears closely correlated with other indicators of health system performance, such as disability-adjusted life expectancy.
- The majority of low- and middle-income countries use essential medicines lists in selecting their medicines and are more likely to use these to limit procurement choices than are high-income countries.
- Generic competition and differential pricing can contribute substantially to the affordability of medicines in low-income countries.
- Bulk purchasing, careful price comparison, compulsory licensing and differential pricing schemes may help countries obtain better purchasing prices for medicines.
- Greater scope for domestic price regulation exists in many low-income countries.

7.1 CURRENT ESTIMATES OF ACCESS TO ESSENTIAL MEDICINES

Inequities in access to medicines reflect failures in health systems and medicines policy. Access to essential medicines remains a major objective of people everywhere, and is widely featured as an objective of countries' national medicines policies. In a strategy document for 2000–2003[1], WHO considers better access to essential medicines a priority health issue. WHO's ongoing World Medicines Survey asks a local medicines expert in each country to estimate the percentage of the population who have access to a minimum list of 20 essential medicines, which are continuously available and affordable at a health facility or medicines outlet, within one hour's walk from the patients' home. Responses to this question form the basis for the access figures reported here and in the statistical annex. Because of the complexity of the access concept and the difficulty of validating respondents' estimates, the statistical annex also uses ranges around each respondent's estimate.

In 1975, less than half the world's population were estimated to have regular access to essential medicines.[2] New estimates from the 1999 World Medicines Survey show that this fraction has fallen to around one-third. However, the absolute number of people without access has remained almost unchanged, at about 1.7 billion. Getting the right medicines to the people who need them at the time they need them remains a major challenge.

In the 1999 survey, 183 of 193 countries responded to this question. **Table 7.1** shows the distribution of countries by WHO region according to reported levels of access to essential medicines.

TABLE 7.1 **Range of access to essential medicines by WHO region, 1999**

WHO Region	Percentage of population with regular access to essential medicines				
	Very low access (< 50%)	Low to medium access (50%–80%)	Medium to high access (81%–95%)	Very high access (<95%)	
	Number of countries	Number of countries	Number of countries	Number of countries	Total Countries
Africa	14	23	5	3	45
Americas	7	14	7	7	35
Eastern Mediterranean	2	7	5	8	22
European	3	12	6	25	46
South-East Asia	2	4	3	0	9
Western Pacific	1	8	8	9	26
Total countries*	29	68	34	52	183

Even from these broad groupings the regional extremes are clear. In Europe, 25 of the 46 countries reporting were in the "very high" access group and only three countries were in the "very low" access group, whilst in the African region only 3 of the 45 countries were in the "very high" but 37 countries (over 80%) were in the "very low" and "low to medium" groups.

Table 7.2 illustrates access in relation to population size.

TABLE 7.2

Number of people without access to essential medicines, by WHO region, 1999

WHO Region	Number of countries	Total population (million)		Estimated numbers, ranges and percentages of population without regular access to essential medicines		
			% of total	Population without access (millions)	Percentage of WHO regional population without access	Percentage of world population without access
African	45	566	10	267 (200–334)	47 (35–59)	15 (11–19)
American	35	813	14	179 (134–224)	22 (16–27)	10 (8–12)
East Mediterranean	22	485	8	143 (107–179)	29 (22–36)	8 (6–10)
European	46	832	14	114 (85–142)	14 (10–17)	7 (5–9)
South-East Asia	9	486	8	127 (95–159)	26 (19–32)	7 (5–9)
India	1	998	17	649 (487–811)	65 (49–81)	38 (28–47)
West Pacific	26	380	7	55 (41–69)	14 (10–17)	3 (2–4)
China	1	1274	22	191 (143–239)	15 (11–19)	11 (8–14)
Total all countries	183	5834	100	1725 (1294–2156)	30 (22–37)	100

Table 7.2 shows that about 30% of the world's population, or between 1.3 and 2.1 billion people, are estimated not to have access to the essential medicines they need. In India, an estimated 499–649 million people (50% to 65% of the population) do not have regular access to essential medicines. Throughout Africa, a further 267 million people (almost half the population or 15% of the world total) also lack access.

Classifying access according to countries' level of income, as in preceding chapters, shows a clear relationship between economic level and access to medicines, as seen in **Tables 7.3** and **7.4**. **Table 7.3** shows the medians and ranges of reported access figures from countries by income level.

TABLE 7.3 **Country income level and access to essential medicines**

Country income group	Median reported access level (%)	Minimum reported %	Maximum reported %
Low-income	60	10	93
Middle-income	85	30	100
High-income	100	98	100

Table 7.4 shows that the percentage of the population estimated to lack adequate access to essential medicines is less than 1% in high-income countries, 39% in low-income countries and 24% in middle-income countries. The 1.3 billion people in low-income countries estimated to lack access account for almost 80% of the total number of people in the world who lack essential medicines.

TABLE 7.4 **People without access to essential medicines, by countries' level of income**

Country income group	Number of countries	Population	Population without access to essential medicines		
		Number (million)	Number (million)	As % of country income group	As % of global total without access
Low-income	63	3548	1369	38.6	79.4
Middle-income	86	1447	350	24.2	20.3
High-income	34	859	5	0.6	0.3
Total countries and population	183	5854	1724	n.a	100

7.2 FACTORS INFLUENCING ACCESS TO MEDICINES

Lack of access to medicines is symptomatic of wider problems relating to the way health services are organized, financed and delivered. However, the measurement of overall health systems performance is still in its infancy. Measures proposed in *The World Health Report 2000*[3] are now undergoing extensive refinement, revision and consultation. Nevertheless, health outcomes, as measured in disability-adjusted life expectancy (DALE) do correlate with the questionnaire-based judgements made in the World Drug Survey on

access levels. Well-performing health systems offer high levels of access, and poorly performing ones result in large numbers of people being excluded from medicines as well as other forms of treatment, prevention and care. **Table 7.5** shows the relationship between health outcomes in DALEs and access to medicines.

TABLE 7.5

Access to essential medicines and life expectancy (DALE),[i] 1999

Level of DALE	Percentage of population estimated to have regular access to essential medicines								
	< 50%		51%–80%		81%–95%		>96%		
	Number of countries	%	Number of countries	%	Number of countries	%	Number of countries	%	Total Countries
Below 50 years	18	62.0	22	42.3	9	21.4	1	1.7	50
50–59 years	5	17.0	13	25.0	12	28.6	5	8.6	35
60 years and over	6	21.0	17	32.7	21	50.0	52	89.7	96
Total countries	29	100	52	100	42	100	58	100	181

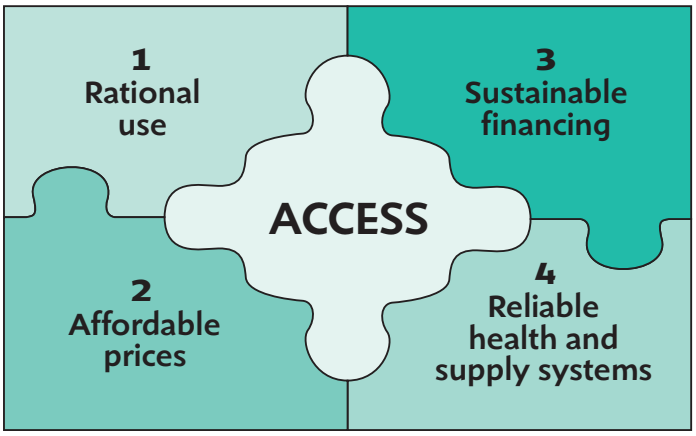
Table 7.5 shows that most countries reporting low access to medicines also had very low disability-adjusted life expectancy. At the other end of the spectrum, almost 90% of countries with very high access to medicines also had the highest level of health outcome.

7.3 KEY FACTORS INFLUENCING ACCESS TO ESSENTIAL MEDICINES

In addition to the general problem of health systems performance, four medicines-specific factors have to be in place to ensure that medicines are accessible to people whenever and wherever they are needed (**Figure 7.1**).

FIGURE 7.1

The access framework



Source: WHO, 2000

As **Figure 7.1** makes clear, *rational medicines selection processes* should be in use, based on national or local essential drugs lists and treatment guidelines; *prices should be at levels*

[i] DALE. *Disability-adjusted life expectancy.*

affordable by governments, health care providers and consumers; *fair and sustainable financing* for the medicines component of health care should be ensured through adequate funding levels and equitable prepayment mechanisms, such as government revenues or social health insurance, to ensure that poor people do not face proportionally higher costs than the better off; and finally, *reliable health and supply systems* need to be in place, incorporating an efficient and locally-appropriate mix of public and private service providers. Failure in any one of these processes will jeopardize people's access to medicines.

The financing aspects of access were discussed separately in **Chapter 5**. The remaining sections of this chapter examine in turn the evidence on each of the other three components of access.

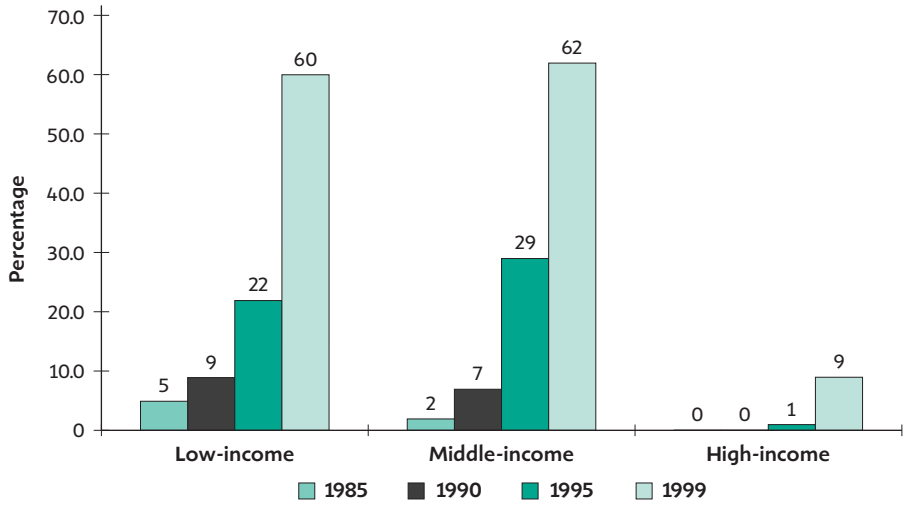
7.4 RATIONAL SELECTION

Rational selection of medicines means choosing medicines appropriate to the country's health situation on the basis of their safety and cost-effectiveness. Institutionalizing rational choice involves using essential medicines lists (EMLs), based on the best available evidence on local disease burden, efficacy, safety and cost of treatment for those diseases. However, there is a significant difference between having an EML and using it effectively. WHO has developed model lists of essential medicines since 1977, which have served as a reference for countries in the establishment of their own national EML. The first Model List, published one year before the Alma Ata Declaration of Health for All, contained around 200 active substances. Approximately every two years, WHO updates the List on the basis of evidence presented to a committee of experts. Following the revision in March 2003, the Model List now contains 316 active substances.[4,5,6]

Figure 7.2 indicates that the number of countries which revised their national EML increased from 1985 to 1999: from 5 to 60 among low-income countries; from 2 to 62 among middle-income countries; and from 0 to 9 among high-income countries.

FIGURE 7.2

Cumulative number of countries with a national essential medicines list revised within the last five years



Source: World Drug Situation Survey (1999)

Table 7.6 shows that there is a clear relationship between a country's EML status and its level of income. Less than 10% of low- and middle-income countries had not established an EML in 1999, compared with over two-thirds of high-income countries. However, institutional use of EMLs, by hospitals or health insurers is often widely practised in high-income countries and likely to be under-represented in these figures.

TABLE 7.6 **Essential medicines list and countries' level of income, 1999**

	Low-income		Middle-income		High-income	
Status of EML	No. Countries	%	No. Countries	%	No. Countries	%
EML updated within 5 years	47	75	70	74	11	31
EML updated over 5 years	13	21	17	18	0	0
No EML/not known	3	4	8	8	24	69
Total	63	100	95	100	35	100

Source: World Drug Situation Survey (1999)

Table 7.7 shows that the number of items on a national EML tends to be associated with the level of a country's income: the median list size is 276 medicines in low-income countries, 420 in middle-income countries and 903 in high-income countries.

TABLE 7.7 **Average size of essential medicines list by countries' level of income, 1999**

Level of income	Total Countries	Median number of medicines	Minimum number of medicines	Maximum number of medicines	Standard deviation
Low-income	45	276	134	6000	911
Middle-income	49	420	35	2348	450
High-income	5	903	531	3280	1036

Source: World Drug Situation Survey (1999)

The following chapter analyses experiences, challenges and approaches to ensuring the rational use of medicines, once they have been selected and purchased.

7.5 AFFORDABLE PRICES

The price of medicines plays an essential role in access to medicines. When a course of treatment for peptic ulcer costs almost twice the monthly wage of a government employee, as in Cameroon,[7] it is clearly not generally affordable. Several strategies are available to countries to influence price, and they fall into two main categories: (i) obtaining the best possible price through the selection and purchasing process and (ii) ensuring price regulation throughout the supply chain from manufacturer or importer to patient.[8] Many countries use combinations of these two approaches in their attempt to keep medicine prices down, though responses to the World Drug Survey indicate that almost 40% of respondent countries (53/135) implement no price regulation policy at all.

A policy focus on cost-effective selection and purchasing is likely to be based on an EML, and to use competitive purchasing methods for medicines available from multiple manufacturing sources. Major economies in the national medicines bill can also be made by ensuring that public procurement focuses on generic medicines of assured quality wherever possible, rather than innovator brand products with patent protection and higher prices.

Table 7.8 shows that, of the 121 countries responding to this question in the World Medicines Survey, low-income countries are more likely to restrict procurement to items on the national EML than middle- or high-income countries.

TABLE 7.8 **Public medicines procurement and country income level, 1999**

Level of income	Limitation to EML	
	Number	%
Low-income	37	77
Middle-income	25	43
High-income	2	13
Total countries	64	47

Source : World Drug Situation Survey (1999)

Estimates of the proportion of procurement done by international tender also indicate that this mechanism is somewhat more used by low-income countries.

TABLE 7.9 **Percentage of procurement done by international competitive tender**

	Number of respondents	Median % by international tender	Minimum	Maximum
Low-income	22	91	10	100
Middle-income	40	80	1	100
High-income	2	54	8	100

For patented medicines, international competitive tenders are seldom possible and purchases have to be negotiated on a country-by-country and medicine-by-medicine basis. The price offered by the manufacture is likely to vary according to the size of the country, its level of income and local manufacturing capacity. Many countries lack the ability to negotiate medicine prices in a professional, evidence-based way. In this situation, access to price information by purchasers in all sectors may have a crucial role to play in successful negotiated purchases. Prices of therapeutic competitors, where these exist, can help purchasers assess value for money. In addition, prices paid in other markets may provide useful evidence as to what a particular manufacturer is getting elsewhere for a particular medicine with patent protection. A number of countries use international reference prices systematically in their medicines purchasing and a number of price information services, both national and international, are now available.[i] Pricing practice in Greece, for

[i] A regularly updated list of this can be consulted on the WHO website: http://www.who.int/medicines/organization/par/ipc/drugpriceinfo.shtml

example, takes account of prices for the same medicine in the three lowest-priced countries in the European Union. Prices for the most clinically effective new medicines in France are set with reference to prices in four other European countries.[9] Eight other OECD countries take formal account of prices elsewhere.[10,11] **Figure 7.3** shows some of these price information links.

FIGURE 7.3

International reference pricing arrangements, 2001

Source: E. Schoonveldt

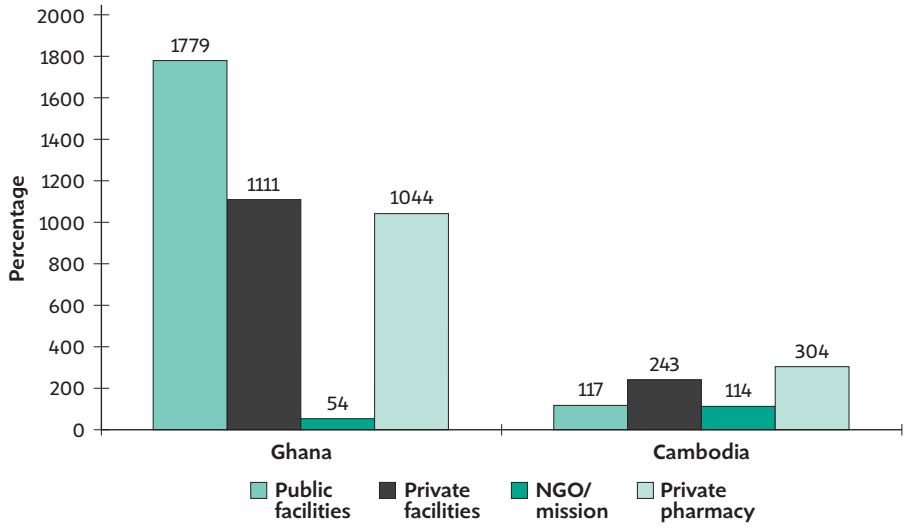
In a small but growing number of mainly high-income countries, systematic use is made of pharmacoeconomic analysis in assessing and negotiating medicine prices. This entails rigorous comparison of the clinical effectiveness of a new medicine, and its price, with the effectiveness and price of the closest existing alternative medicine. In this way, public purchasing bodies can assemble the evidence on cost-effectiveness in a systematic manner, and judge whether the therapeutic advantage of a new medicine offsets its additional cost. The Australian government's Pharmaceutical Benefits Scheme pioneered the use of this approach, and since 1993 has used it to determine which new medicines will qualify for insurance reimbursement. Countries including the Netherlands, UK and France employ similar techniques in evaluating new medicines for public purchase and reimbursement.

As **Chapter 4** illustrates, generic medicines, particularly unbranded generics, are usually much less expensive than newer patented medicines, and in both high- and low-income countries many governments encourage their use to control overall costs. In value terms, the USA is the leading consumer of generic medicines in the world, as **Chapter 4** shows. But the use of generic medicines offers important opportunities for low-income countries, where over the half of households live below the poverty threshold, to maintain affordable access to medicines.

A study carried out in Ghana and Cambodia highlights the "brand premium" or gap between prices of generic and brand medicines. Systematic surveys of the price of generic and brand medicines were carried out in public health, private for-profit facilities, private not-for-profit facilities (NGOs/religious missions) and private retail outlets (private pharmacies). These surveys were based on 30 essential medicines (20 essential medicines selected for diseases that are common throughout the world and 10 medicines that each country selected according to the local disease situation). **Figure 7.4** indicates that prices vary greatly between generic and brand medicines. In Ghana, brand medicines are much more expensive than generic medicines by a factor of 18 in public facilities, 11 in private facilities, and 10 in private pharmacies but by only 50% more in the pharmacies of NGOs and religious missions.[12] In Cambodia, price differences between brand and generic medicines are higher in private pharmacies than others: a two to threefold brand premium in private pharmacies, and in private facilities, and about 100% in public facilities and in the pharmacies of NGOs and missions.

FIGURE 7.4

Price differences between generic and brand medicines for standard treatments in Ghana and Cambodia

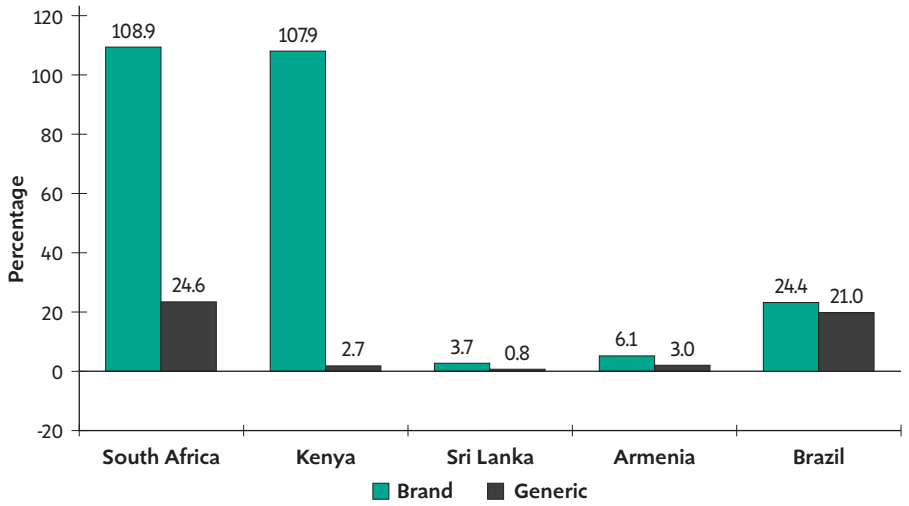


Using a slightly different approach but based on systematic surveys, brand and generic prices for a fixed list of essential medicines were also compared in five other low- and middle-income countries. **Figure 7.5** shows that for one diuretic medicine, furosemide, local retail prices ranged from a high of over 100 times the international reference price (South Africa and Kenya, brand) to slightly below it (Sri Lanka, generic). For the full set of medicines compared, generic prices were close to international reference prices in Kenya, Sri Lanka and Armenia, while half of the innovator medicines in South Africa cost from 11 to 62 times the reference prices.

Clearly, big price differences exist not only between generic and innovator medicines, but also between prices for the same brand or generic in different countries. Many countries thus have considerable scope for taking steps to ensure that they are not paying more than necessary for their essential medicines. National, regional or even global bulk purchasing schemes greatly improve the prospect for achieving lower prices. Regional medicine purchasing schemes exist in francophone West Africa, in the Caribbean, in Latin America through the WHO/PAHO revolving drug fund, and in the countries of the Gulf

FIGURE 7.5

Brand and generic furosemide prices in relation to international generic price, five countries, 2001



Source: http://www.haiweb.org/medicineprices

Cooperation Council. Global purchasing arrangements exist for vaccines through UNICEF and GAVI and for contraceptives through UNFPA; for tuberculosis, the Green Light Committee purchases medicines for multi-drug resistant forms of the disease and the Global Drug Facility purchases first-line tuberculosis drugs. Most recently established, the Global Fund to Fight HIV/AIDS, Tuberculosis and Malaria is currently evolving its procurement and price monitoring arrangements for medicines for these three diseases.

The high price of medicines for common diseases has been highly publicized in recent years. At the national level in high-income countries such as the USA and Switzerland there is widespread concern about high medicine prices. At the international level, the debate has centred on the high price of patented medicines used to treat HIV/AIDS and AIDS-related opportunistic infections — many of them life-saving medicines which have to be taken for life. At prevailing high-income country prices they are beyond the reach of governments and the great majority of people in low-income countries.

7.5.1 Voluntary price discounts and approaches to "equity pricing" for new essential medicines

Manufacturers' discounts on selected medicines under patent are occasionally offered to approved buyers in low-income countries. Novartis, in a framework established with WHO, offers public sector purchasers in developing countries a special price for its antimalarial medicine Coartem (artemether + lumefantrine). For HIV/AIDS medicines, an "Accelerated Access Initiative" focused on Africa was launched by several UN agencies and five pharmaceutical companies in May 2000. A detailed history of treatment price levels and a database of current prices for these medicines is maintained by Médecins Sans Frontières.[i] Treatment costs with the innovators' medicines have fallen from over US$ 10 000 a year to around US$ 730 a year, although generic medicines are available at less than half of these prices and one participating manufacturer has made no price reduction on one key medicine, which is still over US$ 3000 for one year's supply.

[i] http://www.accessmed-msf.org/prod/publications.asp

This voluntary approach has had only a modest impact on peoples' access to care. Although about 60 000 patients in Africa are reported to be receiving medicines through the programme, they represent less than 1% of the HIV-infected population in need of treatment. Moreover, demand from countries for medicines under this initiative is limited, as cheaper generic sources of supply are increasingly available.[13] Finally, countries have little control over voluntary price discounts in terms of which medicines are available, over what period, through which channels, and in what volume.

An alternative gesture by patent-holding manufacturers is to offer patent waivers. Commitment by the patent holder not to prosecute low-income countries for patent infringement would open the door to differential pricing. Such waivers have, in fact, already been granted for African countries by at least one company for a limited range of products. The WTO Ministerial Declaration on the TRIPS Agreement and Public Health has in effect given a limited patent waiver for the least-developed countries by extending their transition period with respect to pharmaceutical products to at least 2016.[i]

A more systematic approach to lower prices for the poorer countries might be achieved by low- and high-income country governments working together with manufacturers and consumer groups through an explicit differential pricing framework, as outlined in recent publications.[ii] The common concern in these has been to establish more thorough market segmentation between high-income and an identified group of low-income countries, entailing the cooperation of manufacturers and governments in both high- and low-income countries. Prices related to countries' purchasing power would be the target for new essential medicines, and measures (by both manufacturers and governments) established to prevent exportation of differentially priced medicines to higher price regions would be necessary. Regulatory mechanisms in high-income countries already exist to prevent such reimportation. Mechanisms such as bulk purchasing could help to guarantee both financing and volume for manufacturers.

7.5.2 Domestic price regulation

Prices increase between the factory or importer and the patient due to transportation costs, tariffs and taxes, and the mark-ups of distributors, wholesalers and retailers. Since these can easily double the ex-factory price of a medicine, some governments try to control these add-ons.

Yet a surprisingly high number of countries do not attempt to control local elements of medicine prices. **Table 7.10** shows that, of the 135 countries responding to the World Drug Survey questionnaire:

- over 40% have no regulation of medicine prices
- 8% use a combination of regulation on the producer price with control of wholesale and retail mark-up
- 16% apply regulation on wholesale and retail mark-ups
- 12% regulate only through a maximum retail mark-up.

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[i] Declaration on the TRIPS Agreement and Public Health. Ministerial Conference, Fourth Session. Doha, 9–14 November 2001, WT/MIN(01)/DEC/W/2, 14 November 2001. It should be noted, however, that the 48 Least Developed Countries, as specified by the United Nations, account for less than 650 million people, less than half of the world's poor, and only one major pharmaceutical production country (Bangladesh).

[ii] http://www.who.int/medicines/library/edm_general/who-wto-hosbjor/who-wto-hosbjor.html and *Report to the Prime Minister: UK working group on increasing access to essential medicines in the developing world.* Department for International Development, London, November 2002.

TABLE 7.10

Price regulation in WHO Member States, 1999

Type of regulation	None	Producer price	Retail mark-ups	Wholesale mark-ups	Retail + wholesale mark-ups	Producer price + retail mark-ups	Producer price + retail + wholesale mark-ups	Total number of respondents and percentage
Number of countries	54	10	15	7	20	6	10	122
Percentage	44.3	8.2	12.3	5.7	16.4	4.9	8.2	100

Source: World Drug Situation Survey (1999)

When the data are analysed by country income level (**Table 7.11**), only 22% (4 of 18) of high-income countries responding use no price regulation, whereas around half of low- and middle-income countries (50/104) do not regulate prices. Proportionally twice as many high-income countries (22%) as low- and middle-income respondents (10%) use all of the identified regulatory approaches and combinations surveyed to control domestic prices. In both purchasing practices and in domestic price regulation measures many low- and middle-income countries appear to be missing opportunities to ensure that medicine prices are affordable.

TABLE 7.11

Price regulation according to countries' level of income, 1999

Level of income	None	Producer price only	Retail mark-ups	Wholesale mark-ups	Retail and wholesale mark-ups	Producer price + retail mark-ups	All	Total
Low-income	20	2	8	0	6	1	2	39
Middle-income	30	4	7	4	12	4	4	65
High-income	4	4	0	3	2	1	4	18
Total	54	10	15	7	20	6	10	122

Source: World Drug Situation Survey (1999)

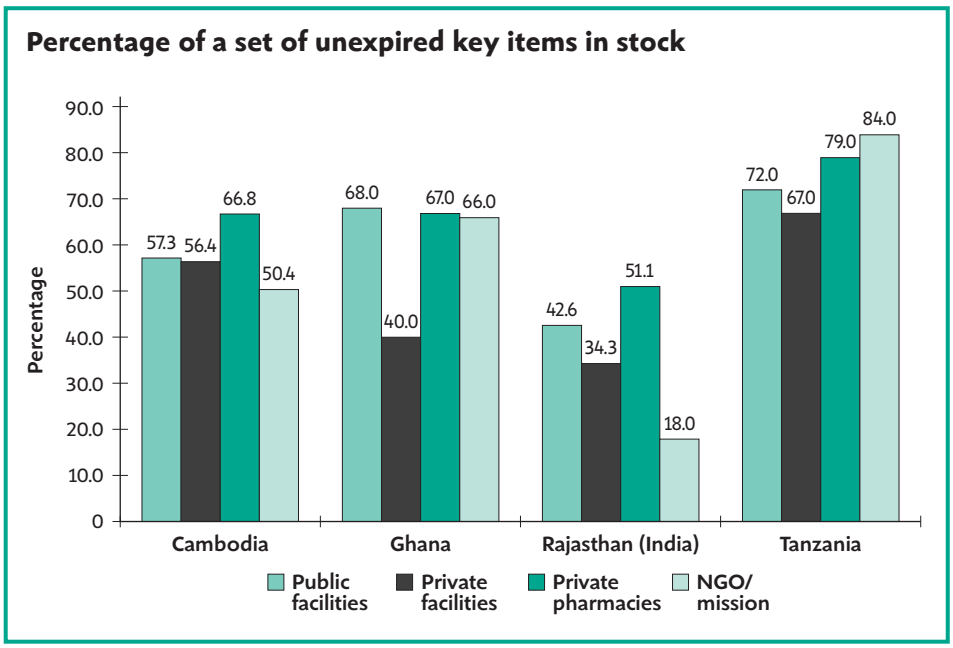
7.6 RELIABLE HEALTH AND SUPPLY SYSTEMS

Reliable medicine supply systems have two components: procurement and distribution. Procurement patterns have been described above in **section 7.5**. Distribution is the process which delivers medicines from their origin to their destination. A good distribution system ensures the timely availability of essential medicines at all levels of the health system. Information available through recent studies in several low-income countries[14] shows that physical accessibility of medicines outlets or health facilities remains a problem for many people. In Ghana, the majority (62%) of the rural population have to travel more than 30 minutes to a health facility, compared with only 20% of the urban population. In Rajasthan (India), only 45% and 55% of households respectively are within 20 km of a public health centre and a public or private hospital. Yet in Tanzania, 73% of households are within 5 km of a health facility and 86% within the same distance of a pharmacy.

Timely distribution of medicines means that they must be distributed and dispensed within their expiry date. **Figure 7.6** shows the percentage of unexpired items in a defined set of important medicines in the stock at dispensing facilities in four countries, with

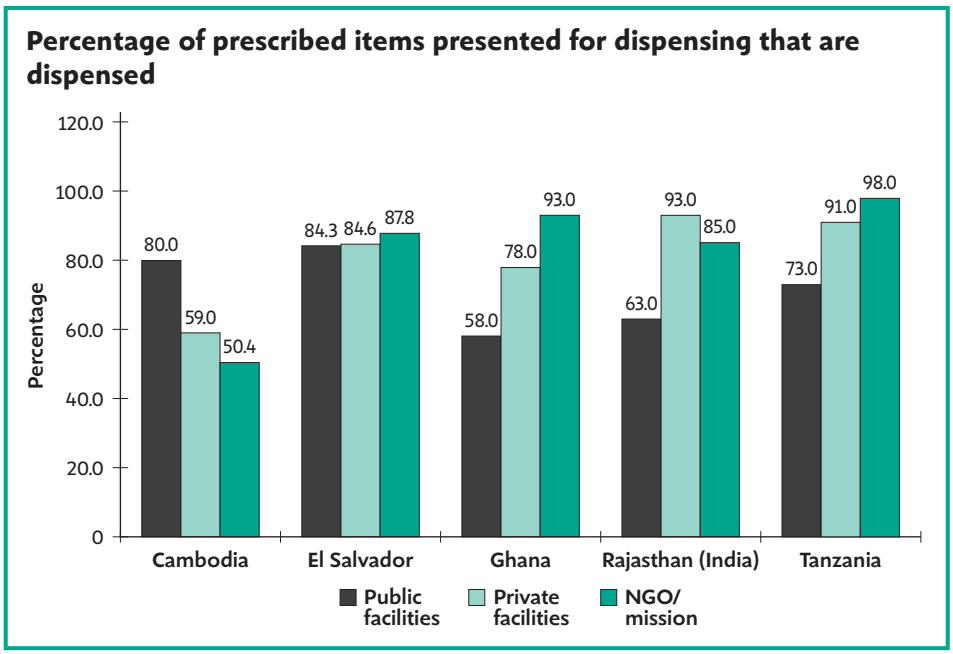
separate data for each sector (public, NGO, private health facilities and private dispensaries). All sectors in each country had expired items in stock, with the lowest level of expired stock (16%) at NGO facilities in Tanzania and the highest, also at NGO facilities (82%), in Rajasthan. All sectors in Rajasthan compared poorly with those in Tanzania. Private health facilities (hospitals, clinics) compared poorly: in three of the four countries they had the lowest percentage of unexpired key items in stock, though private pharmacies everywhere appeared to have better distribution systems.

FIGURE 7.6



Source: MSH

FIGURE 7.7



Another indicator of the performance of the supply system is the percentage of prescribed items which are actually dispensed. A low percentage of dispensing of prescribed items may result from either out-of-stock facilities or unaffordable prices. **Figure 7.7** uses

limited survey data from public, private for-profit and private not-for-profit facilities in four countries and in one state in India to show the percentage of prescribed items actually dispensed at facilities in each sector. The findings indicate that in Ghana, Tanzania and Rajasthan, India, the public facilities perform less well than those in other sectors, while in Cambodia the reverse is true. In Cambodia, NGO and private facilities are able to dispense only 50% and 59% respectively of prescribed medicines.

REFERENCES

1 *WHO medicines strategy: framework for action in essential drugs and medicines policy 2000-2003.* Geneva, World Health Organization, 2000.

2 *The world drug situation.* Geneva, World Health Organization, 1988.

3 *The world health report 2000. Health systems: improving performance.* Geneva, World Health Organization, 2000.

4 Laing R, Waning B, Gray A, Ford N, 't Hoen E. 25 years of the WHO essential medicines lists: progress and challenges. *Lancet* 2003, May 17:1723–9.

5 *WHO model list of essential medicines,* 13th list (April 2003), (http://www.who.int/medicines/organization/par/edl/eml.shtml).

6 *The selection and use of essential medicines.* Report of the WHO Expert Committee, including the Model List of Essential Drugs, thirteenth list (WHO Technical Report Series 920) in press, (http://www.who.int/medicines/organization/par/edl/expertcomm13.shtml).

7 Are medicine prices a problem? *Essential Drugs Monitor No.33,* Geneva, World Health Organization, 2003.

8 *Cost-containment mechanisms for essential medicines, including antiretrovirals, in China.* Geneva, World Health Organization, 2003.

9 French outline new pricing policy. *SCRIP,* No.2814, 2003.

10 *Pharmaceutical price regulation: the current debate.* London, Institute for Fiscal Studies, (http://www.ifs.org.uk).

11 Jacobzone S. *Pharmaceutical policies in OECD countries: reconciling social and industrial goals.* Paris, OECD, 2000. DEELSA/ELSA/WD(2000)1.

12 *Strategies for enhancing access to medicines.* Boston, Management Sciences for Health, (http://www.msh.org/seam/3.1.3.htm).

13 Grace C. *Equitable pricing of newer essential medicines for developing countries.* Geneva, World Health Organization, 2002, (available electronically at: http://www.who.int/medicines/library/par/equitable_pricing.doc).

14 Quick JD, Rankin JR, Laing RO, O'Connor RW, Hogerzeil HV, Dukes MNG, Garnett A, eds. *Managing drug supply.* West Hartford, CT, Kumarian Press, 1997.

8

RATIONAL USE OF MEDICINES

SUMMARY

- Worldwide, it is estimated that half of all medicines are inappropriately prescribed, dispensed or sold, and that half of all patients fail to take their medicine properly.
- An estimated two-thirds of global antibiotic sales occur without any prescription, and studies in Indonesia, Pakistan and India show that over 70% of patients were prescribed antibiotics. The great majority – up to 90% – of injections are estimated to be unnecessary.
- The inappropriate use of medicines is not only widespread, it is costly and extremely harmful both to the individual and the population as a whole. Adverse drug events rank among the top 10 causes of death in the USA and are estimated to cost that country between US$ 30 and US$ 130 billion each year.
- Growing resistance to antimicrobial medicines is a particularly serious challenge in countries at all economic levels, and results largely from inappropriate prescribing and use. For the treatment of malaria, chloroquine resistance is now established in 81 of the 92 countries in which the disease is endemic.
- Much greater use of evidence-based diagnostic and treatment guidelines by health professionals is needed.
- More effective monitoring and regulation of medicines, and public education and information are important components of a strategy for increased rational use.

8.1 INTRODUCTION

Worldwide, it is estimated that over half of all medicines are prescribed, dispensed or sold inappropriately, and that half of all patients fail to take their medicine correctly.[1,2] Medicines are used rationally when patients receive the appropriate medicines, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost both to them and their community.[2,3] Irrational use occurs when one (or more) of these conditions is not met.

In spite of available tools and information on how to measure medicines use and the intervention strategies needed to achieve this, irrational use continues to occur. This is wasteful, expensive and dangerous, both to the health of the individual patient and to the population as a whole. Inappropriate use of medicines, and the related illness and deaths, are not restricted to low-income countries. Studies in Canada, Australia, Kuwait and the USA, as well as in middle-income countries such as South Africa and Thailand, have revealed that inappropriate use of medicines is widespread in teaching hospitals[1]. In many countries, the problem extends well beyond hospitals. Two-thirds of all antibiotics are sold without prescription, through under-regulated private sectors. A recent review of adverse drug events in the USA[4] shows these to be the fourth to sixth ranked cause of death in that country, with economic costs of between US$ 30 to US$ 130 billion per year.

Common examples of irrational drug use are:

- too many medicines are prescribed per patient (polypharmacy)
- injections are used where oral formulations would be more appropriate
- antimicrobial medicines are prescribed in inadequate doses or duration or antibiotics prescribed for non-bacterial infections, thereby contributing to the growing problem of antimicrobial resistance
- prescriptions do not follow clinical guidelines
- patients self-medicate inappropriately or do not adhere to prescribed treatment.

In many countries, the problem is entrenched. Few countries currently monitor inappropriate use of medicines – partly due to a lack of awareness of the scale of the problem and its economic and health costs – and decision-makers often lack knowledge of the most cost-effective ways to tackle this problem. Meanwhile, some countries lack the financial and human resources needed to promote more accurate diagnostic procedures, to implement effective regulation of prescribing and dispensing behaviour and to promote adherence to treatment by patients, in both the public and private sectors. In addition, the high cost of medicines contributes to low adherence levels by patients: in some studies, an estimated 90% of consumers buy three days' supply, or less, of antibiotics, making compliance with the recommended dosage impossible.[5,6]

Institutions, health professionals and patients all have roles to play in promoting more rational use of drugs. Effective regulation, clear clinical guidance, supportive incentive structures, training, education and management, are key components of an effective policy in this area.

8.2 METHODOLOGY FOR ASSESSING MEDICINES USE

In 1969, the European Drug Utilization Research Group was established to develop methods for drug utilization research. The Anatomical Therapeutic Chemical Classification (ATC) system and the defined daily dose (DDD) established by this group have been important in the development of drug utilization research. The system was originally developed in Scandinavia and then administered through WHO's European Regional Office. In 1996, WHO accepted the system as its official international standard and established the WHO International Working Group for Drug Statistics Methodology in order to strengthen the system and promote its use, particularly in developing countries.

Drug utilization data are essential in order to:

- monitor trends in medicines consumption
- provide a benchmark for comparison with similar countries or regions
- carry out an audit of medicines use against practice guidelines
- increase awareness among stakeholders, including governments
- assess the accessibility, quality and cost-effectiveness of care.

In most developed countries, research on medicines use is routine in health care facilities and numerous studies have demonstrated its effectiveness.[7] However, most developing countries do not have data on this at the national level.

A recent article by Ronning et al reviewed antibacterial usage in 16 European countries. This study demonstrated that despite the countries being very similar economically and epidemiologically the use varied by a factor of 2.5 between countries.[8]

Pharmacoepidemiology, the study of the utilization and effects of drugs in large numbers of people is also crucial in the promotion of rational drug use. These studies use information on medicines use to estimate the likely beneficial and adverse effects of medicines in populations. This kind of information is provided by the International Society for Pharmacoepidemiology.[9,10]

A major step towards rational use of medicines was the launch by WHO in 1977 of the 1st Model List of Essential Drugs, designed to help countries formulate their own national lists. In 1989, the International Network for the Rational Use of Drugs (INRUD) was formed to conduct multidisciplinary intervention research to promote the rational use of medicines.[7] In 1993, WHO and INRUD developed and published a standard methodology for selected drug use indicators in health facilities.[11,12] Since then, several intervention studies have been conducted using these indicators, and a review of the published studies with adequate study design was presented at the 1st International Conference for Improving the Use of Medicines (ICIUM) in Thailand in 1997.

Box 8.1 shows the selected WHO/INRUD drug use indicators for health care facilities. These indicators can be used to identify problems in general prescribing and quality of care at these facilities. Results from the use of these indicators can help identify the motives for irrational use and other problems in the use of medicines. The data collected can then be used to design appropriate interventions and to measure the impact of those interventions.[11–14]

BOX **8.1**

Selected WHO/INRUD drug use indicators for primary health care facilities

Prescribing indicators

- average number of medicines prescribed per patient encounter
- percentage of medicines prescribed by generic name
- percentage of encounters with an antibiotic prescribed
- percentage of encounters with an injection prescribed
- percentage of medicines prescribed from an EML or formulary.

Patient care indicators

- average consultation time
- average dispensing time
- percentage of medicines actually dispensed
- percentage of medicines adequately labelled
- percentage of patients with knowledge of correct dose.

Facility indicators

- availability of essential medicines list or formulary to practitioners
- availability of clinical guidelines
- percentage of key medicines available.

Complementary drug use indicators

- average medicine cost per encounter
- percentage of prescriptions in accordance with clinical guidelines.

8.3 STUDIES OF MEDICINES USE

This section details the results of 35 country studies from 1988 to 2002 which have been evaluated using the WHO standard methodology. Although some studies were conducted prior to the publication of the WHO methodology manual in 1993, the indicator results and definitions used are consistent with the manual.

8.3.1 Core prescribing indicators

Most of the studies evaluated are from low-income countries. However, Oman is an example of a middle-income country which uses the same indicators to measure drug use.[14–27]

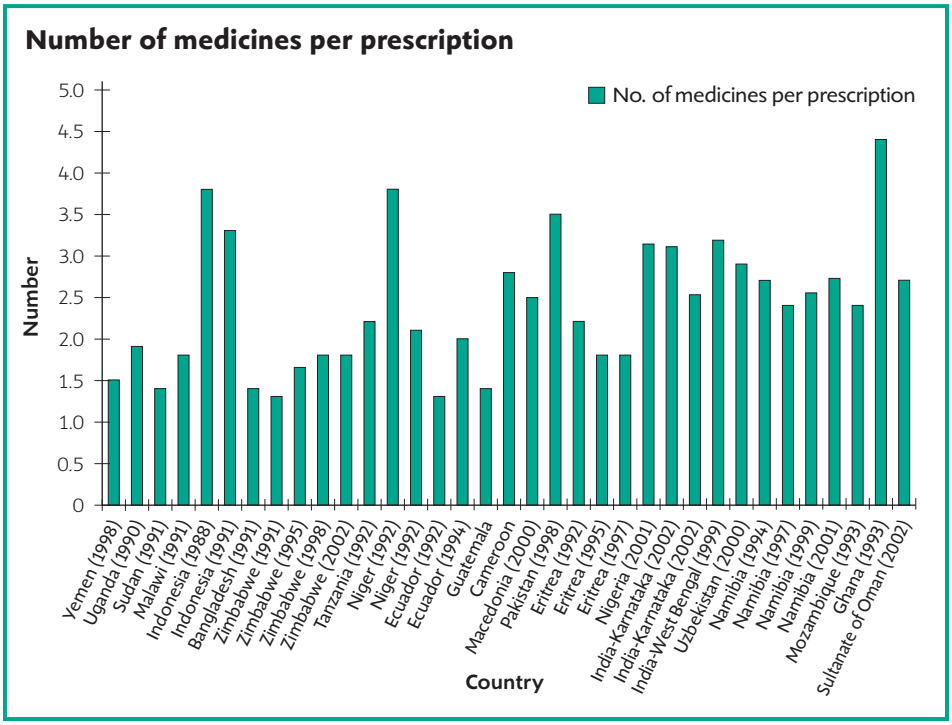
TABLE 8.1 **Core prescribing indicators for 35 countries**

	No. of drugs prescribed per encounter	% Antibiotics	% Injections	% Generic	% EML
Numbers of studies	35	35	34	26	8
Mean	2.39	44.8%	22.8%	60.3%	71.7%
Maximum	4.4	76.5%	74%	99%	99.6%
Minimum	1.3	22%	0.2%	24.6%	12%

• Indicator: Average number of drugs per prescription

Figure 8.1 shows the average number of drugs prescribed per patient. The common range of drugs prescribed per patient is two to three. However, in Ghana, the maximum number of drugs per prescription was 4.4 and in several countries (Indonesia, Niger, Nigeria, India and Pakistan) the prescriptions were for three or more drugs.[12,14–26]

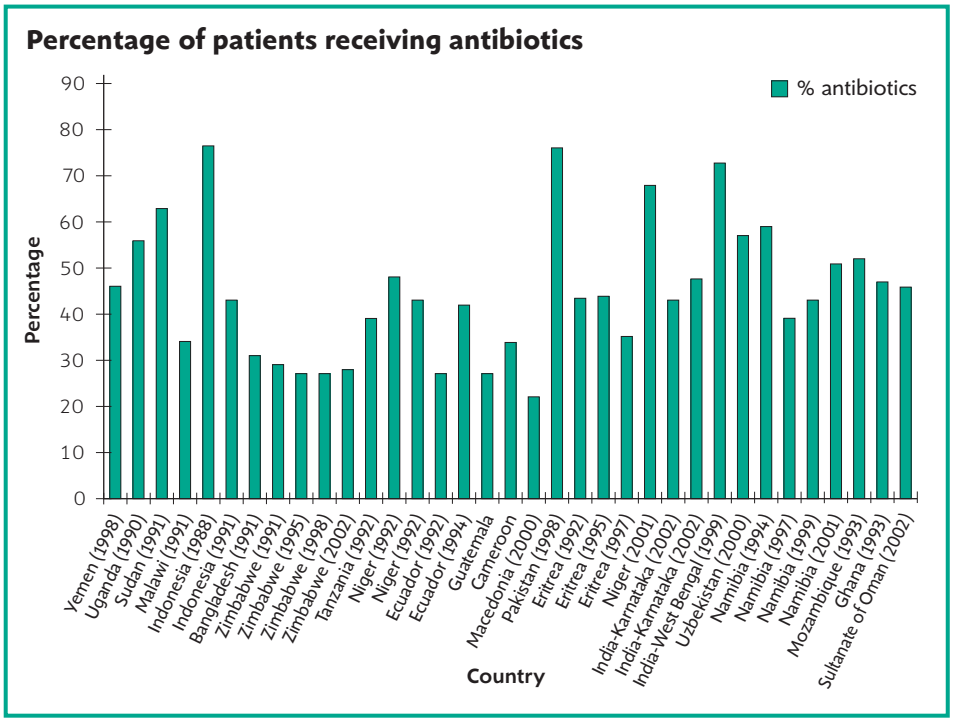
FIGURE 8.1



• Indicator: Percentage of patients prescribed antibiotics

Figure 8.2 shows data from the same countries on antibiotic prescribing. Overall about 45% of the patients were prescribed antibiotics. However, in Indonesia (1990), Pakistan (1998) and West Bengal, India, (1999) rates in excess of 70% were observed.

FIGURE 8.2

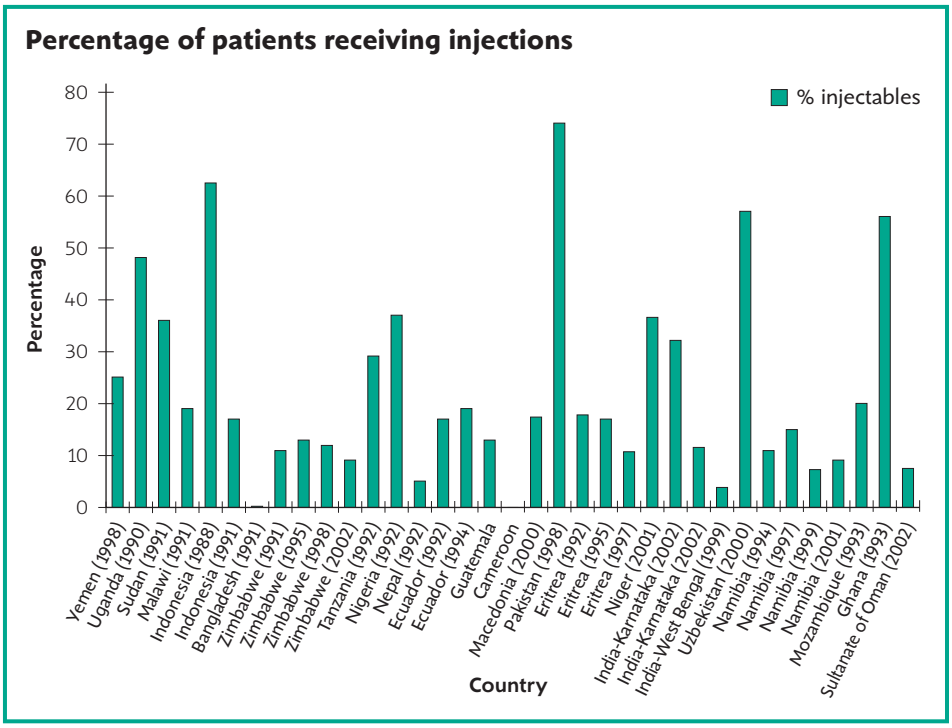


Analysis of data from Uzbekistan, Pakistan, Indonesia and Eritrea revealed that 75%–99% of patients diagnosed with an upper respiratory tract infection (URTI) received antibiotics.[16–19] In Eritrea, for example, it was confirmed that 75% of the adults and children diagnosed with URTI were prescribed antibiotics even though the cause of the infection may have been viral.[16] Results from Indonesia demonstrated that 46% of patients aged under five years received oral rehydration salts (ORS) for the treatment of diarrhoea while 73% of these same patients received oral antibiotics. Among patients aged over five years, 36% received ORS, 91% received oral antibiotics, and 25% of patients received an antibiotic injection.[17]

• Indicator: Percentage of patients prescribed injections

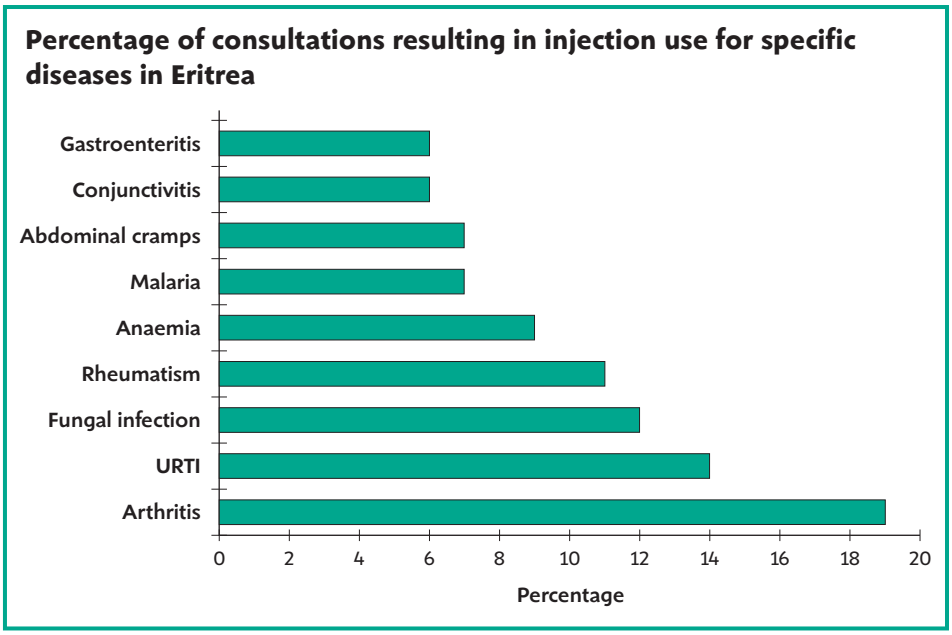
Figure 8.3 shows the percentage of patients receiving injections. On average over 23% of consultations resulted in an injection. Countries with the highest percentage of injections (over 60%) included Indonesia (1988), Pakistan, Uzbekistan and Ghana.[15–19] However, a serial survey in an area of Indonesia in 1991 revealed that injection use had improved significantly and the percentage of patients prescribed injections had been reduced to 17%.[17] Overall, it is estimated that up to 90% of injections are unnecessary, because alternative, safer routes of administration are available.[17] Study results from Uzbekistan revealed that excessive injection prescribing occurred mainly for: URTI (54.8%); urinary tract infection (79.8%); anaemia (32.2%); digestive disorders, including diarrhoea (47.7%); and hypertension (68.9%).[18]

FIGURE 8.3



Results from Eritrea also indicated the percentage of irrational use of injections for specific diseases (with no significant difference between overall results and results by age or province).[16] Results of the study are shown in **Figure 8.4**.

FIGURE 8.4

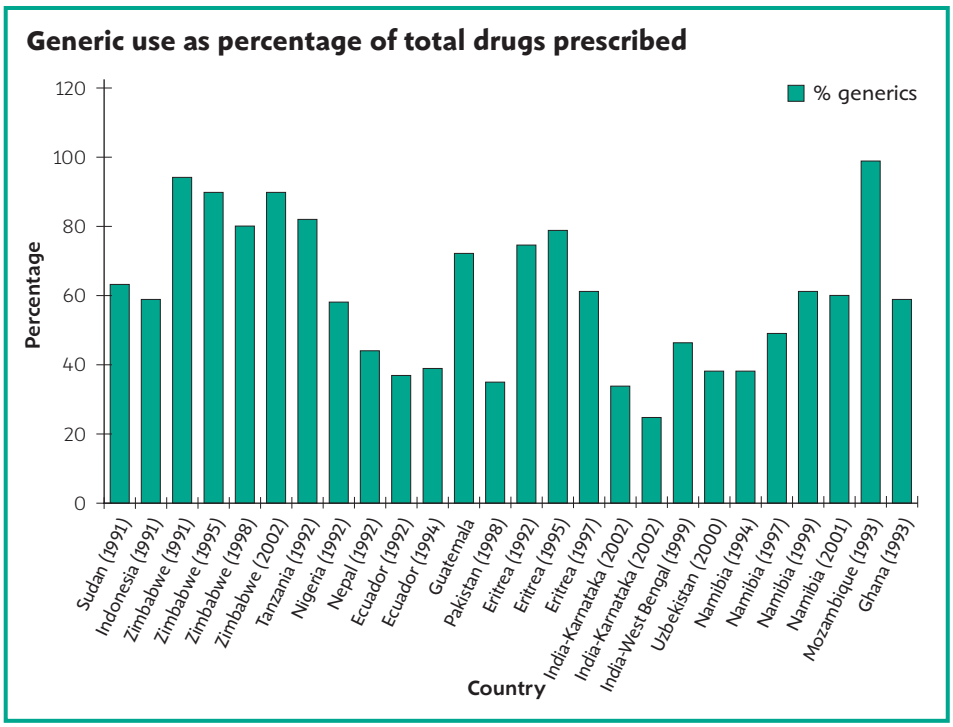


Excessive use of injections, particularly prevalent in low-income countries, is a widespread hazard to health in countries where injection safety cannot be guaranteed. Worldwide, it is estimated that unsafe injections account for 8 million infections of hepatitis B a year, 2 million of hepatitis C, and 75 000 cases of HIV.[28] In a survey in Zaire, two-year-olds had received an average of 24 injections.[29] In Moldova, where 50% of hepatitis B cases are associated with unsafe injection practices, 39%–57% of the population received at least one injection per year.[30]

• Indicator: Percentage of medicines prescribed by generic name

Figure 8.4 shows the percentage of medications prescribed by generic name. On average more than 60% of medications were prescribed by generic name for the 26 countries that reported on this. In Pakistan, India, Uzbekistan and Namibia less than 50% of medications were prescribed as generics.[15–28]

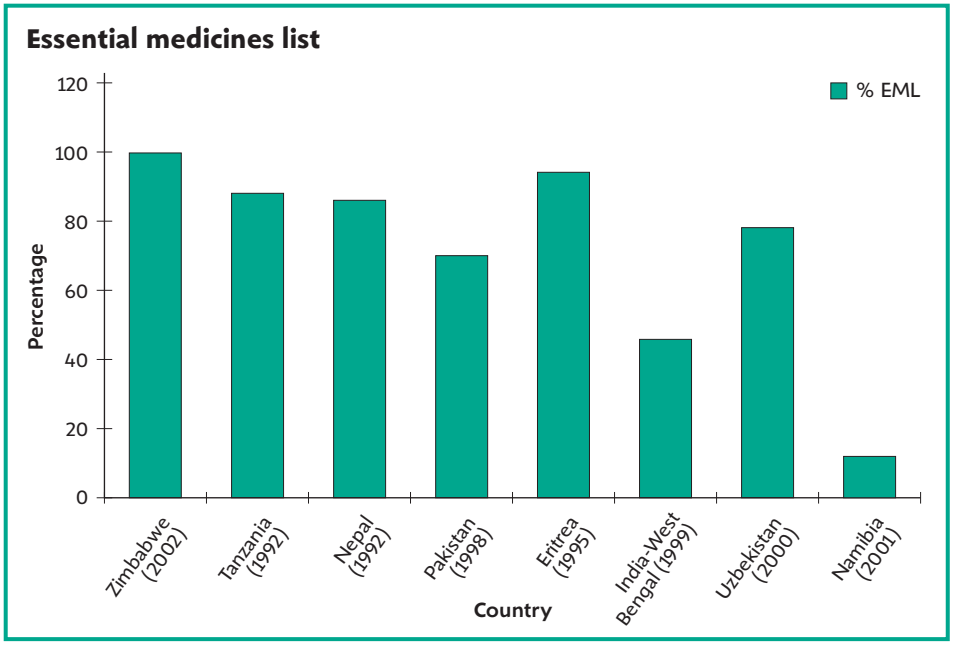
FIGURE **8.5**



• Indicator: Percentage of drugs prescribed from an essential medicines list

Only eight out of the 37 indicator studies report the percentage of drugs prescribed from an essential medicines list (**Figure 8.6**). On average, over 60% of the drugs were prescribed from an essential medicines list. At the bottom end of the scale, in Namibia (2001), only 12% of medicines prescribed were from the essential medicines list.

FIGURE **8.6**



8.3.2 Patient care indicators

Only 20 out of the 37 studies reported partial results on patient care indicators. Four countries, Zimbabwe, Pakistan, Eritrea and Niger, reported results on all patient care indicators.[16,19,23–28] The average consulting time in 10 countries was 4.0 minutes. The average dispensing time in seven countries was 105 seconds. On average, 89% of the medicines were dispensed (12 countries); 54% were adequately labelled (eight countries); and 71.4% of patients (16 countries) understood the correct dosage.

TABLE 8.2 **Patient care indicators**

Indicator	Count	Mean	Maximum	Minimum
Consultation time (minutes)	10	4.0	6.3	2.3
Dispensing time (seconds)	7	105	204	12.5
Percentage of drugs dispensed	12	89%	100%	70%
Percentage adequately labelled	8	54%	89.7%	20%
Percentage knowledge of dosage	16	71.4%	98.6%	27%

Zimbabwe conducted serial surveys on patient care indicators from 1995 to 2000, which were then compared. Information was collected on patients' knowledge of their medicines in relation to the *dose, frequency, duration and indication*. The study revealed that over 70% of patients were knowledgeable about the dose, frequency and indication – the same as in previous years. However, the study identified a need for greater emphasis in staff training on the importance of telling patients the *duration* of their treatment. The Zimbabwe study also reported on the average time patients spent in consultation with prescribers. The time was measured for a range of prescribers at the institutions, including doctors and nurses. The average consultation time was five minutes per patient. The average dispensing time was 2.5 minutes and the dispensers included pharmacists, pharmacy technicians, dispensary assistants, nurses and auxiliary nurses.[27]

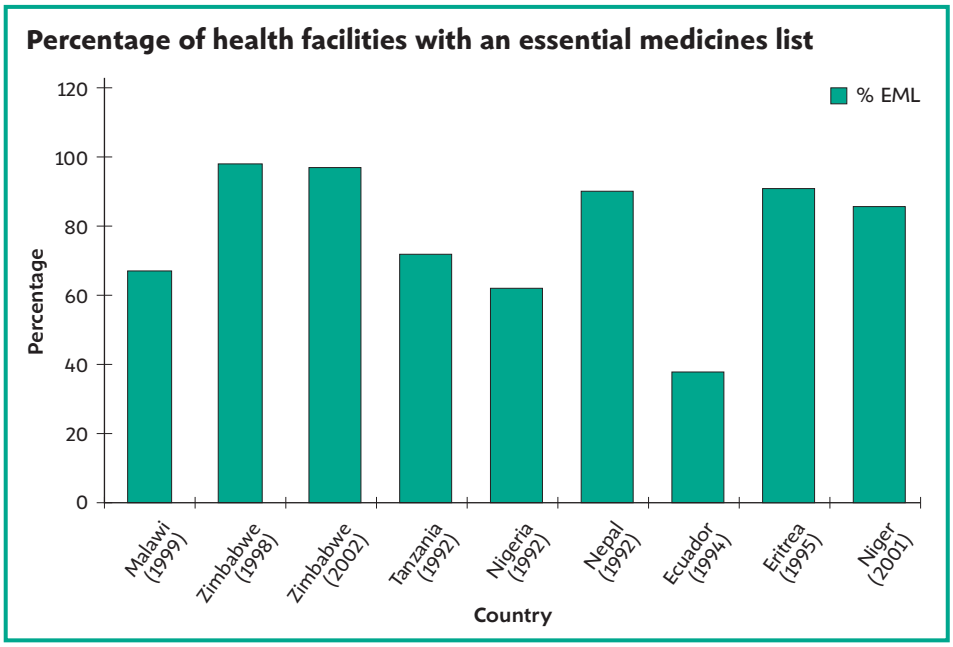
Very few countries reported data on the percentage of drugs that were adequately labelled. Of the eight countries that did so, the average was 54%. Zimbabwe carried out additional analysis of the labelling by collecting information on the name of the drug, the strength, quantity, dose and the date dispensed, as well as the name of the patient and health facility. The results reflected a need to include on the label the strength of the medicine, the date dispensed and the name of the patient and health facility.[27]

8.3.3 Facility indicators

- **Indicator: Percentage of health facilities with an essential medicines list**

Only nine studies reported information on the percentage of health facilities with an essential medicines list but these do not indicate the level of the facilities involved. On average, 78% of the facilities had an essential medicines list. However, in Ecuador, only 38% of facilities had an essential medicines list.

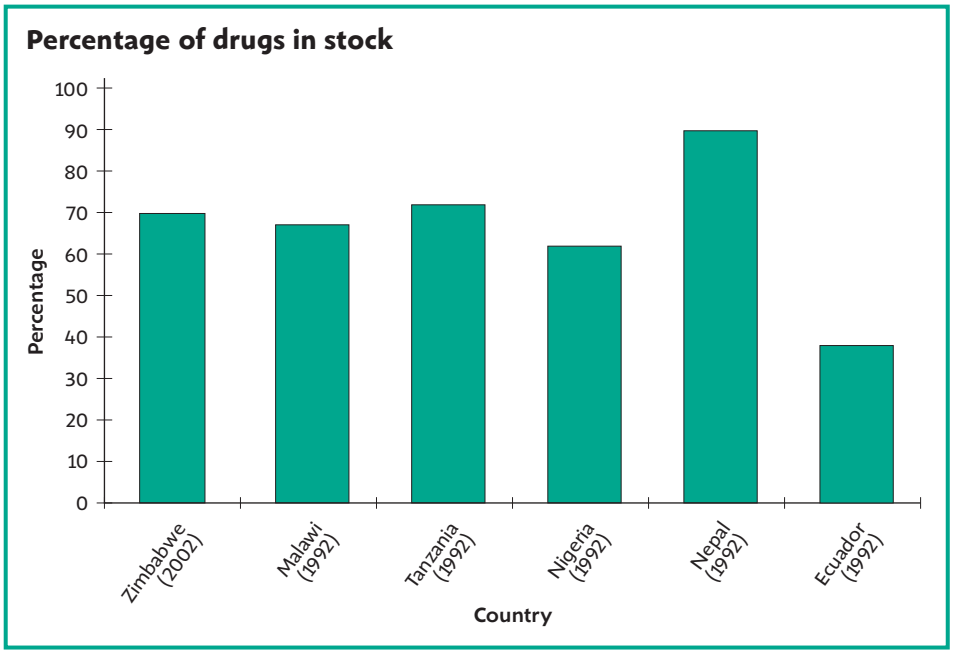
FIGURE 8.7



• Indicator: Percentage of drugs in stock

Six countries reported information on the percentage of drugs in stock. On average, 66.5% of the countries had drugs available. At the top end of the scale, Nepal reported having up to 90% of its drugs currently in stock, while at the bottom end, Ecuador had only 38% of its drugs in stock.

FIGURE 8.8



• Indicator: Percentage of facilities with impartial information on medicines

Only four studies — Eritrea (1995), Zimbabwe (1998), Zimbabwe (2002) and Niger (2001) — reported any information on the availability of impartial information on medicines available at health facilities. The studies showed that on average 74% of health facilities had impartial information available.

BOX 8.2

Serial surveys

Three countries, Namibia, Zimbabwe and Eritrea, conducted serial surveys for monitoring purposes. Serial surveys can be useful in the evaluation of rational prescribing at baseline and to determine the success of subsequent prescribing as a result of specific strategies. For example, results from Namibia show that the average number of drugs prescribed per patient was higher than in previous years and that the use of the essential medicines list had improved. However, the percentage of generic prescribing had not improved and the percentage of antibiotics prescribed had increased. Many low-income countries such as these have been hard hit by the HIV/AIDS epidemic which may account for the increased number of drugs prescribed per patient, including the number of antibiotics and injections prescribed. Since no information is available to confirm this, future serial surveys should aim to incorporate this.

8.3.4 Analysis of sub-speciality prescribing (Oman)

The Oman INRUD studied sub-speciality prescribing at hospital facilities in the regions of Muscat and Dhofar and, to a lesser extent, some other regions.[27] The methodology used a large sample size of 600 prescriptions per facility. Results from the Muscat Governorate hospitals and polyclinics are shown in **Table 8.3**.

TABLE 8.3 **Medicine use in Omani health facilities**

Health facility	A	B	C	D	E	F	G
Ave. no. of drugs per prescription	1.71	2.4	2.96	2.64	2.54	2.24	2.61
Percentage of drugs written as generics	14%	18%	30%	10%	14%	15%	*83%
Percentage of prescriptions with an antibiotic	14%	29%	9%	0%	25%	23%	21%
Percentage of prescriptions with an injection	0%	2%	3%	6%	7%	6%	1%

Notes on type of facility:
A = Specialist orthopaedics and trauma
B = General medical, ENT, dermatology, dental, ophthalmology
C = Full service tertiary care hospital
D = Psychiatric hospital
E = Urban polyclinic
F = Suburban health centre (PHC)
G = Suburban health centre (PHC)

*Analysis of the results shows that the high percentage of medicines written as generics in the suburban health centre (facility G) reflects the fact that this was the first computerized facility studied and drugs appear automatically by generic name.

8.4 SECONDARY ANALYSIS (INDICATORS BY LEVEL OF CARE, DISTRICT, AGE, DISEASE AND DRUG)

A secondary evaluation of indicator by age, category and diagnosis can be very useful in targeting interventions for managing the rational use of medicines.

• Drug use by level of care, and by geographic/district/province level

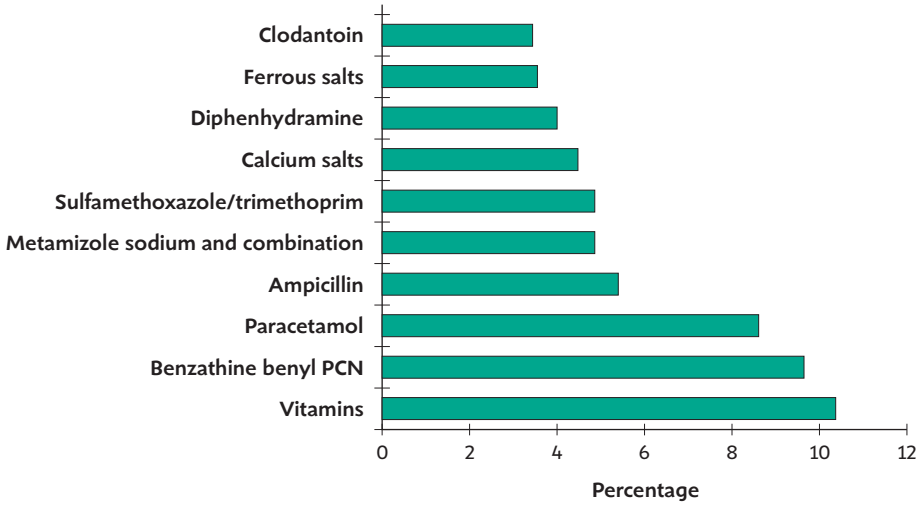
Four countries, Namibia, Uzbekistan, Pakistan and Eritrea, show indicator results by level of care and by provincial or district level.[16,18,19,21] The Eritrea study revealed that the average number of drugs prescribed per patient was higher in hospitals. The level of generic prescribing was generally lower in hospitals and lowest of all in Hamasien Province. The use of injections varied little between the different levels of care or at the province level, with the exception of Hamasien, where it was very high. The percentage of patients knowledgeable about the medicines dispensed was generally lower at health centres and in the province of Seraye. The availability of drugs in stock was good overall and varied little between the different levels of care. However, the labelling of medicines was generally poor, especially at health centres, health stations and in Hamasien.[16] The collection and presentation of indicator data by level of care and province can be very valuable since the results can be used to help evaluate and implement focused strategies to improve rational use of medicines.

• Drug use by age group, diagnosis and drug prescribing

Figure 8.9 shows data from Uzbekistan on the level of prescribing of their top 10 medicines – several of which are non-essential and indicate irrational use.[18]

FIGURE 8.9

The 10 most frequently prescribed medicines, by percentage, Uzbekistan



Uzbekistan also determined prescribing by category of diagnosis and rates of prescribing by diagnosis and province. This was extremely valuable since it identified key areas of intervention in relation to a specific indicator. For example, it revealed irrational prescribing of injections for urinary tract infections, hypertension and digestive diseases, including diarrhoea. It also identified generally poor generic prescribing for medications for these common diseases, as shown in **Table 8.4**.

TABLE 8.4 **Indicator data by diagnosis for Uzbekistan**[16]

Diagnosis	Respiratory	URTI	Anaemia	Digestive, incl. diarrhoea	Hypertension
Average no. of drugs	3.2	2.9	2.2	2.6	3.1
Percentage of generics	47.3	38.3	17.9	18.8	16.7
Percentage from EML	83	78.5	60.6	79.4	79
Percentage with antibiotic	78.9	93.5	1.7	30.2	2.2
Percentage with injection	54.8	79	32.2	47.7	68.9

Elsewhere, in Pakistan, results shown by level of care, district and age group reveal that both antibiotics and injections are over-prescribed in each of these categories, as shown in **Table 8.5.**[17] In general the differences between levels, districts and age groups are small.

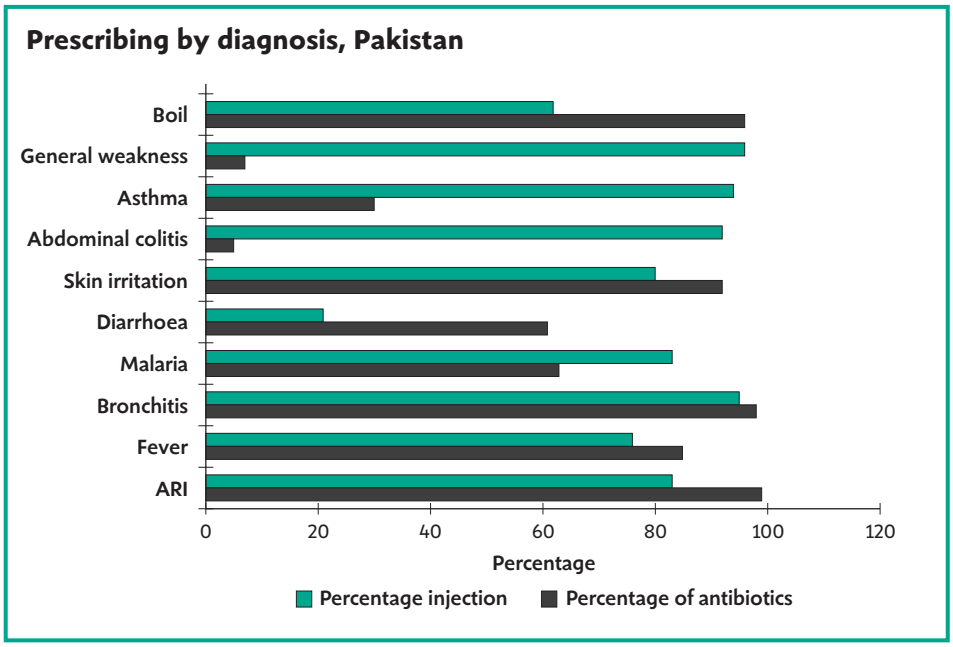
TABLE 8.5 **Prescribing indicator data by level of care, district and age group, Pakistan**

	Average no. of drugs	Percentage generics	Percentage with antibiotic	Percentage with injection	Percentage from EML
Level of care					
Rural health centre	3.2	38	78	74	72
Basic health centre	3.7	33	75	73	68
District					
Larkhana	3.4	34	75	72	66
Thar	3.6	37	75	74	74
Surkur	3.5	35	79	75	71
Age group					
0–1 years	2.4	33	72	22	74
1–4 years	3.1	34	84	65	72
5–14 years	3.4	37	84	78	70
15–45 years	3.7	35	69	81	70
>45 years	4	37	72	85	66
Average	**3.5**	**35**	**76**	**74**	**70**

A further analysis of prescribing by diagnosis and indicator for Pakistan is shown in **Figure 8.10.**[19]

The over-prescribing of antibiotics and injections identified in the Pakistan study is confirmed by the breakdown of prescribing for the 10 most frequently diagnosed diseases (**Figure 8.10**), in particular for acute respiratory infections (ARI), bronchitis and fevers of unknown etiology which may have a viral cause.[17]

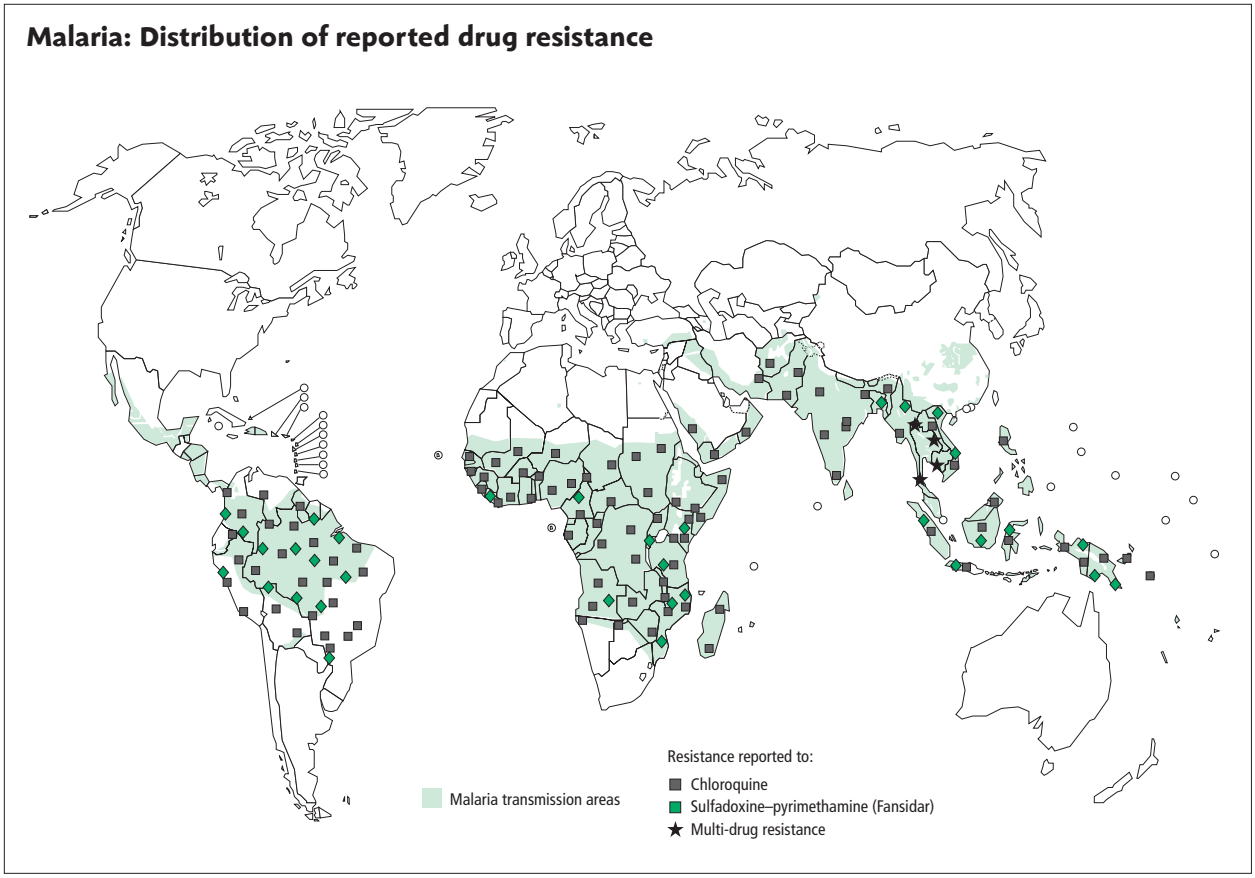
FIGURE 8.10



8.5 ANTIMICROBIAL RESISTANCE

Overuse and misuse of antimicrobials are contributing to growing resistance to treatment for the very diseases that contribute most to the burden of illness in low-income countries. Resistance to the use of chloroquine for the treatment of malaria, for example, is now established in 81 of the 92 countries where the disease is endemic — substantially raising

FIGURE 8.11



the costs of treatment with second- and third-line antimalarial medicines. **Figure 8.11** shows the distribution and reported resistance to antimalarials.

Estimates of resistance to primary multi-drug therapy for tuberculosis from 28 countries at all income levels range from a low of 2% to a high of 40% of cases.[31] Resistance to penicillin treatment is estimated to be between 5% and 98% for gonorrhoea *(N. gonorrhoeae)*[32] and between 12% and 55% for pneumonia and bacterial meningitis.[33]

In Bangladesh, resistance to ampicillin in the treatment of shigellosis diarrhoea is estimated to be over 90%. In addition, resistance to treatment with nalidixic acid increased from less than 10% in 1987 to over 90% in 1992.[34] A study of antibiotics use in 13 countries from 1992 to 1996 revealed that antibiotics were wrongly prescribed for approximately 30% of cases of URTI. More recently, studies in low-, middle- and high-income countries showed that antibiotics were wrongly prescribed in 50% to almost 100% of URTI cases. Elsewhere, a large study in the USA (JAMA 1997) found that 51% of patients with colds and URTI were receiving antibiotics and estimated that over 20% of all antibiotic prescriptions were clinically useless.[35] The highest overall rate for the use of antibiotics for URTI was 97% in China (1997).[36] Yet in 1994, only 8% of cases were found to be treated with antibiotics. One important change in the intervening period was the increasing dependence of health providers on revenue from sales of medicines to supplement low incomes. Perverse financial incentives almost certainly have a role to play in China's recent irrational use of antibiotics and in the development of antimicrobial resistance. Similar trends have been identified in other countries, particularly those in transition to market economies.

Antimicrobial resistance is not only a problem for the individual patient, it also reduces the effectiveness of established treatment and poses a major threat to public health by increasing the complexity and cost of treatment and reducing the probability of a successful outcome.

BOX **8.3**

Interventions to improve rational use of medicines

Since 1988, a number of intervention studies have been undertaken to identify effective methods to improve rational use of medicines. These findings represent a major improvement in the world drug situation. A recent WHO publication proposed 12 core policies to promote more rational use of medicines.[3] These include:

- a mandated multi-disciplinary national body to coordinate medicine use policies
- clinical guidelines
- essential medicines list based on treatment choice
- drug and therapeutics committees in districts and hospitals
- problem-based learning in pharmacotherapy in undergraduate curricula
- continuing in-service medical education as a licensure requirement
- supervision, audit and feedback
- independent information on medicines
- public education about medicines
- avoidance of perverse financial incentives
- appropriate and enforced regulation
- sufficient government expenditure to ensure availability of medicines and staff

Table 8.6 indicates that standard treatment guidelines do not exist in a majority of WHO's Member States.

TABLE 8.6 **Global status of standard treatment guidelines, 1999**

Status of STGs	STGs revised within last 5 years	STGs over 5 years old	No STGs/ unknown	Total
Number of countries	55	32	106	193
Percentage	28.5%	16.6%	54.9%	100%

Source: World Drug Situation Survey, 1999

Where countries do have STGs, their use is not always adequately supported by training, information and incentives. Survey results included in the WHO database on rational use of medicines indicate that the percentage of prescriptions conforming to guidelines in nine countries varied between a low of 25% and a high of 59%.[37]

8.5 RESEARCH AND INFORMATION NEEDS

While much is known about the use of medicines in low-income countries, based on indicator surveys on medicines use and on studies of childhood illnesses and acute infections, there is little information about the impact of the HIV/AIDS epidemic on prescribing or about the treatment of chronic diseases such as diabetes, hypertension and depression. In hospitals where computerized record systems exist, extensive reporting of medicines use may occur, often facilitated by the ATC/DDD system. However, in hospitals without such computerized systems, little has been done and only partial information is available on the indicators. Other unmet needs include information on drug utilization studies in transitional and middle-income countries and information on rational drug use for providers by level of care both in the public, private and NGO sectors.

The detection, assessment and prevention of adverse drug reactions, known as pharmacovigilance, is also becoming increasingly important. Pharmacovigilance requires the rapid transmission of drug information detected by monitoring systems used both nationally and internationally. The information it provides is very useful for prescribing and for patient counselling and efforts are needed to improve the dissemination of this information at all levels.[7,38]

REFERENCES

1 Hogerzeil HV. Promoting rational prescribing: an international perspective. *British Journal of Clinical Pharmacy*, 1995; 39:1–6.

2 *The rational use of drugs. Report of the Conference of Experts.* Geneva, World Health Organization, 1985.

3 *Promoting rational use of medicines: core components 2002.* WHO Policy Perspectives on Medicines No.5, Geneva, World Health Organization, 2002.

4 White TJ, Araekelian A, Rho JP. Counting the costs of drug-related adverse events. *Pharmacoeconomics,* 1999; 15(5): 445–458.

5 Lansang M, Lucas-Aquino R, Tupasi T, et al. Purchase of antibiotics without prescription in Manila, the Philippines: inappropriate choices and doses. *Journal of Clinical Epidemiology*, 1990; 43(1):61–67.

6 Van der Geest S, Hardon A. Self-medication in developing countries. *Journal of Social and Administrative Pharmacy*, 1990; 7(4): 199–204.

7 *Proceedings of the twentieth anniversary symposium. ATC/DDD classification.* WHO Collaborating Centre for Drug Statistics Methodology. *WHO Drug Information* Vol.16, No 3, 2002.

8 Ronning M, et al. *Problems in collecting comparable national drug use data in Europe: the example of antibacterials.* Berlin, Springer-Verlag. 2003.

9 Dukes MNG, ed. *Drug utilization studies. Methods and uses.* WHO, European Series No.45. Copenhagen, World Health Organization, Regional Office for Europe, 1993.

10 International Society for Pharmacoepidemiology, (http://pharmacoepi.org).

11 *How to investigate drug use in health facilities. Selected drug use indicators.* Geneva, World Health Organization, 1993.

12 Quick JD, Rankin JR, Laing RO, O'Connor RW, Hogerzeil HV, Dukes MNG, Garnett A, (eds). *Managing drug supply.* 2nd ed. West Hartford, CT, Kumarian Press, 1997.

13 Ross-Degnan D, Laing RO, Quick J, et al. A strategy for promoting improved pharmaceutical use: the International Network for Rational Use of Drugs. *Soc. Sci. Med.* 1992; 35:1329–41.

14 Hogerzeil HV, et al. Field-tests for rational drugs use in twelve developing countries. *Lancet* 1993; 342: 1408–1410.

15 Embaye A. *Drug use studies in Eritrean health facilities.* September 1999, (http://dcc2.bumc.bu.edu/richardl/IH820/Embaye_concentration_paper.htm).

16 Arustiyono. *Promoting rational use of drugs at the community health centres in Indonesia,* (http://dcc2.bumc.bu.edu/prdu/Other_Documents/ARUS_INDONESIA_PRDU.htm).

17 Pavin M, et al. Prescribing practices of rural primary health care physicians in Uzbekistan. *Trop Med. & Int. Health,* 2003;8 (2):182–190.

18 Memon K. *Use of drugs in Sind Province Pakistan primary health care facilities.* (http://dcc2.bumc.bu.edu/prdu/Other_Documents/Khalil_Concentration_Paper.htm).

19 Chorliet S, Gulija M, Andreeva V. *Drug use survey in Macedonia 2000.* (http://dcc2.bumc.bu.edu/richardl/IH820/Resource_materials/Drug_use_survey_in_Macedonia1.doc).

20 Lates J, Shiyandja N. *Third national survey on the use of drugs in Namibia's public health institutions including monitoring the implementation of the National Drug Policy.* July 2001. (http://dcc2.bumc.bu.edu/richardl/IH820/Resource_materials/FINAL_Drug_use_survey_2001_Report.doc).

21 Groom A, Hedlund A. *Promoting appropriate drug use in missionary health facilities in Cameroon.* Geneva, World Health Organization, 1998.

22 Mallet PH, Njikam A, Scouflaire MS. *Évaluation des habitudes de prescription et de l'usage rationnel des médicaments au Niger. Enquêtes successives dans 19 centres de santé intégrés de la région de Tahoua. Cahiers d'études et de recherches francophones / Santé,* Vol. 11, Numéro 3, Mai–Juin 2001: 185–93.

23 Srinivas SC, Chaudhury RC, Delhi Society for Promotion of Rational Use of Drugs, Karnataka State Pharmacy Council, Bangalore. *Results for rational drug use indicators for 8 government hospitals and 4 private hospitals.* 2002, E-mail correspondence.

24 Srinivas SC, Chaudhury RC, Delhi Society for Promotion of Rational Use of Drugs, Karnataka State Pharmacy Council, Bangalore. *Results for rational drug use indicators for 7 dispensaries of ESI in Karnataka.* 2002, E-mail correspondence.

25 Hazra A, Tripathi SK, Alam MS. Prescribing and dispensing activities at the health facilities of a non-governmental organization. *Natl Med J India,* 2000 Jul–Aug; 13(4): 177–82.

26 Gunn BC Sr, Ali SA. *Drug utilization studies in the Sultanate of Oman.* December 2002, E-mail correspondence.

27 *Public sector survey 2000.* Harare, Directorate of Pharmacy Services Ministry of Health and Child Welfare. Zimbabwe, 2000; p.35–42.

28 Simonsen L, Kane A, Lloyd J, Zaffran M. Unsafe injections in the developing world and transmission of bloodborne pathogens: a review. *Bulletin of the World Health Organization,* 1999; 77(10):789–800.

29 Mann J, et al. Risk factors for human immunodeficiency virus seropositivity among children 1–24 months old in Kinshasa, Zaire. *Lancet,* 1986; 2(8508): 654–7.

30 Report from the International Field Epidemiology Course, Chisanu, Moldova [editorial]. *Weekly Epidemiological Record,* 1999, p.84.

31 Espinal MA. Epidemiology of multi-drug resistant tuberculosis in low and middle income countries. In: Bastian I, Portaels F, (eds), *Multidrug-resistant tuberculosis.* Dordrecht, the Netherlands, Kluwer Academic Publishers, 2000.

32 Tapsall J. *Antimicrobial resistance in Neisseria gonorrhoea.* Geneva, World Health Organization, 2001. WHO/CDS/CSR/DRS/2001.3.

33 Schrag S, Beall B, Dowell SF. *Resistant pneumococcal infections: the burden of disease and challenges in monitoring and controlling antimicrobial resistance.* Geneva, World Health Organization, 2001. WHO/CDS/CSR/DRS/2001.6.

34 Sack DA, et al. *Antimicrobial resistance in shigellosis, cholera and campylabcater.* Geneva, World Health Organization, 2001, WHO/CDS/CSR/DRS/2001.8.

35 Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. *JAMA,* 1997, 278(11):901–4.

36 Hui L, Li X, Zeng X, Dai Y, et al. Patterns and determinants of use of antibiotics for acute respiratory tract infection in children in China. *Paed. Infectious Disease Journal,* 1997, 16(6):560–564.

37 Holloway K. *Measuring use of medicines. How have we progressed in the last decade?* Presentation of results from the WHO Database on the Rational Use of Medicines made at the 2nd International Conference on Improving Use of Medicines, Chiang Mai, Thailand, 30 March 2004.

38 The UMC Global Intelligence Network for Benefits and Risks in Medicinal Products. World Health Organization Collaborating Centre for International Drug Monitoring. Uppsala Monitoring Centre, (http://www.who-umc.htm).

9

MEDICINES REGULATION

SUMMARY

- Most countries have a medicines regulatory authority and formal requirements for registering medicines. However, medicines regulatory authorities differ substantially in their human and financial resources, and in their overall effectiveness. Fewer than one in six WHO Member States have well-developed drug regulation and two in six have no or very little drug regulatory capacity.
- The quality of medicines varies greatly, particularly in low-income countries, both in manufacturing and in the distribution system.
- Regulatory gaps are common, with the informal sector for medicines supply often neglected.
- Three types of common imbalance have been identified in regulatory practice:
  - over-concentration on pre-market, rather than post-market monitoring (e.g. of adverse reactions).
  - too much focus on registration and not enough emphasis on regulating the distribution system
  - more attention given to inspection of manufacturing practice than of distribution channels.
- Whilst international harmonization of regulatory guidelines is desirable, the current process allows inadequate expression of the needs of developing countries.

9.1 INTRODUCTION

The production and distribution of medicines require public oversight and stewardship. Unlike ordinary goods and services, an unregulated medicines market place will fail: it will be not only inequitable, but also inefficient, and probably dangerous to public health.[1] Most countries recognize this need and many have done so for a long time: legal guidelines on the use of drugs by physicians date from as far back as Egypt's late Pharaonic period.

The task of overseeing and regulating the medicines market place is often formidable. Thousands of products may be available, supplied by large numbers of manufacturers and handled by numerous importers, wholesalers and retailers. Three main components of stewardship in the medicines market are identified in a recent review:[2]

- product registration: assessing and authorizing products for market entry, and monitoring their effectiveness and safety after entry
- regulation of manufacturing, importation and distribution
- regulation of medicine promotion and information.

Institutional arrangements and the resource support for carrying out these components differ widely among countries. If a national drug regulatory authority (DRA) is an arm of an existing ministry, its director may not be able to make major policy decisions on

his/her own. It may well be that many drug regulation activities are carried out by another agency with overlapping jurisdictions and functions.[3] Delegation of tasks by a DRA to external groups of experts or to sub-committees can be risky, as these outside groups may acquire a considerable influence on the system as a whole:

- this influence can make it hard to allocate tasks to a wider potential group of experts
- the outside groups may acquire such authority that other experts routinely defer to them, bypassing the NDRA procedures or at least, making balanced debate difficult.[4]

The experience of decentralized, as opposed to national medicines regulatory authorities has also revealed problems. For instance, under the Indian Drugs and Cosmetics Act (1940), the regulation of manufacture, sale and distribution of drugs is primarily the concern of the state, rather than federal, authorities. The federal authorities are responsible for approval of new drugs, provision of standards, quality control over imported drugs, coordination of the activities of state drug control organizations, and supplying advice to allow for uniformity in enforcement of the Act. Responsibility for Indian drug regulation is therefore divided and this can lead to inefficiencies. Each of the 31 states has its own drug control organization that is responsible for drug quality and a system of licensure for the manufacture, sale and distribution of drugs within that state. The federal authorities are supposed to coordinate the activities of individual states.[5]

In some countries, a fourth component, price control, is a recognized objective of medicines policy (**Chapter 6**). Price control is usually implemented through separate mechanisms, such as procurement and/or insurance organizations, rather than through the medicines regulatory authority. However, in some settings (e.g. Cyprus, Tunisia and Cuba), price control is part of the mandate of the national regulatory authority.

A recent WHO 10-country review[2] found considerable variation between countries in both the human and financial resources of the regulatory authority. The review revealed an approximately 10-fold difference in the number of medicines regulatory staff per million population between Estonia (the highest) and Uganda (the lowest), and an even greater discrepancy between average per capita expenditure on medicine regulation between Australia (highest) and Venezuela (lowest).

Registration fees charged by DRAs may be used as a policy instrument to speed up regulatory approval, to encourage retention of quality staff and to stimulate introduction of generics versus new chemical entities. Often, however, the cost recovery function of these fees is not related to the true cost of the pharmaceutical regulatory process, and there is little relationship between DRA registration fees and drug approval times in developing countries.[6] DRA registration fees for most countries could be increased without disincentive to the pharmaceutical industry.

Most countries have a national authority responsible for medicines regulation, and information from the World Drug Situation Survey 1999 indicates that a country's income level has little bearing on this.

A 1995 WHO document describes the limitations of developing countries' DRAs as follows: "…despite all the efforts made to improve drug regulation at national and international levels, fewer than one in six WHO Member States have well-developed drug regulation. Those that do are usually wealthy, industrialized counties. About three in six Member States undertake drug regulation of varying levels of development and operational capacity, while two in six have either no drug regulatory authority or very limited drug regulation capacity".[7]

9.2 REGULATORY FUNCTION 1: PRODUCT REGISTRATION

9.2.1 Dual health systems and medicines regulation

Western medicine and "traditional" medicine, of which herbal medicines are a key component, exist simultaneously in most countries. In the Republic of Korea, for example, the two systems legally coexist. Herbals are covered by the country's medical insurance and are regulated by the Ministry of Health. A registration dossier is required for all new herbal medicines and must include information on toxicity, mutagenicity, efficacy, pharmacokinetics and, significantly, clinical trial data and tables of comparison between the new drug and similar products on the domestic market.[8] Viet Nam possesses an old system of traditional medicine and the Government has adopted a policy of integrating modern and traditional systems. The *Viet Nam Pharmacopoeia*, with national standards for 215 plants commonly used in traditional medical practice and 27 indigenous medicines prepared from medicinal plants, has been published. The monographs on medicinal plants, in addition to protocols for quality control, testing methods and storage, also include regulations on processing and formulation methods, properties, therapeutic efficacy, use, dosage and contraindications.[9]

These dual medical systems pose interesting problems for most countries, however, as regulatory controls are often lacking for "traditional"/herbal products. WHO has produced guidelines for the assessment of herbal medicines[10,11] that define basic criteria for the evaluation of quality, safety and efficacy of herbal medicines to assist national regulatory authorities and manufacturers. However, these guidelines appear not to have been widely acknowledged since only 65 of the 192 Member States of WHO have regulatory systems dealing with traditional medicines.[12] In the WHO 10-country study, all 10 countries have a registration system for allopathic/modern drugs, but only certain countries (Australia, Malaysia, the Netherlands, Tunisia, Uganda and Venezuela) make registration of herbal medicines compulsory.[2] Herbal medicines are not registered in Cuba, Cyprus, Estonia or Zimbabwe. Although more than 20% of the plant species known in the world exist in Brazil, drugs derived from plants have been legally exempt from drug registration since 1976.[13] In 1995, Brazil finally established the legal requirements for phytopharmaceutical drug registration. There are practical difficulties in implementing this in Brazil: resistance from drug companies unwilling to spend the money to install GMP and quality control for these products; limited qualified centres to perform the clinical trials; and ineffective government inspection agencies.[13] It is highly unlikely that these barriers are unique to Brazil.

9.2.2 New medicines approval

There is between–country variation and within-country variability in the time required to approve a new drug (**Tables 9.1** and **9.2**[6] and previously unpublished results). Approval time is defined as time between submission of a "new drug"-type or "generic drug"-type application and DRA approval, and this is exclusive of any clinical testing phase. With regard to developed countries with large shares of the global pharmaceutical market, the median approval times of Canada, Australia, Europe and the United States for non-fast track procedures tends to converge on 15 to 20 months. Japan is the exception. At least until 1997, Japan had no filing fees for new drugs. Recent data on Japanese approval times would be useful to see if introduction of user fees has increased approval times. U.S. approval times have steadily improved since 1995 and are fastest for "fast track" products and slowest for generic products.

TABLE 9.1

Market authorization approval time for industrialized countries

	Median approval time (months)								
	1993	1994	1995	1996	1997	1998	1999	2000	2001
United States (non priority NDA)	27	22	19	18	16	12	13.8	12	14
United States (priority NDA)	22	15	6	8	7	7	6	6	6
United States (generic)			27	23	19.3	18	18.6	18.2	18.1
EP Mutual Recognition Procedure				14	11	22	20		
EP Centralized Procedure				13	15	14.5	15		
Japan			26.5	29	16	29	34		
Canada			20	19	16	17	17.5		
Australia			19	18	17	15.5	17		

EP = European Parliament

The limited data available for other countries (**Table 9.2**) suggest that average approval times, even for new products, are often faster than in developed countries with the largest pharmaceutical market share. In particular Costa Rica has approval times approaching 1.5 months.

TABLE 9.2 **Market authorization approval time (months) for various countries**

	1990–1994	1995–1999	2000–2002
Algeria	7	7	7
Bulgaria		9	7
Costa Rica	6	3	1.5
Cuba	12	12	
Cyprus	5	5	
Czech Republic		25	25.3
Nigeria	36	7	4.5
Malaysia	6	6	
Tunisia	18	18	
Uganda	6	6	
Uruguay	24	9.5	5
Venezuela	6	6	
Zimbabwe	18	18	

9.2.3 The WHO Certification Scheme

The WHO Certification Scheme was established in 1975 and updated in the 1990s to provide minimum safeguards for drugs moving in international commerce. It is a non-binding set of guidelines which can be accessed by both developed and developing countries. The WHO Scheme has no legal status and it can be superseded by national legislation. The Scheme allows importing countries to request basic information about the manufacturing facility and the product of the exporting country. Under the Scheme, the approval of drugs for import depends on the documentation provided by the DRA of the exporting country. It is therefore an administrative mechanism whereby the national DRA is assured that: (i) a given product has been authorized to be marketed in the exporting country, and, if applicable, it can obtain information on the reasons for a product not being authorized in the country of export; (ii) a product is manufactured subject to

inspections and that it conforms to requirements for good manufacturing practices as recommended by WHO;[14] and (iii) the information on a product, including the labelling, is authorized in the exporting country. WHO and others have published data on the actual use of the Scheme. As expected, most of the exporting countries (such as the EU countries) have accepted the Scheme but have not yet standardized the text of their certificates. Many developing countries do not use it.[15] Only two out of 15 importing countries surveyed use the Scheme as recommended.[15]

9.3 REGULATORY FUNCTION 2: MANUFACTURING AND DISTRIBUTION

Tables 9.3 and **9.4** summarize questionnaire responses on national legislation on medicines manufacturing and distribution, and on regulatory agency inspection practices.

TABLE 9.3 **Countries with law on (i) manufacturing and (ii) distribution (by income groups)**

	Law on manufacturing	Law on distribution
Low-income	35 (55.6%)	36 (57.1%)
Middle-income	53 (56.4%)	57 (60.6%)
High-income	21 (60%)	22 (62.9%)
Total	109 (56.8%)	115 (59.9%)

TABLE 9.4 **Countries where medicines regulatory agency inspects (i) manufacturers and (ii) distributors/medicine outlets**

	MRA inspects manufacturers	MRA inspects distributors and/or medicine outlets
Low-income	32 (50.8%)	38 (60.3%)
Middle-income	52 (55.3%)	54 (57.4%)
High-income	20 (57.1%)	17 (48.6%)
Total	104 (54.2%)	109 (56.8%)

Source: World Drug Situation Survey 1999

The rationale for regulating manufacturing and distribution is to ensure quality and safety. Common steps taken by regulatory agencies to ensure quality include requirement of proof of good manufacturing practices (GMP) during product registration, and sampling and testing of medicines at the procurement or distribution stage. Responses to questions on these practices in WHO's 1999 survey generated a composite indicator of "basic elements of quality control in place", which indicates that low-income countries achieve somewhat less than middle- and high-income countries in this respect (**Table 9.5**).

TABLE 9.5 **Countries with basic elements of quality assurance in place, 1999**

	GMP required, sampling and testing in procurement and/or retail outlets
Low-income	25 (39.7%)
Middle-income	43 (46.2%)
High-income	16 (45.7%)
Total	84 (44.7%)

BOX 9.1

Good Manufacturing Practices (GMP)

Good manufacturing practices (GMP) is a system for ensuring that products are consistently produced and controlled according to quality standards. It is designed to minimize the risks involved in any pharmaceutical production that cannot be eliminated through testing the final product. The main risks are:

- unexpected contamination of products, causing damage to health or even death
- wrong labels on containers, leading to the patient getting the wrong medicine
- not enough or too much active ingredient, resulting in ineffective treatment or adverse effects.

For example, in Haiti in 1996, more than 80 children died after receiving a cough and cold syrup containing glycerol contaminated with diethylene glycol. If the manufacturer had followed GMP, these deaths could have been prevented.

GMP is necessary even if there is a quality control laboratory because:

- not even extensive testing of a product can detect all possible mistakes or accidents that may occur during production
- without GMP it is impossible to be sure that every unit of a medicine is of the same quality as the units of medicine tested in the laboratory.

In the early 1970s, a UK manufacturer produced an infusion fluid which caused the death of five patients because it was heavily contaminated with bacteria. Before distributing the fluid, the manufacturer had tested several bottles and found them to be sterile. Eventually a technical fault was found in the sterilizer. The bottles at the bottom had not been properly sterilized. The bottles that the manufacturer had tested were from the upper part, giving the false impression that all the bottles were sterile.

Source: Making a Difference: Manufacturing Quality Medicines. Quality Assurance. WHO/EDM/QSM/2000.3

In the context of developing countries, a problem arises when a DRA (whose mission it is to protect the public) takes it upon itself to perform GMP inspections. This is likely to ensure duplication of effort and this is particularly resource-inefficient if the DRA merely confirms a previous inspection failure. Developed countries already inspect large-scale pharmaceutical manufacturers. Moreover, international health organizations insist on GMP inspections as well. UNICEF, for instance, contracts out GMP inspection services by arrangements with certain countries such as Australia and South Africa whose DRAs can perform these services. At present, these UNICEF-associated GMP inspection reports are not shared with developing country DRAs. Things are changing, however. In March 2002 WHO published its first list of prequalified manufacturers of AIDS drugs[i] (see also, below).

[i] http://www.who.int/medicines/organization/qsm/activities/pilotproc/ppdoc1.doc

Most drug regulatory authorities determine frequencies for GMP inspection by considering the number of manufacturing plants. Australia, however, uses another system for setting inspection frequency, based on product type and on manufacturer type. Products are classified according to their relative therapeutic and side-effect "risk", i.e. as high-risk, medium-risk or low-risk. Similarly, manufacturers are categorized according to their "risk" in passing GMP compliance, i.e. acceptable, marginal or unacceptable GMP. The frequency of GMP inspection is a function of the product risk and manufacturer risk profile. Frequent inspections are made of plants producing high-risk products.[2]

Regulation of drugs for export

Export laws of developed countries are sufficiently diverse that in some cases the criteria for product export is not the same as for full licensing for use in the country.[16]

A drug that is eligible for commercial distribution within the United States generally may be exported without any additional FDA approval or involvement. As to a product intended for export that could not otherwise be commercially distributed within the United States (i.e., is unapproved), the general rule is that the product may nevertheless be exported if it: (a) accords to the specifications of the foreign purchaser, (b) is not in conflict with the laws of the country of destination, (c) is labelled on the outside of the shipping package that it is intended for export, and (d) is not sold or offered for sale in domestic commerce. Thus, in a nutshell, the exporter shipping products from the United States must comply either with FDA's laws or with the laws of the importing country which may, or may not, be sufficiently comprehensive to assure safety.

However, the U.S. law does provide for export of unapproved products to highly developed countries — presumably relying on the high quality review of these listed countries. Listed countries are Australia, Canada, Israel, Japan, New Zealand, Switzerland, South Africa, and the countries of the EU and the European Economic Area (EEA). Unapproved drug exports must still meet FDA standards for GMP.

BOX **9.2**

This high standard for exporting from the U.S. is not the case for other drug regulatory systems. For example, Norplant® implantable contraceptives were developed mainly for use in developing countries, but first were approved for marketing in Finland in 1983 and in Sweden in 1985. Since then Norplant has been approved in more than 40 countries, most of them in the developing world. Ollila & Hemminki (1996)[17] analysed the Norplant® clinical documentation submitted to the Finnish and Swedish drug control authorities and concluded that the clinical data were of poor quality and were mainly focused on assessing efficacy. Side-effects, acceptability, proper insertions and removals, follow-up and other requirements of the health care system for proper use of the implant in developing countries were poorly studied, if at all. This example of Norplant® licensing in Finland shows that licensing of drugs in industrialized countries is not always sufficient to guarantee safety of new drugs in developing countries.

Greece does not allow unlicensed drugs to be exported but in Germany all exported products should merely be "safe" and should not be misleadingly labelled. As of 1996, drug exports from the Netherlands were not subject to any regulatory restriction. Switzerland issues export-only licences.[18] Most European countries do not have specific procedures covering the export of drugs which have been rejected for licensing on the domestic market.[17] Austria, France, Germany, Greece and Spain do not allow the export of rejected drugs, although exceptions may apply. Notwithstanding the above mentioned restrictions, many rejected drugs may remain unidentified. Drugs may disappear from the market for a number of reasons, and it is often difficult to distinguish between regulatory decisions and action taken by companies themselves.[17]

Prequalification and the "Approved List"

The rationale for "prequalifying" pharmaceutical suppliers is that many countries do not have the capacity or resources to appropriately assess the quality of the products they purchase.[19] Significantly, the assessment of pharmaceutical quality is information that can be used by many users at a negligible additional cost. Comprehensive advice on quality medicines is needed for DRAs who cannot afford to provide their own inspection and GMP services.

In March 2002, the World Health Organization released its first list of "pre-approved" manufacturers of AIDS drugs, which included, besides a number of research-based companies, a large Indian producer of generics and three smaller European ones. The medicines on the list are approved for United Nations purchase, and it is intended to encourage price competition in poor nations by telling health officials which of hundreds of suppliers make safe drugs. By October 2003 the list included 41 different formulations of medicines, among them 11 antiretroviral drugs and five drugs for infections that often accompany AIDS. United Nations inspectors spent up to two weeks at each factory making inspections. WHO has therefore acknowledged that generic drugs can fully meet international standards of quality.

Nonetheless, not only should suppliers be prequalified, but the products must also be selected that have the necessary guarantees about quality, effectiveness and safety.

9.3.1 Quality of medicines

Recent survey data suggest there is cause for concern about the quality of medicines in the distribution system in some countries, both in the public and private sectors. **Table 9.6** shows the percentage failures of samples of two important antimalarial medicines: chloroquine syrup and tablets and sulphadoxine/pyrimethamine tablets in seven countries.[20] Average content failure for chloroquine syrup was 23% and for tablets 38%, with

TABLE **9.6**

Percentage failure of antimalarial medicine samples in seven African countries

Country	Chloroquine syrup	Chloroquine tablets		Sulphadoxine/pyrimethamine tablets*	
	Content	Content	Dissolution	Content	Dissolution
Gabon	0 (0/8)	29.0 (5/17)	5.8 (1/7)	0 (0/10)	–
Ghana	5.0 (1/20)	66.7 (12/18)	20.0 (3/15)	37.5 (3/8)	75.0 (3/4)
Mali	66.7 (4/6)	47.3 (9/19)	5.2 (1/19)	0 (0/7)	100 (7/7)
Kenya	25.0 (2/8)	42.8 (3/7)	28.6 (2/7)	0 (0/12)	91.7 (11/12)
Mozambique	25.0 (3/12)	20.0 (3/15)	6.7 (1/15)	5.5 (1/18)	100 (18/18)
Sudan	26.6 (4/15	5.2 (1/19)	12.5 (2/16)	0 (0/20)	80.0 (12/15)
Zimbabwe	13.3 (2/15)	57.1 (8/14)	7.1 (1/14)	10.0 (1/10)	100 (10/10)
Average failure (%)	23.0	38.3	12.2	7.6	91.1 (n=6)
Range (%)	0–66.7	20–66.7	5.2–28.6	0–37.5	75–100 (n=6)

Source: C. Maponga, C. Ondari[20]

highs of 67% for both. While content failures for SP were much lower (average 7.6%), SP dissolution failure averaged over 90%. The authors of the report conclude: "These figures suggest a significant problem of substandard products being found in most countries and at all levels of the distribution chain".

Table 9.7 shows failure rates in quality tests for a mixed sample of tracer medicines in the public, private and NGO sectors (where applicable) in five countries and one Indian state. No quality failures occurred in private and NGO facilities in Tanzania, Ghana and Rajasthan State (India). However, failure rates of up to 50% were found in El Salvador's public sector and failure rates in excess of 10% were common.

TABLE 9.7 **Percentage of sampled tracer medicines that failed quality testing**

Country	Public facilities	Private facilities	NGO
Brazil	18.18% (n=22)	18.18% (n=22)	15.0% (n=20)
Cambodia	19.57% (n=46)	17.81% (n=73)	–
El Salvador	50% (n=30)	28.6% (n=35)	27.3% (n=22)
Tanzania	11.4% (n=35)	13.0% (n=35)	0.0% (n=7)
Ghana	6.0% (n=50)	0.0% (n=33)	2.97% (n=101)
Rajasthan (India)	6.0% (n=50)	14.08 (n=71)	0.0% (n=4)

Source: MSH (2001, draft)

Quality of manufacturing

Studies in 10 countries show great variation in violations of GMP and in the sanctions taken against violators. Reflecting capacity differences, the percentage of manufacturing plants inspected varied between a low of 22% in Zimbabwe and 100% in Australia and Cuba. Manufacturing plants in violation of GMP varied between a low of 1% (in Australia) and highs of 100% in Estonia and Venezuela. While no sanctions were imposed on GMP violators in Australia and Cuba, there were more than 11 sanctions for 20 inspections and violations in Tunisia, and 78 sanctions for 40 inspections and 10 violations in Venezuela.

TABLE 9.8 **Number of manufacturing plants with GMP inspections, violations and sanctions, 1997**

Country	Manufacturing plants	Inspections	Violations in GMP	(%)	Sanctions
Australia	322	322	3	1%	5
Cuba	26	26	4	15%	–
Cyprus	9	7	1	14%	3
Estonia	6	5	5	100%	4
Malaysia	105	77	6	8%	5
Netherlands	86	28	3	11%	–
Tunisia	23	20	1	5%	11
Uganda	9	5	3	60%	6
Venezuela	41	40	10	25%	78
Zimbabwe	23	5	1	20%	3

BOX 9.3

In May 2002, the FDA announced that Schering-Plough's Corporation had signed a consent decree related to a permanent injunction. The company agreed to measures assuring that the drug products manufactured at its New Jersey and Puerto Rico plants are to be made in compliance with FDA's current good manufacturing practice (GMP) regulations. Schering agreed to pay US$ 500,000,000 to the U.S.Treasury after the consent decree has been entered by the court. The Government sought this money to disgorge profits made by the company on drug products that were produced over the last three years in violation of GMP regulations. The Government's action in this case follows 13 inspections at four New Jersey and Puerto Rico facilities since 1998, during which time the FDA found significant violations of the GMP regulations related to facilities manufacturing, quality assurance, equipment, laboratories, and packaging and labelling. As part of the decree, the company has agreed to suspend manufacture of 73 other products. To ensure that it stays in compliance with GMP requirements after entry of the decree, the firm has agreed to submit comprehensive workplans for each facility for FDA concurrence. Station-trained personnel at each facility will provide full-time oversight of all operations at the facilities, and have their expert consultants conduct yearly inspections of the facilities for a period of three years. For at least five years after entry of the injunction, the company must conduct regular audits of its operations and make reports to the FDA concerning its continuing compliance, and the FDA will periodically inspect Schering Plough's manufacturing operations to evaluate the regulatory status of those operations [nytimes.com May 24, 2002].

9.4 REGULATORY FUNCTION 3: MEDICINES PROMOTION

Drug regulatory authorities exert varied degrees of control over post-marketing aspects of pharmaceutical supply, including labelling of drugs, post-approval safety surveillance, marketing, promotion and advertising.

Table 9.9 summarizes available information on the number of countries with legislation concerning medicines promotion activities, and with regulatory powers governing promotion. No clear pattern emerges.

TABLE 9.9 **Countries with law on medicines promotion and regulation of promotion, by income level**

	Law on promotion	Regulation of promotion
Low-income	35 (55.6%)	25 (39.7%)
Middle-income	54 (57.4%)	46 (48.9%)
High-income	20 (57.1%)	18 (51.4%)
Total	109 (56.8%)	89 (46.3%)

Results from the recent WHO study[2] confirm the widespread existence of regulatory gaps – areas of pharmaceutical activity that fall outside the control of existing laws and institutions. Many regulatory bodies fail to provide the tools, such as guidelines and standards, needed to support effective regulation. Regulatory gaps also occur where laws do apply but where the regulatory agency fails, for one reason or another, to implement its mandate. A common and important area of neglect, for example, was found to be the quality of medicines in the informal sector of the economy, which often accounts for a very high proportion of retail sales.

Labelling

Pharmaceutical regulators in the USA and in a number of countries pay close attention to the product labelling. As pharmaceutical products are likely to be distributed in a variety of ways, some going out through informal channels, the labelling of drugs and the package insert becomes important. Most drug products exported from the United States are in bulk form and are repackaged and labelled elsewhere.[21] A widely-quoted 1993 study by the United States Office of Technology Assessment found that up to two thirds of pharmaceuticals sold by US companies in developing countries were mislabelled.[20] The report found that warnings and precautions were underestimated, and clinical and descriptive pharmacological information was lacking in many foreign labels.

If the regulatory authority considers a pharmaceutical to be a prescription-only item, it may well be that the package insert provides only limited information, on the assumption that the physician (or drug seller) will be instructing the user. In reality, this is often not the case, since many drugs in developing countries can be obtained without a prescription and patients often do not receive important information.[20] The problem is exacerbated where literacy is at a low level.

In addition, many regulatory agencies were found to devote excessive resources to pre-marketing assessments for registration purposes, and too little to the monitoring of adverse reactions to registered products or their routine re-evaluation. Similarly, it was found that regulators paid scant attention to the inspection and regulation of national distribution systems and channels, and focused too much on the regulation of manufacturers.

Post-marketing pharmacovigliance

Adverse drug reactions (ADRs) may not be detected until a drug is used after launch, in part because animal toxicology studies are often poor predictors of human effects, the sample size of the clinical trials are usually small, the duration of the clinical trials are often short, and susceptible patients (e.g., those with concurrent disease or medications) are often not included in trials.[22] The main sources of information on the safety of drugs in regular use can be from spontaneous reports, published case reports, so-called "phase IV" procedures and controlled prospective or retrospective studies. Reliance on these sources of reporting has been criticized as being inadequate.[23] For many drugs, especially those not widely used or in developing countries, there is virtually no post-marketing safety monitoring.[24,22] This is because comprehensive post-marketing surveillance is constrained by many factors including: a general under-reporting because of lack of knowledge of ADRs, fear of medical negligence or non-compliance; specific under-reporting because of lack of patient follow-up; inability to measure cumulative toxicity because of the lack of systematic records of repeated use; and lack of information on populations at risk. In developing countries, other systemic factors that are relevant to many DRAs come into play, such as difficulty in transmitting reports, lack of resources for promotion of ADR reports, and difficulties in DRAs implementing policy decisions so that health warnings are circulated in a limited way.[25]

In the WHO 10 country survey, only Uganda did not have a system for monitoring ADRs.[2] Each of the other nine countries uses a spontaneous reporting system for health professionals. Reporting by the pharmaceutical industry is mandatory in most of the countries.[2] The launching of drugs in most developing countries often requires that the sponsor monitor the patients for adverse reactions in collaboration with the national government or DRA.[23] However, the sponsor frequently has neither the time, money nor

infrastructure to do this adequately. The increase in access to the Internet and the general trend towards globalization, in theory at least, support the idea that DRAs should create globally standardized ADR reporting systems. Uniformity of data collection, processing, evaluation and reporting can remove the potential for disputes and misunderstandings. In addition, it eliminates duplication of effort throughout various DRAs.[26]

In the early 1970s, the WHO set up an international programme for adverse reaction monitoring in order to identify rare adverse drug reactions that could not be found through clinical trial programmes.[27] This international database of ADR case reports has expanded over time to accommodate the totality of drug safety monitoring. The international centre is called the WHO Collaborating Centre for International Drug Monitoring and is located in Uppsala, Sweden (now known as the Uppsala Monitoring Centre (UMC)). The Centre maintains the international database and serves various national centres associated with WHO. National centres are appointed by the governments of each of the countries participating in the WHO programme and they are responsible for collecting spontaneous ADR reports originating from health professionals. At present, national pharmacovigilance centres in 60 countries report adverse reactions to a central database maintained by the Uppsala Monitoring Centre in Sweden. The database is large. In 2001, it contained almost 2.5 million reports.[28] Nevertheless, to find new adverse reactions from combinations of drugs and also to identify previously unknown patterns may require sophisticated "data mining" procedures.[27] A recent WHO publication[29] highlights the strengths and weaknesses of present pharmacovigilance systems.

9.5 INTERNATIONAL HARMONIZATION OF REGULATORY REQUIREMENTS

The ability of an individual country to safeguard public interests through national legislation is inherently diminished once national pharmaceutical industries begin to expand beyond national borders.[30] Consequently, policies of global standardization of regulatory requirements have been set up,[29] the most notable example being the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).[31] The ICH has promulgated a common set of technical requirements relating to quality control (validation of procedures), drug safety, and certain aspects of manufacturing practice for active ingredients.[30,32] The ICH steering committee consists of the DRAs and industry associations from the three ICH regions but does not allow any reconsideration of, or amendment to, its decisions. ICH decisions have no direct effects on implementation, except to the extent participating countries adopt the standards.[33] The ICH is not meant to deal with safety and clinical efficacy of the final product.

Harmonization of these technical guidelines is a desirable goal for following reasons:

- in theory, only one set of guidelines need be set for all regions, and consequently the amount of duplicative human and animal experimentation is reduced
- there can be cross-country exchange of expertise with minimum duplication of effort
- improved and coordinated technical harmonization will give developing country DRAs greater bargaining/negotiating power when dealing with outside DRAs, multinationals and/or foreign manufacturers
- the cost of development of new drugs can be reduced, which ought to lead to lower prices; local products are more likely to be acceptable for export to other countries.

ICH and make-up of membership

The key members of the ICH are the European Union, Japan and the United States as well as representatives of the pharmaceutical industry trade associations in these regions (European Federation of Pharmaceutical Industries, Japanese Pharmaceutical Manufacturers Association, International Federation of Pharmaceutical Manufacturers Association and Pharmaceutical Research and Manufacturers of America).[32] The three major members represent over 75% of world pharmaceutical sales, as **Chapter 4** (**Table 4.5**) shows.[32] The countries it represents control more than 90% of the worldwide market. The ICH standards have been criticized as reflecting Western and Japanese industrial concerns. Developing countries lack any effective mechanism to influence the ICH either alone or through the WHO, as the latter currently lacks means to implement international policies in this regard.

There are many examples of regional pharmaceutical harmonization, the first being the 1965 European Directive on the marketing authorization for medicinal products, the precursor of the European Agency for the Evaluation of Medicinal Products (EMEA). Other regional efforts include creation of the Pharmaceutical Inspection Convention (PIC) which provides for mutual recognition of GMP inspections within the European Free Trade Association.[30] There are several mutual recognition agreements between the EU and Australia, New Zealand, Canada, Japan on GMP.[33] Transnational cooperation in this regard varies from region to region, with that of Latin America lagging behind others in the world.

BOX **9.4**

Regional efforts in harmonization of medicines regulation

CADREAC

The Collaboration Agreement of Drug Regulatory Authorities in European Union Associated Countries (CADREAC)[34] signatories are DRAs in Central, Eastern and Southern Europe, i.e. Bulgaria, Cyprus, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Slovak Republic, Slovenia and Turkey. The first CADREAC agreement in 1999 allowed products authorized in the European Union to be recognized in the member country DRAs through a simplified procedure.[30] In 2001, CADREAC approved a simplified "decentralized" procedure which is designed to lead to faster product approvals in the CADREAC countries for products that have been approved by the EU.

ASEAN

The Association of Southeast Asian Nations includes the governments of Brunei Darussalam, the Republic of Indonesia, the Lao People's Democratic Republic, Malaysia, the Union of Myanmar, the Republic of the Philippines, the Republic of Singapore, the Kingdom of Thailand and the Socialist Republic of Viet Nam. Efforts toward ASEAN harmonization were initiated in 1992. Full implementation of a harmonized ASEAN drug regulatory process is not expected for several more years.

Harmonization activities in the Americas

The degree of progress in harmonizing regulatory and technical standards in Central and South America is variable and generally lags far behind similar activities in other parts of the world.

The North American Free Trade Agreement

To date, in the North American Free Trade Agreement (NAFTA: Canada, United States, Mexico), established in 1994, the topic of pharmaceutical regulation has been

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limited to information exchange on regulatory matters, Good Clinical Practices (GCPs), postmarketing surveillance and adverse event reports, approval of new products, and joint reviews.

MERCOSUR

The Mercado Comun del Sur (MERCOSUR), is the South American "Common Market" consisting of Brazil, Bolivia, Argentina, Chile, Paraguay and Uruguay. It has made the most structured effort among the Central and South American trade groups for regulatory harmonization of pharmaceuticals. Many of the common standards are based on recommendations of WHO such as Good Manufacturing Practices (GMPs). Difficulties lie in the adoption and implementation of MERCOSUR agreements and resolutions by participant countries.[35]

The Andean Group

The Andean Group, established in 1969 and including Bolivia, Colombia, Ecuador, Peru and Venezuela, has since the 1970s been attempting to develop a common market, but with limited success, despite several agreed proposals.

The Caribbean Community

In the Caribbean Community (CARICOM) established in 1973, a legal or administrative framework for pharmaceutical regulatory harmonization has yet to be established. The Caribbean Regional Drug Testing Laboratory in Jamaica is responsible for drug quality analysis in the sub-region.

Central American Integration System

Economic integration in the Central America area is being sought by the Central American Integration System (SICA), established in 1961 with Costa Rica, El Salvador, Guatemala, Honduras and Nicaragua as members. There have been several attempts to establish a free trade in pharmaceuticals, but without success. There is no sub-regional legal or administrative framework for participating countries to adopt the decisions of sub-regional technical meetings. Implementation of those agreements depends on the interest and political capacity of the individual regulatory authorities.[34]

Pan American Health Organization

Since 1997, PAHO has convened three conferences related to pharmaceutical regulatory harmonization in the Americas.[36] Generally the different political, health, and legislative realities among the countries of the region makes this difficult to achieve, although arguably no more so than in the ASEAN or CADREAC regions.

REFERENCES

1 *Effective drug regulation: what can countries do?* Theme paper for discussion. (11)99.6. Geneva, World Health Organization, 1999. WHO/HTP/EDM/Mac

2 Ratanwijitrasin S, Wondemagegnehu E. *Effective drug regulation: a multicountry study.* Geneva, World Health Organization, 2002.

3 Agege C. Products and the consumer: an analysis of food and drug legislation in Nigeria. *Food Drug and Cosmetic Law Journal,* 1987, 43 (i):200–214.

4 Dukes G, Hill S, Summers R, Bannenberg W. *The medicines regulatory system in South Africa: review and proposals for reform.* Pretoria, Department of Health, South Africa, 1998.

5 *Counterfeit drugs guidelines for the development of measures to combat counterfeit drugs.* Geneva, World Health Organization, 1999[a]. WHO/EDM/QSM/99.1.

6 Kaplan W, Laing R. Paying for pharmaceutical registration in developing countries. *Health Policy & Planning,* 2003, 18:237–248.

7 *Use of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce.* Geneva, World Health Organization, 1995.

8 Chang I-M. Phytomedicines in Korea: regulatory affairs. *Drug Information Journal,* 1993, 27 (i):160–168.

9 *Regulatory situation of herbal medicines: a worldwide review.* Geneva, World Health Organization, 1998. WHO/TRM/98.1.

10 *Guidelines for the assessment of herbal medicine programme.* Geneva, World Health Organization, 1993.

11 *Handbook for drug supply management at the first level health facility.* Geneva, World Health Organization, 1998. (http://whqlibdoc.who.int/hq/1998/WHO_CHD_98.4d.pdf).

12 *Traditional medicines strategy 2002–2005.* Geneva, World Health Organization, 2002.

13 Petrovick PR, Marques LC, de Paula IC. New rules for phytopharmaceutical drug registration in Brazil. *Journal of Ethnopharmacology*, 1999, 66 (i):51–55.

14 WHO Expert Committee on Specifications for Pharmaceutical Preparations. *Thirty-third Report.* Geneva, World Health Organization, 1993. (WHO Technical Report Series, No. 834:1–30).

15 *Use of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce.* Geneva, World Health Organization, 1995. WHO/DAP/94.21 edn.

16 Horton L. Pharmaceuticals and medical devices: international harmonization and mutual recognition agreements. *Seton Hall Law Review,* 1998, 29:692.

17 Ollila E, Hemminki E. Secrecy in drug regulation: licensing documentation on the Norplant contraceptive. *International Journal of and Risk and Safety in Medicine,* 1999, 9:161–72.

18 Bruneton C, Naboulet P, van der Heide B, Rey JL. The drug trade between European countries and developing countries. *Med. Tropicale,* Mar 1997, 57 (iv): 375–379.

19 *Quality assurance for TB Drugs.* Issues paper prepared by Management Sciences for Health for the WHO/Stop TB Global Drug Facility, 2001, (http://www.stoptb.org/gdf/drugsupply/MSH_QA_Paper_Final_version4.pdf).

20 Maponga C, Ondari C. *The quality of antimalarials. A study in selected Africa countries.* Geneva, World Health Organization, 2003.

21 Gelband H, Corrigan J, McDonough R. Methodology of OTA's report on drug labelling in developing countries. *International Journal of Technology Assessment in Health Care,* 1993, 9 (ii):238–250.

22 Edwards IR. Who cares about pharmacovigilance? *European Journal of Clinical Pharmacology,* 1997, 53(ii):83–88.

23 Edwards IR. Safety monitoring of new anti-malarials in immediate post-marketing phase. *Med. Tropicale,* 1998, 58: 93S–96S.

24 Lindquist M, Edwards IR. The WHO programme for international drug monitoring, its database, and the technical support of the Uppsala Monitoring Centre. *J.Rheumatol.*, 2001, 28 (v):1180–1187.

25 Hartigan-Go K. From signals to policies: academic and regulatory perspective in the Philippines. *Drug Information Journal,* 1999, 33:949–954.

26 Peachey J. From pharmacovigilance to pharmacoperformance. *European Pharmaceutical Review,* 2000, 5(ii).

27 Olsson S. The role of the WHO Programme on International Drug Monitoring in coordinating worldwide drug safety efforts. *Drug Safety,* 1998, 19(i):1–10.

28 Coulter D, Moulter D, Bate A, Meyboom R, Lindquist E, Edwards IR. Antipsychotic drugs and heart muscle disorder in international pharmacovigilance: data mining study. *British Medical Journal,* 2001, 322:1207–1209.

29 *The importance of pharmacovigilance.* Geneva, World Health Organization, 2002.

30 Trouiller P, Salmen R, Myhr K, Folb P, Weerasuriya K, Gray A. *The globalization of regulatory requirements, and the development and availability of medicinal products in developing countries: quality, efficacy and safety issues.* MSF/DND/Working Group: The Crisis of Neglected Diseases, Developing Treatments and Ensuring Access. New York, March, 2002.

31 ICH requirements for registration of pharmaceuticals for human use (http://www.ich.org/) (http://www.ifpma.org/Issues/issues_reg.aspx).

32 Murano G. International Conference on Harmonization – critical discussion of the biotech "specifications document". *Curr.Opin.Biotechnol.*, 2000, 11(iii):303–308.

33 Trouiller P, Folb P, Weerasuriya K. *Legal and regulatory issues affecting drug development for neglected diseases: Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and Neglected Diseases Act,* MSF/DND Working Group The Crisis of Neglected Diseases, Developing Treatments and Ensuring Access. New York, March 2002.

34 CADREAC Secretariat 2001. State Institute for Drug Control.

35 Calam DH. Design and international harmonization of pharmacopoeial standards. *J.Pharm.Biomed.Anal.* 2001, 14 (i–ii):1–5.

36 Pharmaceutical regulatory harmonization in the Americas. CD42/13, Rev.1. Pan American Health Organization and World Health Organization, 52nd Session of the Regional Committee, Washington D.C., 25–29 September 2000, (http://www.paho.org/english/gov/cd/cd42_13e.pdf).

CONCLUSION

In the 15-year interval since the publication of the first review of the world pharmaceutical situation *(The World Drug Situation)* there has been both progress and failure. Almost 2 billion people today still lack access to essential medicines. While this is a smaller percentage of the global population than in 1985, when the first survey was carried out, gross inequity in access to medicines remains the overriding feature of the world pharmaceutical situation.

One encouraging finding is that many more countries now have national policies on medicines than in 1985. However, in low-income countries, all too often these policies lack implementation plans and supporting strategies, such as price regulation, generic promotion or the effective regulation of quality.

Meanwhile, over the past 15 years there has been a notable change in the global context in which national medicines policies are being implemented. Nothing illustrates this more clearly than the tragedy of the HIV/AIDS epidemic. The global burden of disease has undergone a major shift, as the scale and impact of HIV/AIDS has become fully apparent. In 1988, there were an estimated 6.3 million HIV/AIDS cases worldwide. By the end of 2002, an estimated 42 million people were living with HIV/AIDS and in that year alone 3.1 million people died of AIDS. The global response to the HIV/AIDS pandemic has brought to the fore a number of key issues in medicines policy. Firstly, it has confirmed the importance of innovation. The R&D of new, safe and effective medicines is critical in saving lives and reducing suffering from a new disease on an epidemic scale.[i] However, many of these medicines have been at the centre of continuing controversies about prices and the legal limits to competition through intellectual property rights in the form of patents. Patents have "unusual importance" in medicines policy.[1] A major shift towards the development of a global trading system with a single set of rules has occurred since *The World Drug Situation* was published. Intellectual property rights occupy an important place in this system, and medicines have held centre stage in arguments in and around the World Trade Organization about whether, and at what speed, to implement a single set of international trade rules.

The high price of new medicines for HIV/AIDS in relation to their production cost has reopened interest in competition. Brazil began supplying its domestic market with generic HIV/AIDS drugs and Indian manufacturers of generic HIV/AIDS medicines entered into the markets of sub-Saharan Africa. Meanwhile, the authority of national governments to regulate their national medicines market by invoking compulsory licensing arrangements has been both asserted and challenged over medicines for HIV/AIDS.

The high price of medicines for HIV/AIDS has also highlighted the importance of risk-pooling mechanisms that can ensure access to treatment on the basis of medical need rather than ability to pay. This reinforces the importance of financing medicines through government revenues, health insurance, or a mix of both. Brazil's social security system

[i] Antiretroviral medicines went on the WHO Model List of Essential Medicines for the first time in 2002.

and numerous employers, including several large firms in South Africa, offer examples of middle-income countries where access to treatment has been made possible through health insurance schemes.

Finally, the human and physical capacity limits of health systems in many low-income countries have been brought into sharp focus as they attempt to deal on a national scale with prevention and counselling, and to provide treatment and care for those living with HIV/AIDS.

Elsewhere, the overall production of medicines has undergone important changes over the past 15 years, as the number of pharmaceutical manufacturers has fallen and market share has increased. In 1987, the largest single manufacturer had a 3.4% share of global sales. By 2000, the largest manufacturer had a 7.3% share of the global market, and the top 10 manufacturers 45.7%.[i] This concentration is the result of more than 30 mergers among major manufacturing companies that occurred between 1988 and 1999.[ii]

Today, following a period of record profitability in the late 1990s, manufacturers are attempting both to improve their product pipeline and rationalize the high fixed costs of R&D and marketing. There have been substantial changes in both the process and content of R&D, following the development of the biotechnology industry and its concentration in small specialist firms. Another development is the emergence of very large generic medicine production markets in India and China, consisting of thousands of small manufacturers and a small number of very big enterprises. By 1999, India had become the world's tenth largest net exporter of pharmaceuticals.

Overall, the dominant picture that emerges from our analysis is of extreme and worsening disparity. As documented in the 1988 report, the pharmaceutical situation is one of extraordinary, and sometimes growing, asymmetries: in production, trade, consumption, and in people's access to the medicines they need. A small number of countries and companies dominate the global market and the best market opportunities are provided by the lifestyle-related illnesses of the affluent. At the same time, the needs of almost two billion people in the lowest income groups remain unmet.

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[i] IMS data based on audit of 59 countries plus estimates of the remainder, cited in "Pharmaceuticals – Global Insights" presentation by John Morris of KPMG, February 2002.

[ii] Windhover's Health Care Strategies, 2000.

REFERENCE

1 Scherer FM. The pharmaceutical industry. In: *Handbook of health economics,* vol.1. Culyer AJ, Newhouse JP, eds. Amsterdam, Elsevier BV, 2000.

STATISTICAL ANNEX NOTES

Income level

1= low income, 2= middle income, 3= high income. Income classification is based on the World Bank classification of countries (valid through to July 2000) as reported in the Human Development Report 2000 (UNDP). High income countries are those with GNP per capita of US $9,361; middle income have a GNP per capita between $761 and $9360; and low income countries have a GNP per capita of $760 or less. All income figures relate to 1998.

Disability-adjusted life expectancy

Data show rankings of countries from 1 to 191 in terms of expectation of life lived in equivalent full health (estimates for 1997). The country ranked 1 (Japan) has the longest expectation of disability-free life, the country ranked 191 (Sierra Leone) the shortest. Data reprinted from *The World Health Report 2000: Health Systems - Improving Performance.* World Health Organization, Geneva. Details of estimation methods can be found in: *Estimates of DALE for 191 Countries* by Mathers, C and others, http://www.google.com/u/who?q=estimates+of+DALE&sitesearch=who.int&domains=who.int

Production

Data show estimated production values in US$ for 1985, 1991 and 1997 using the Standard Industrial Trade Classification Revision 1 code 54. Based primarily on UNIDO data reported in Balance, R Pogany, J and Forster, H, *The World's Pharmaceutical Industries,* UNIDO, 1992, with projections to 1991 and 1997 based on trends 1975–1990. Supplemented by data from OECD health database and from data supplied by the International Federation of Pharmaceutical Manufacturers Associations, and individual country estimates, where available.

Imports and exports

Data show imports and exports in US $ for 1985, 1991 and 1997 using SITC 3 code 54 "medicinal and pharmaceutical products". Data source was United Nations Statistics Division Comtrade database (customized study) and International Trade Centre.

Total sales

Data show total sales for selected countries for 1990 and 2000. Sales data in US $ at exchange rate values in effect at time of sale. **Licensed brands** are defined as sales of products manufactured and marketed by a company under a licensing agreement with the originating corporation. **Original brands** are medicines marketed by the originating corporation. **Other brands** are branded products marketed by a company that is not the originator. A branded product in this context has its own (non-generic) name and registered trademark. **Unbranded products** are marketed under the generic name for the molecule rather than their own brand name (registered trademark). **Patent n/a** means patent status was not available. Source: IMS Health, IMS MIDAS Customized study, February 2001.

Pharmaceuticals expenditure data

Data estimates are all in US $ at average exchange rate values for the years 1995 and 2000. Columns 1 and 2 show per capita health expenditure from all sources; columns 3 and 4 show total expenditure on pharmaceuticals (all sources) as a percentage of total health expenditure. Columns 5 and 6 show total per capita expenditure on pharmaceuticals. The following columns show government and private sources of pharmaceuticals expenditure in per capita terms. The final column shows private health expenditure as a percentage of total health spending. All estimates are from the WHO National Health Accounts database.

Data from world medicines survey 1999

This questionnaire survey of all WHO Member States is the source of data for all remaining columns in the annex. Columns 1 and 2 show estimates of the proportion of the population with access to affordable essential medicines, the first figure being the respondent's single point estimate, the second being the broader range which is used in the analysis in Chapter 7. Columns 3–4 summarize responses on the status of national policy on medicines. Columns 5 and 6 summarize responses on the implementation of national medicines policies. The following columns summarize responses: on the existence and actions of national medicines regulatory bodies; on selected aspects of quality assurance; and on tendering and procurement practice. The next 2 columns identify the year in which standard treatment guidelines were last updated and whether, and at what levels essential medicine training is part of health worker training. The final column brings together responses on price regulation practices.

STATISTICAL ANNEX

Annex Table 1: Production, trade, sales

Country	Region	Inc level	Health system performance DALE	Production 1985 US$'000	Production 1991 US$'000	Production 1997 US$'000	Imports 1985 US$'000	Imports 1991 US$'000	Imports 1997 US$'000	1985 US$'000
Afghanistan	EMRO		168							
Albania	EURO	2	102						11567	
Algeria	AFRO	2	84				218887	217287	373379	64
Andorra	EURO		10							
Angola	AFRO	1	165				23918			
Antigua and Barbuda	AMRO	2	48							
Argentina	AMRO	2	39				103406	182540	663596	20438
Armenia	EURO	1	41						43751	
Australia	WPRO	3	2	797547	1693463	2261537	241766	727671	1642104	82725
Austria	EURO	3	17	540854	1634564	2352284	338437	1014271	1913743	252512
Azerbaijan	EURO	1	65							
Bahamas	AMRO	3	109				11501		19453	30656
Bahrain	EMRO	2	61				10984	19914		
Bangladesh	SEARO	1	140	100519	212973	320541	28068	37290	92188	23
Barbados	AMRO	2	53				11231	16852	24785	197
Belarus	EURO	2	83							
Belgium	EURO	3	16	2656000			546585	1767455	3623509	662445
Belize	AMRO	2	94				2789		4871	160
Benin	AFRO	1	157						23231	
Bhutan	SEARO	1	138					1329		
Bolivia	AMRO	2	133		24049		12433	18591	26515	3
Bosnia and Herzegovina	EURO		56							
Botswana	AFRO	2	187							
Brazil	AMRO	2	111				120232	425829	1461421	61480
Brunei Darussalam	WPRO	3	59				6730	14010	27426	
Bulgaria	EURO	2	60						93618	
Burkina Faso	AFRO	1	178							
Burundi	AFRO	1	179							
Cambodia	WPRO	1	148							
Cameroon	AFRO	1	156						53177	
Canada	AMRO	3	12	2050561	4067311	5561960	424535	1010655	2259765	165048
Cape Verde	AFRO	2	118						4137	
Central African Republic	AFRO	1	175							
Central America										
Chad	AFRO	1	161							
Chile	AMRO	2	32		413884	633444	30987	77574	232511	1638
China	WPRO	1	81	48904	106419	214025		520372	330757	
Colombia	AMRO	2	74	471819	547631	1209985	73645	70185	400942	20440
Comoros	AFRO	1	146							
Congo	AFRO	1	150				21267			19
Cook Islands	WPRO		67							
Costa Rica	AMRO	2	40	54694	58485	75207	44735	66146	119639	25637
Côte d'Ivoire	AFRO	1	155				58938			966
Croatia	EURO	2	38						185122	
Cuba	AMRO	2	33							
Cyprus	EMRO	3	25	5549	27018	54945		50284	80508	6115
Czech Republic	EURO	2	35				20229		694135	
Democratic People's Republic of Korea	SEARO		137							
Democratic Republic of the Congo	AFRO	1	174				27187			
Denmark	EURO	3	28	570000	1618552	4595983	221000	551958	835047	451988
Djibouti	EMRO	2	166				4429	5872		
Dominica	AMRO	2	26				674	1117	1769	
Dominican Republic	AMRO	2	79				39089			1534
Ecuador	AMRO	2	93	40471	76532	128760	56274	131366	206868	2816
Egypt	EMRO	2	115	873599	464108	1237811	88843	155494	315199	4693

PRODUCTION, TRADE & SALES DATA											
Exports		Total sales*									
1991	1997	1990					2000				
US$'000	US$	Licensed Brands	Original Brands	Other Brands	Patent N/A	Unbranded	Licensed Brands	Original Brands	Other Brands	Patent N/A	Unbranded
	34										
	329	3943									
57299	284437	107582	270532	780626	147814	49547	307881	802472	1901959	307815	105620
	1090										
229177	678135	65442	519557	439861	109028	6908	339734	1318686	708676	133382	17766
781188	1324880	133204	353219	298992	134907	58981	316309	749349	381394	113385	67652
332											
343	240	7358	15014	67950	23453	4675	10658	27460	201359	46151	4053
5557	4327										
1911686	4885516	163245	833697	417308	165962	36595	391550	1330255	510930	148551	42402
	98										
19	229										
99710	217291	217489	781237	1273883	413132	81158	505088	1630017	2287858	571517	164758
	150										
	137113										
	303										
254340	964549	306098	1400589	1377406	357296	158030	989770	2895646	1379043	349923	549049
	11										
		8419	46439	95586	34975	8662	42685	140569	243516	62105	36387
15282	31148	7409	35639	83004	27465	27296	29479	114601	288792	65468	51285
773787	1536246										
20476	175066	31182	281416	202240	110437	21120	62425	217779	340347	101289	74405
35984	69928										
	156594										
23128	38543										
	213736	19328	15054	107817	43818	36031	67073	226688	262644	56275	46922
1200325	2272449										
8											
	1										
	1945	2493	14631	48719	12316	4790	12481	50032	137264	27550	16096
2920	25096										
20715	55604	61346	83220	175583	57094	16957	128244	165203	351362	100928	24661

Annex Table 1: Production, trade, sales

Country	Region	Inc level	Health system performance DALE	Production 1985 US$'000	Production 1991 US$'000	Production 1997 US$'000	Imports 1985 US$'000	Imports 1991 US$'000	Imports 1997 US$'000	1985 US$'000
El Salvador	AMRO	2	87			118200	61003	45978	115171	14550
Equatorial Guinea	AFRO	2	152							
Eritrea	AFRO	1	169							
Estonia	EURO	2	69						70263	
Ethiopia	AFRO	1	182					17141		
Fiji	WPRO	2	106				4930	8911		7
Finland	EURO	3	20	227980	578391	652663	148941	445117	618586	63287
France	EURO	3	3	6022557	14998263	22517920	787038	3084597	5875385	1536065
French West Africa										
Gabon	AFRO	2	144							
Gambia	AFRO	1	143						4727	
Georgia	EURO	2	44							
Germany	EURO	3	22	6623913	17870548	23087608		4226912	7117795	
Ghana	AFRO	1	149							
Greece	EURO	3	7	252476	672868	1793245	122810	387016	984078	36528
Grenada	AMRO	2	49				1414	1971	2891	
Guatemala	AMRO	2	129	130808	112534	273817	45576	63591	124565	47466
Guinea	AFRO	1	167						15040	
Guinea-Bissau	AFRO	1	170							
Guyana	AMRO	2	98					1388		
Haiti	AMRO	1	153							
Honduras	AMRO	1	92	18821	17484	26837	55916	50748	76058	1624
Hungary	EURO	2	62				144839	227243	485755	349415
Iceland	EURO	3	19				12392	31505	47807	
India	SEARO	1	134	2116391	3312667	6012453	146202	227729	388862	129697
Indonesia	SEARO	1	103	497705	992013	1314302	83097	138586	262638	15400
Iran, Islamic Republic of	EMRO	2	96						393045	
Iraq	EMRO	2	126							
Ireland	EURO	3	27				178532	503605	897235	198163
Israel	EURO	3	23				59461	201609	486678	20934
Italy	EURO	3	6	4011000	4450230	4937558	966903	3029695	4763626	859591
Jamaica	AMRO	2	36				11316	22951	60392	2640
Japan	WPRO	3	1	15972432	39775216	56768000	1291884	3114112	4243178	391051
Jordan	EMRO	2	101		74339		42887	58465	64485	36339
Kazakhstan	EURO	2	122						59222	
Kenya	AFRO	1	162				28410	56040	95651	5351
Kiribati	WPRO		125				238	390		
Kuwait	EMRO	3	68					21569	169845	
Kyrgyzstan	EURO	1	123							
Lao People's Democratic Republic	WPRO	1	147							
Latvia	EURO	2	82						98418	
Lebanon	EMRO	2	95							
Lesotho	AFRO	1	171							
Liberia	AFRO		181							
Libyan Arab Jamahiriya	EMRO	2	107				38699	83842	106664	
Lithuania	EURO	2	63						180610	
Luxembourg	EURO	3	18							
Madagascar	AFRO	1	172	7527			7947	9995	23838	5
Malawi	AFRO	1	189				5344	12264	23717	100
Malaysia	WPRO	2	89	55456	96143	177699	118110	193868	370132	17798
Maldives	SEARO	2	130						3585	
Mali	AFRO	1	183						18011	
Malta	EURO	3	21				9121	25375	47895	3486
Marshall Islands	WPRO		121							
Mauritania	AFRO	1	158							

PRODUCTION, TRADE & SALES DATA

Exports		Total sales*									
1991	1997	1990					2000				
US$'000	US$	Licensed Brands	Original Brands	Other Brands	Patent N/A	Unbranded	Licensed Brands	Original Brands	Other Brands	Patent N/A	Unbranded
14529	53111										
	31773										
116											
18											
139368	214488	63922	222499	307133	66907	13874	119036	468018	322216	51904	24916
3955696	7900846	1432934	4918394	3470982	1798168	217160	2811085	7665118	3872697	1835293	503023
		17568	65763	113511	73024	9966	10737	61054	86689	42465	6927
	27										
6575126	11654976	1307245	3555786	4779724	1633470	670638	1990510	5648584	5721883	1728055	1139085
70663	89493	41319	290077	223378	38528	5746	188165	598055	292521	38982	4427
61857	68540										
1219	1291										
	357260	42757	51587	125922	41668	14146	115082	325088	243651	57290	34683
227	5861										
483471	947204										
21638	41357	16706	96219	221617	57863	14101	28413	149655	315352	72109	29173
	2267										
1150583	3356685	15474	101890	68955	13818	3353	78066	227474	130934	17216	5525
95745	416716	6604	27421	65061	18289	1521	28517	109657	124741	18500	2143
1629241	4430346	1953233	3228248	4017128	1150457	383122	2692809	4484176	2879652	709474	169767
2996	828										
1089475	1952405	5318803	9409592	8096757	2223624	1222166	10946413	20969289	14474656	3648654	1423052
50633	21362										
	5176										
8949	30740										
53	685										
	47276										
	67265										
		3313	25319	17637	5869	607	10452	52030	21345	5489	924
1	3										
111											
43829	72287	2958	29155	34971	10370	2521	14503	97429	69185	23959	5994
	215										
9235	24246										

Annex Table 1: Production, trade, sales

Country	Region	Inc level	Health system performance DALE	Production 1985 US$'000	Production 1991 US$'000	Production 1997 US$'000	Imports 1985 US$'000	Imports 1991 US$'000	Imports 1997 US$'000	1985 US$'000
Mauritius	AFRO	2	78	1463	2064	3006	6321	21660	31095	
Mexico	AMRO	2	55	1070000	1783514	2972824	130064	346270	898716	36669
Micronesia, Federated States of	WPRO		104							
Monaco	EURO		9							
Mongolia	WPRO	1	131							
Morocco	EMRO	2	110			261149	32587	85101	136471	5003
Mozambique	AFRO	1	180							
Myanmar	SEARO	1	139		24632	129425		24187		
Namibia	AFRO	2	177							
Nauru	WPRO		136							
Nepal	SEARO	1	142		5744		18733	25175	45422	5
Netherlands	EURO	3	13	1001686	2648596	3536068	579921	1540705	3478147	609201
New Zealand	WPRO	3	31	95000			110915	258646	417075	23632
Nicaragua	AMRO	1	117	21456			52872	40132	75203	563
Niger	AFRO	1	190						9489	
Nigeria	AFRO	1	163		483793		187274	71106	123258	
Niue	WPRO		85				3			
Norway	EURO	3	15	155399	455812	1336975	145853	432658	618804	43246
Oman	EMRO	2	72				24775	41506	62044	97
Pakistan	EMRO	1	124	311866	595313	711129	134353	207286	265335	2523
Palau	WPRO		112							
Panama	AMRO	2	47	16837	18234	20383	50390	64982	113085	4103
Papua New Guinea	WPRO	2	145				9188			3
Paraguay	AMRO	2	71				7160	24486	59194	5
Peru	AMRO	2	105	172364	404747	425144	38882	63789	179516	2395
Philippines	WPRO	2	113	353678	724527	1146765	54450	148048	350559	6727
Poland	EURO	2	45				255442	435776	1311086	233708
Portugal	EURO	3	29	192357	687843	2459635	124780	341109	699953	46763
Qatar	EMRO	3	66				10790	23152		
Republic of Korea	WPRO	2	51	1380198	3636616	4814558	113211	352742	724741	42207
Republic of Moldova	EURO	1	88						44106	
Romania	EURO	2	80					55468	181179	
Russian Federation	EURO	2	91						1768492	
Rwanda	AFRO	1	185							
Saint Kitts and Nevis	AMRO	2	86						1613	
Saint Lucia	AMRO	2	54				1482	2227	3816	
Saint Vincent and the Grenadines	AMRO	2	43						1905	
Samoa	WPRO	2	97							
San Marino	EURO		11							
São Tomé and Principe	AFRO	1	132							
Saudi Arabia	EMRO	2	58				365011	622688		135
Senegal	AFRO	1	151			16927		44416	37355	
Seychelles	AFRO	2	108				1096	2319		
Sierra Leone	AFRO	1	191							
Singapore	WPRO	3	30	230342	832956	3012111	108677	219181	722278	135717
Slovakia	EURO	2	42		121349				347933	
Slovenia	EURO	3	34						187582	
Solomon Islands	WPRO	1	127				890			
Somalia	EMRO		173							
South Africa	AFRO	2	160	413700	1125915	1943961				
Spain	EURO	3	5	1837172	6712343	16038176	244642	1175290	2746540	233103
Sri Lanka	SEARO	2	76		9399		22328	38855		291
Sudan	EMRO	1	154				22542		48239	
Suriname	AMRO	2	77					8489	7339	
Swaziland	AFRO	2	164							

PRODUCTION, TRADE & SALES DATA											
Exports		Total sales*									
1991	1997	1990					2000				
US$'000	US$	Licensed Brands	Original Brands	Other Brands	Patent N/A	Unbranded	Licensed Brands	Original Brands	Other Brands	Patent N/A	Unbranded
1697	929										
128346	636834	105272	491553	603353	164245	30553	505459	1880508	1929867	544840	43595
17322	9397	36047	32410	76792	33464	4213	76344	85576	171772	45849	6386
662											
	21										
1513097	3770552										
40946	54969	18627	154862	83754	25190	7754	35062	222798	109185	27384	14047
292	1182										
	12										
157											
140838	217871	32003	206625	125947	39480	16984	87077	480915	162293	35849	23799
69	1996										
14520	32104	44524	143400	162417	71652	23236	63039	205917	361070	70324	14187
7143	14045										
1											
453	3770										
4196	22523	14697	60364	99088	30428	2874	17069	68514	134678	29837	18558
9444	31044	36380	136223	258787	60777	9467	98000	400138	489505	104094	25883
322468	294560										
89443	171707	83491	332247	288810	67161	4105	236131	679797	515540	81574	9547
139363	289844	196047	182208	1293735	312651	195542	386885	598777	1603405	335107	272616
	3495										
13181	30850										
	116472										
	10										
7227		22252	158762	141255	39791	3443	79361	291129	261901	48758	4853
346	1547										
220652	616571	2451	22529	18330	6212	2628	19109	100454	47324	14039	5851
	145649	13908	6553	60149	26431	23992	38825	122572	119242	30792	19727
	402036										
		43018	212922	232491	56283	7708	79143	330594	320687	61790	17255
737529	1516932	529465	1031739	1481231	309273	90861	1556136	2876284	1909587	448197	302162
785											

Annex Table 1: Production, trade, sales

Country	Region	Inc level	Health system performance DALE	Production 1985 US$'000	Production 1991 US$'000	Production 1997 US$'000	Imports 1985 US$'000	Imports 1991 US$'000	Imports 1997 US$'000	1985 US$'000
Sweden	EURO	3	4	646217	2409411	4391386	332181	805130	1230853	405469
Switzerland	EURO	3	8				493288	1357707	3517053	1603645
Syrian Arab Republic	EMRO	2	114				133459		23706	136
Tajikistan	EURO	1	120							
Thailand	SEARO	2	99		740297		110335	238667	511711	10080
Macedonia, The former Yugoslav Republic of	EURO	2	64						41531	
Togo	AFRO	1	159					21017	15105	
Tonga	WPRO		75				695	1056		
Trinidad and Tobago	AMRO	2	57		4428		322265	41164	37021	278
Tunisia	EMRO	2	90		33282	75684	53250	136400	168332	1092
Turkey	EURO	2	73	446566	1716517	2160366	76711	288834	811079	15952
Turkmenistan	EURO	1	128						15570	
Tuvalu	WPRO		119				25		22	
Uganda	AFRO	1	186							
Ukraine	EURO	2	70							
United Arab Emirates	EMRO	3	50				51250	99349		4377
United Kingdom	EURO	3	14	5184499	13278308	23326532	760807	2422256	5194598	1846018
United Republic of Tanzania	AFRO	1	176							
United States of America	AMRO	3	24	31500000	60840000	97505440	1717992	3092086	8819067	2790444
Uruguay	AMRO	2	37	108249			15712	37807	111934	3288
Uzbekistan	EURO	2	100							
Vanuatu	WPRO	2	135							
Venezuela, Bolivarian Republic of	AMRO	2	52	415467	436003	457554	104902	116685	247036	2556
Viet Nam	WPRO	1	116							
Yemen	EMRO	1	141					8256		
Yugoslavia (renamed Serbie & Montenegro)	EURO		46						78449	
Zambia	AFRO	1	188							
Zimbabwe	AFRO	1	184	30335	163220		12917	24751	48380	3845
	*6/2/03	*6/2/03	*6/2/03	*7/2/03	*7/2/03	*7/2/03				

PRODUCTION, TRADE & SALES DATA

Exports		Total sales*									
1991	1997	1990					2000				
US$'000	US$	Licensed Brands	Original Brands	Other Brands	Patent N/A	Unbranded	Licensed Brands	Original Brands	Other Brands	Patent N/A	Unbranded
1724648	3057619										
4658423	8208497	75901	493796	405571	160514	23129	236853	903457	433505	149020	36519
	7342										
34234	106551	10367	86519	183503	70523	31759	33663	232525	301058	81722	46115
	18818										
25											
1942	2163										
4501	14561	5099	26230	36534	17925	2901	16885	59198	67850	20696	3166
53498	113568	113835	128675	342895	80114	16241	420732	726703	1009636	136315	27718
421		947	9011	11300	3648	171	6046	45851	38199	10315	777
4515065	8940218	410344	2495569	1370253	470506	467107	1291394	5349022	2434297	653919	1402711
4608533	8036944	5212904	11453723	9902688	2291962	1928474	22761819	60951686	17895806	4844184	6776252
14552	22572	2257	7522	26129	9826	3142	8464	26347	85080	23051	7314
7322	48304	16271	92904	128790	46170	10046	98668	416918	471275	145229	94757
	65408										
2849	5693										

* IMS Health & Area Classifications

Annex Table 2: Expenditure

Country	EXPENDITURE DATA					
	Total expenditure on health (per capita at average exchange rate)		Total expenditure on pharmaceuticals (% total expenditure on health)		Total expenditure on pharmaceuticals (per capita at exchange rate)	
	1995	2000	1995	2000	1995	2000
Afghanistan	13	9	9.6	15	1	1
Albania	27	46	15.1	16.5	4	8
Algeria	73	68	23.8	21.3	17	15
Andorra	1282	1200	5.4	7.6	70	92
Angola	17	25	19.7	20.3	3	5
Antigua and Barbuda	415	509	31.5	26.9	130	137
Argentina	620	683	26.7	28.9	165	198
Armenia	23	22	61.7	52.6	14	12
Australia	1700	1808	11.2	13.5	191	245
Austria	2498	1873	13.3	17.3	331	323
Azerbaijan	19	31	7.7	7.8	1	2
Bahamas	587	863	13.8	13.4	81	115
Bahrain	455	483	15	15.3	68	74
Bangladesh	10	14	53.3	37.9	5	5
Barbados	451	603	19.2	24.7	87	149
Belarus	56	61	11.2	11.9	6	7
Belgium	2407	1916	16.0	16.4	386	315
Belize	137	156	18.4	20.9	25	33
Benin	13	15	22.5	15.2	3	2
Bhutan	5	9	48.8	26.2	2	2
Bolivia	39	52	24.2	24.1	10	13
Bosnia and Herzegovina	37	87	n/a	n/a	n/a	n/a
Botswana	170	173	23.2	26.3	39	45
Brazil	316	265	16.8	23.2	53	61
Brunei Darussalam	458	469	22.3	23.3	102	109
Bulgaria	69	75	23.9	22	16	16
Burkina Faso	7	6	53.1	44.1	4	3
Burundi	7	5	32.1	29.8	2	2
Cambodia	20	30	37.9	36.7	7	11
Cameroon	27	19	32	44.5	9	9
Canada	1818	2102	13.7	14.9	248	313
Cape Verde	40	56	54.7	32.4	22	18
Central African Republic	12	12	28	32.6	3	4
Central America						
Chad	8	5	27.8	38.3	2	2
Chile	307	328	10.7	14.2	33	46
China	22	45	51.7	45.1	11	20
Colombia	158	108	11.5	17.4	18	19
Comoros	12	9	44.8	53.7	5	5
Congo	19	18	79.9	46.7	15	9
Cook Islands	288	196	18.3	25.6	53	50
Costa Rica	230	280	15.5	14.9	36	42
Côte d'Ivoire	44	42	18.9	17.5	8	7
Croatia	363	388	18.1	18.3	66	71
Cuba	122	175	27.8	25.9	34	45
Cyprus	860	904	24.1	32.1	208	290
Czech Republic	367	358	25.6	22	94	79
Democratic People's Republic of Korea	8	21	n/a	n/a	n/a	n/a
Democratic Republic of the Congo	4	10	6.8	19.9		
Denmark	2826	2474	9.1	8.7	256	215
Djibouti	60	58	34.6	22.9	21	13
Dominica	173	200	20	28.5	35	57
Dominican Republic	100	145	15.6	16.1	16	23
Ecuador	73	52	24.1	25.6	18	13
Egypt	36	52	43.9	40.3	16	21

Government expenditure on pharmaceuticals (per capita at exchange rate)		Private expenditure on pharmaceuticals (per capita at exchange rate)		Private expenditure as % total health spending
1995	2000	1995	2000	1997 exch rate
		1	1	47.4
3	4	1	4	28.5
12	11	5	4	20.2
53	70	16	22	13.4
	1	3	4	52.1
94	96	36	41	37.1
39	41	127	157	44.8
3	5	4	13	58.5
103	133	88	112	30.7
212	227	120	97	28.6
	1	1	2	26.6
25	43	56	73	46.3
26	28	42	46	28.7
	1	5	5	65.3
29	46	58	103	39.8
6	6	1	1	12.8
166	157	220	157	29.0
6	6	19	27	47.1
1	1	1	1	51.5
2	2			9.6
2	3	7	10	36.1
n/a	n/a	n/a	n/a	44.6
22	23	18	23	29.5
4	5	49	57	59.7
95	100	7	9	59.4
9	13	7	4	20.0
2	2	1	1	32.4
1	1	1	1	57.8
	1	7	10	90.6
2	1	7	7	70.6
81	113	167	200	30.1
13	12	8	7	28.2
1	2	2	2	48.6
1	n/a	n/a	n/a	20.7
5	10	28	37	62.1
4	6	8	14	60.6
5	6	13	13	42.4
n/a	n/a	n/a	n/a	31.8
n/a	n/a	n/a	n/a	35.4
n/a	n/a	n/a	n/a	32.9
13	17	23	25	21.7
1	1	7	6	54.0
56	61	9	10	19.5
14	21	20	24	12.5
68	82	139	208	63.7
79	73	15	18	8.3
n/a	n/a	n/a	n/a	16.5
n/a	n/a	n/a	n/a	25.9
124	106	132	109	17.7
13	6	8	8	55.6
24	37	10	20	30.4
3	5	12	18	70.9
6	3	12	10	49.2
3	3	12	17	68.2

Annex Table 2: Expenditure

Country	EXPENDITURE DATA					
	Total expenditure on health (per capita at average exchange rate)		Total expenditure on pharmaceuticals (% total expenditure on health)		Total expenditure on pharmaceuticals (per capita at exchange rate)	
	1995	2000	1995	2000	1995	2000
El Salvador	107	169	28.6	26.6	31	45
Equatorial Guinea	19	56	14.6	12.4	3	7
Eritrea	8	9	38.4	38.8	2	4
Estonia	153	222	24	22.3	37	49
Ethiopia	3	3	53.5	39.4	2	1
Fiji	98	80	11.4	15.6	11	12
Finland	1906	1550	14.1	15.5	268	240
France	2555	2067	17.6	20.4	450	421
French West Africa						
Gabon	93	130	43.7	25.5	41	33
Gambia	23	20	20.1	16.3	5	3
Georgia	12	20	37.5	39.1	4	8
Germany	3101	2408	12.7	13.6	405	328
Ghana	16	11	28.2	32.8	5	4
Greece	1082	1018	15.7	13.3	170	136
Grenada	146	245	24.3	20.9	36	51
Guatemala	54	79	38	31.8	21	25
Guinea	17	13	18.1	21.3	3	3
Guinea-Bissau	19	10	78.3	70.5	5	3
Guyana	39	48	24.8	20.4	10	10
Haiti	16	22	18.4	12.5	3	3
Honduras	38	54	43.4	42.1	16	23
Hungary	323	305	25	24.9	81	76
Iceland	2149	2794	15.5	14.7	333	412
India	21	23	13.5	14.5	3	3
Indonesia	24	20	18.5	26.7	4	5
Iran, Islamic Republic of	98	312	15.7	12.6	15	39
Iraq	147	214	n/a	n/a	n/a	n/a
Ireland	1254	1579	10.4	10.6	131	168
Israel	1596	1612	9.3	10.7	149	173
Italy	1415	1512	20.9	22.2	296	336
Jamaica	96	173	29.9	24.8	29	43
Japan	2857	2890	22.4	18.3	641	528
Jordan	115	154	52.4	34.5	60	53
Kazakhstan	57	62	5.7	8.4	3	5
Kenya	25	30	27.4	22.9	7	7
Kiribati	53	45	11.3	12.5	6	6
Kuwait	611	553	23	27.5	140	152
Kyrgyzstan	16	12	20.7	39.9	3	5
Lao People's Democratic Republic	10	9	16.4	20.4	2	2
Latvia	119	191	22.4	39.8	26	76
Lebanon	384	607	27.5	21.2	106	128
Lesotho	30	29	13	12.1	4	4
Liberia	32	2	24.7	21.4	8	1
Libyan Arab Jamahiriya	163	175	17.6	17.8	29	31
Lithuania	98	197	29.2	20	29	39
Luxembourg	2810	2442	12	12.1	338	295
Madagascar	6	6	24.8	24.7	1	1
Malawi	12	12	21.4	21.7	3	3
Malaysia	113	129	12.4	11.2	14	15
Maldives	64	104	21.8	19.7	14	20
Mali	10	10	35.2	28.4	4	3
Malta	713	811	17.4	21.8	124	177
Marshall Islands	213	188	16.2	16	35	30
Mauritania	16	13	33.1	29.6	5	4

Government expenditure on pharmaceuticals (per capita at exchange rate)		Private expenditure on pharmaceuticals (per capita at exchange rate)		Private expenditure as % total health spending
1995	2000	1995	2000	1997 exch rate
3	6	27	39	61.3
1	3	1	4	44.0
1	2	1	2	34.2
26	22	10	28	11.5
1	1	1	1	58.6
5	5	6	7	33.3
121	121	147	120	23.9
276	273	174	148	23.9
2	2	38	21	33.5
n/a	n/a	n/a	n/a	21.3
1	1	4	6	91.4
272	227	127	102	23.4
n/a	n/a	n/a	n/a	44.9
121	100	50	36	44.8
10	15	26	36	34.3
3	5	17	20	55.1
n/a	n/a	3	2	42.8
n/a	n/a	n/a	n/a	36.0
6	6	3	3	18.5
		3	2	66.5
3	5	13	18	44.6
54	57	27	19	24.7
224	265	109	147	16.3
1	1	2	2	84.7
1		4	5	76.2
8	20	7	19	53.6
n/a	n/a	n/a	n/a	41.1
101	134	30	34	24.4
22	26	127	147	31.9
113	149	183	187	27.8
2	4	26	39	46.5
438	348	203	180	20.5
15	14	45	39	37.4
2	3	1	2	23.6
1		6	6	71.8
6	5	n/a	n/a	0.9
119	116	22	36	12.6
1	1	2	4	30.6
		2	2	63.2
12	26	14	50	39.4
6	8	99	121	79.4
n/a	n/a	n/a	n/a	24.0
n/a	n/a	n/a	n/a	33.3
n/a	n/a	n/a	n/a	52.4
14	22	15	17	26.1
276	241	62	54	7.5
		1	1	42.8
1		2	2	49.4
4	4	10	11	42.4
8	11	6	10	25.5
2	2	1	1	54.2
75	106	49	71	29.1
n/a	n/a	n/a	n/a	38.1
n/a	n/a	1	1	30.3

Annex Table 2: Expenditure

Country	EXPENDITURE DATA					
	Total expenditure on health (per capita at average exchange rate)		Total expenditure on pharmaceuticals (% total expenditure on health)		Total expenditure on pharmaceuticals (per capita at exchange rate)	
	1995	2000	1995	2000	1995	2000
Mauritius	111	127	39.1	35.5	43	45
Mexico	182	327	21.1	24.9	39	8
Micronesia, Federated States of	149	140	n/a	n/a	n/a	n/a
Monaco	1895	1610	n/a	n/a	n/a	n/a
Mongolia	22	23	15.7	15	3	3
Morocco	54	54	41.1	36.2	22	20
Mozambique	8	12	23.1	18.6	2	2
Myanmar	52	164	16.7	16	9	26
Namibia	136	126	16.4	15.1	22	19
Nauru	416	643	n/a	n/a	n/a	n/a
Nepal	10	12	28.9	29.9	3	4
Netherlands	2253	2003	11	10.1	247	202
New Zealand	1195	1054	14.8	12.3	177	129
Nicaragua	50	55	34.1	46.5	17	26
Niger	7	6	16.2	17.1	1	1
Nigeria	7	13	23.7	18.2	2	2
Niue	326	290	n/a	n/a	n/a	n/a
Norway	2689	2817	9.1	9.6	245	272
Oman	230	227	14.7	15	34	34
Pakistan	21	18	28.2	27.1	6	5
Palau	429	454	n/a	n/a	n/a	n/a
Panama	231	260	11.1	15	26	39
Papua New Guinea	30	27	31.1	34.3	9	9
Paraguay	130	112	27.3	38.9	35	44
Peru	101	96	29.5	24.2	30	23
Philippines	37	34	46	43.5	17	15
Poland	198	244	27.6	25	54	61
Portugal	892	934	23.2	23.1	207	216
Qatar	738	860	16.5	13.9	122	120
Republic of Korea	507	577	21.9	15.9	111	92
Republic of Moldova	28	18	8.3	12.2	2	1
Romania	55	104	17.9	23.3	10	25
Russian Federation	126	95	14.1	17.8	18	12
Rwanda	12	13	26.9	21.3	3	3
Saint Kitts and Nevis	255	364	15	16.4	38	60
Saint Lucia	150	195	12.2	16.1	27	36
Saint Vincent and the Grenadines	134	170	26.7	23.7	36	40
Samoa	60	80	13.9	13.7	8	11
San Marino	1127	1196	22.1	28.8	249	338
São Tomé and Principe	1	7	20	16.1	11	8
Saudi Arabia	356	376	22.5	19.9	80	75
Senegal	25	22	26.4	30	7	7
Seychelles	418	444	23.5	22.5	98	100
Sierra Leone	6	6	30.5	29	2	2
Singapore	879	826	32.4	34.2	285	282
Slovakia	239	208	23.7	34	57	71
Slovenia	737	765	18.9	17.6	140	135
Solomon Islands	38	39	13.9	8.8	5	3
Somalia	4	6	26.1	26.5	1	2
South Africa	311	253	14.1	12.3	44	31
Spain	1133	1048	18	17.7	204	186
Sri Lanka	24	32	27	25	7	1
Sudan	13	13	21.1	29.9	3	4
Suriname	119	186	11.4	17.1	14	32
Swaziland	45	46	34.9	27.4	16	13

Government expenditure on pharmaceuticals (per capita at exchange rate)		Private expenditure on pharmaceuticals (per capita at exchange rate)		Private expenditure as % total health spending
1995	2000	1995	2000	1997 exch rate
13	11	31	34	48.9
9	19	29	62	56.4
n/a	n/a	n/a	n/a	43.3
n/a	n/a	n/a	n/a	50.0
2	2	1	1	37.3
2	2	20	18	71.4
1	1	1	1	43.8
1	1	8	25	79.7
2	5	20	14	45.7
n/a	n/a	n/a	n/a	2.6
1	1	2	3	79.4
220	123	28	80	31.1
124	87	53	43	22.7
6	6	11	20	38.7
		1	1	48.9
1	1	1	2	73.0
n/a	n/a	n/a	n/a	2.7
141	147	104	125	17.0
17	18	16	16	17.9
4	3	2	2	77.1
n/a	n/a	n/a	n/a	12.5
10	12	15	27	33.3
9	9	1	1	10.6
9	12	26	31	66.9
4	5	26	18	44.5
2	1	15	13	56.6
29	27	25	34	28.0
131	151	76	65	32.9
92	50	30	30	23.7
3	16	108	76	59.0
1	1			24.6
7	16	3	10	37.1
13	7	5	4	29.5
1	1	3	2	65.9
11	17	27	43	31.6
16	21	12	15	37.7
19	23	16	18	36.2
7	7	1	4	28.6
170	236	79	102	14.8
n/a	n/a	n/a	n/a	33.3
64	60	16	15	19.8
2	2	5	5	44.3
44	58	13	16	27.7
				58.6
53	45	232	237	65.6
44	58	13	12	8.6
90	98	50	37	20.7
4	2	2	1	4.7
				37.5
9	6	35	25	52.7
155	164	49	21	23.4
19	35	6	7	50.5
n/a	n/a	n/a	n/a	79.1
5	10	8	22	39.8
n/a	n/a	n/a	n/a	27.7

Annex Table 2: Expenditure

Country	EXPENDITURE DATA					
	Total expenditure on health (per capita at average exchange rate)		Total expenditure on pharmaceuticals (% total expenditure on health)		Total expenditure on pharmaceuticals (per capita at exchange rate)	
	1995	2000	1995	2000	1995	2000
Sweden	2293	2269	12.3	13.9	282	315
Switzerland	4352	3572	10	10.7	435	382
Syrian Arab Republic	42	64	7	6	3	4
Tajikistan	4	5	41.2	13.4	2	1
Thailand	99	73	29.7	29.3	29	21
Macedonia, The former Yugoslav Republic of	119	106	11	18.2	13	19
Togo	12	8	39.6	36.8	5	3
Tonga	91	81	26.2	26.7	24	22
Trinidad and Tobago	189	248	34.9	37.6	66	93
Tunisia	136	126	21.6	28	29	33
Turkey	93	150	23.2	28	21	58
Turkmenistan	33	42	21.2	26.7	5	7
Tuvalu	63	74	n/a	n/a	n/a	n/a
Uganda	11	14	26.4	15.4	3	2
Ukraine	47	30	12.6	17.8	6	5
United Arab Emirates	617	820	15.9	18.8	98	155
United Kingdom	1372	1786	15.3	14.1	209	253
United Republic of Tanzania	8	11	18.7	10.4	2	1
United States of America	3654	4540	8.9	11.9	324	541
Uruguay	552	653	20.2	17.1	112	112
Uzbekistan	22	30	12.8	7.6	3	2
Vanuatu	47	47	20.9	22.6	10	11
Venezuela, Bolivarian Republic of	168	296	21.7	14	36	42
Viet Nam	11	21	38.1	41	4	9
Yemen	38	21	37.5	37.8	14	8
Yugoslavia	96	89	11.2	9.6	11	9
Zambia	19	18	32.2	26.7	6	5
Zimbabwe	43	42	13.9	20.6	6	9

Government expenditure on pharmaceuticals (per capita at exchange rate)		Private expenditure on pharmaceuticals (per capita at exchange rate)		Private expenditure as % total health spending
1995	2000	1995	2000	1997 exch rate
207	221	75	95	15.7
232	232	203	150	44.8
2	3	1	1	48.3
	1	1		34.0
18	13	12	8	42.8
11	13	3	7	15.2
n/a	n/a	n/a	n/a	57.2
16	11	8	10	53.2
8	11	58	82	56.6
11	10	19	23	59.6
n/a	34	n/a	21	28.5
3	5	2	1	25.5
n/a	n/a	n/a	n/a	28.6
1		2	2	49.3
4	3	2	2	25.0
n/a	n/a	n/a	n/a	20.7
133	167	76	86	16.3
1	1	1	1	52.9
50	99	224	442	54.5
19	16	93	95	54.1
2	1	1	1	17.1
n/a	n/a	n/a	n/a	35.8
9	6	28	35	49.4
1	2	4	8	79.7
1		14	8	62.1
11	9	3	7	41.4
3	3	3	2	43.5
4	7	1	2	40.9

Annex Table 3: 1999 World drug survey – access, national medicines policies

Country	DATA FROM 1999 WORLD DRUG SURVEY							
	Questionnaire response – % with access to EMs	% with access to EMs	Status of NMP	Date of latest EM policy document	NMP implementation		Drug registration	
	1997 int $				Date	Less than five years of NMP	There is DRA	Law on registration
	Med Strat comp 3 indicator	Med Strat comp 3 indicator	1=NMP official <10yrs; 2=NMP official >10yrs; 3=draft NMP; 4=no NMP; 5=no response		Col H regional policy	(use yes or no from col I in regional policy)	1=yes	1=yes
Afghanistan	50	50–80	4				1	0
Albania	60	50–80	1	1998	1995	Yes	1	1
Algeria	95	>95	4				1	1
Andorra	–		5					
Angola	20	<50	4				1	0
Antigua and Barbuda	66	50–80	5					
Argentina	70	50–80	4				1	1
Armenia	40	<50	1	1995			1	1
Australia	100	>95	3	1999			1	1
Austria	100	>95	4				1	1
Azerbaijan	66	50–80	5					
Bahamas	80	50–80	4				1	0
Bahrain	100	>95	4				1	1
Bangladesh	65	50–80	2	1982			1	1
Barbados	100	>95	4				1	0
Belarus	70	50–80	1	1998			1	1
Belgium	99	>95	5					
Belize	80	50–80	4				0	0
Benin	77	50–80	3	1998	1998	Yes	1	1
Bhutan	85	81–95	2	1985			0	0
Bolivia	70	50–80	1	1997	1999	Yes	1	1
Bosnia and Herzegovina	88	81–95	3	1997				
Botswana	90	81–95	3	1987			1	1
Brazil	40	<50	1	1998	1998	Yes	1	1
Brunei Darussalam	99	>95	5			Yes		
Bulgaria	88	81–95	5				1	1
Burkina Faso	60	50-80	1	1996	1997	Yes	1	1
Burundi	20	<50	3	1998			1	0
Cambodia	30	<50	1	1998	1995	Yes	1	1
Cameroon	66	50–80	3	1997				
Canada	100	>95	4				1	1
Cape Verde	80	50–80	5				1	1
Central African Republic	50	50–80	1	1995			1	1
Central America								
Chad	46	<50	1	1995	1998	Yes	1	1
Chile	88	81–95	1	1996				
China	85	81–95	1	1997	1997	Yes	1	1
Colombia	88	81–95	1	1993				
Comoros	90	81–95	3	1997			1	0
Congo	61	50–80	1	1997	1999	Yes	1	1
Cook Islands	60	50–80	4				0	0
Costa Rica	100	>95	1	1997			1	1
Côte d'Ivoire	80	50–80	4		1997		1	1
Croatia	100	>95	3	1998	1999	Yes	1	1
Cuba	100	>95	1	1998	1998	Yes	1	1
Cyprus	100	>95	4				1	1
Czech Republic	88	81–95	5				1	1
Democratic People's Republic of Korea	–		3	1983				
Democratic Republic of the Congo	–		3					
Denmark	99	>95	5					

			Manufacturing			Importation		Pharma registration		
Date	DRA registers drug	List of registered drugs maintained	Law on manufacturing	Date	DRA inspects manufacturers	Law on importation	Date	Law on distribution	Date	DRA inspects drug outlets
	1=yes	1=yes	1=yes		1=yes	1=yes		1=yes		1=yes
	1	1	1	1980		1	1980	1	1980	1
1998	1	1	1	1998	1	1	1998	1	1998	1
1995	1	1	1		0	1	1969	1	1995	0
	0	0	0		1	0		0		1
1964	1	1	1	1964	1	1	1964	1	1977	
1992	1	1	1	1998	1	1	1995	1	1991	1
1998	1	1	1	1998	1	1	1998	1	1998	0
1994	1	1	1	1984	1	1	1997	1	1994	1
	0	0	0		0	1	1987	1	1987	1
1997	1	1	1	1997	1	1	1997	1	1997	1
1982	1	1	1	1982	1	1	1982	1	1982	1
	0	0	1	1969	1	1	1969	0		1
1993	1	1	1	1998	0	1	1998	1	1998	1
	0	0	0		0	1	1958	0		0
1997	1	1	1	1975	1	1	1975	1	1975	1
	0	0	0		0	0		0		0
1997	1	1	1	1997	0	1	1997	1	1997	1
1992	1	1	1	1992	1	1	1992	1	1992	1
1976	1	1	1	1995	1	1	1996	1	1973	
1995	1	1	1	1995	1	1	1995	1	1995	1
1992	1	1	0		0	1	1998	1	1998	0
	0	0	0		0	0		0		1
1994	1	1	1	1998	1	1	1998	1	1996	1
	1	1	1			1		1		
1993	0	1	0		1	1	1993	1	1993	1
1994	1	1	0			0		0		1
1967	1	1	1	1965	1	1	1965	1	1965	1
1985	1	1	1	1985	1	1	1985	1	1985	1
	1	0	1	1991	1	1	1990	1	1991	1
1985	1	1	1	1933	1	1	1933	1	1933	1
			0		0	0		0		
1994	1	1	1	1992	1	1	1994	1	1973	1
1994	1	1	1	1994	0	1	1994	1	1994	1
1997	1	1	1	1997	1	1	1997	1	1997	1
1995	1	1	1	1922	1	1	1995	1	1922	0
1995	1	1	1	1990	1	1	1993	1	1993	1
1997	1	1	1	1998	1	0		1	1998	1

Annex Table 3: 1999 World drug survey – access, national medicines policies

Country	DATA FROM 1999 WORLD DRUG SURVEY							
	Questionnaire response – % with access to EMs	% with access to EMs	Status of NMP	Date of latest EM policy document	NMP implementation		Drug registration	
	1997 int $				Date	Less than five years of NMP	There is DRA	Law on registration
	Med Strat comp 3 indicator	Med Strat comp 3 indicator	1=NMP official <10yrs; 2=NMP official >10yrs; 3=draft NMP; 4=no NMP; 5=no response		Col H regional policy	(use yes or no from col I in regional policy)	1=yes	1=yes
Djibouti	80	50–80	4				1	0
Dominica	90	81–95	4				0	0
Dominican Republic	66	50-80	3	1997	1997	Yes	1	1
Ecuador	40	<50	3	1998			1	1
Egypt	88	81–95	5				1	1
El Salvador	80	50–80	4				1	1
Equatorial Guinea	44	<50	1	1990			1	0
Eritrea	57	50–80	3	1997	1998	Yes	1	1
Estonia	100	>95	4				1	1
Ethiopia	66	50–80	1	1993				
Fiji	100	>95	1	1995	1996		1	0
Finland	98	>95	4				1	1
France	99	>95	4				1	1
French West Africa								
Gabon	30	<50	3	1993			1	1
Gambia	90	81–95	1	1996	1994	Yes	1	1
Georgia	30	<50	1	1995			1	1
Germany	100	>95	4				1	1
Ghana	44	<50	3	1995				
Greece	100	>95	1	1995			1	1
Grenada	98	>95	4				1	0
Guatemala	50	50–80	1	1996			1	1
Guinea	93	81–95	3	1992	1998	Yes	1	1
Guinea-Bissau	44	<50	5					
Guyana	44	<50	5					
Haiti	30	<50	1	1997	1997	Yes	1	0
Honduras	40	<50	1	1995			1	1
Hungary	100	>95	5				1	1
Iceland	100	>95	4				1	1
India	35	<50	1	1994			1	1
Indonesia	80	50–80	2	1983			1	1
Iran, Islamic Republic of	85	81–95	1	1998	1998	Yes	1	1
Iraq	85	81–95	1	1991			1	1
Ireland	99	>95	5					
Israel	99	>95	5					
Italy	99	>95	5					
Jamaica	95	81–95	1	1995			1	1
Japan	100	>95	5		1950		1	1
Jordan	100	>95	1	1998	1998	Yes	1	1
Kazakhstan	66	50–80	1	1995				
Kenya	35	<50	1	1994			1	1
Kiribati	75	50–80	3	1998		Yes	1	0
Kuwait	99	>95	5					
Kyrgyzstan	66	50–80	1	1994				
Lao People's Democratic Republic	66	50–80	1	1992	1992	Yes	1	1
Latvia	90	81–95	1	1995	1999	Yes	1	1
Lebanon	88	81–95	4				1	1
Lesotho	80	50–80	3	1996			0	0
Liberia	30	<50	3	1998	1999	Yes	1	1
Libyan Arab Jamahiriya	100	>95	4		1999	Yes	1	1

			Manufacturing			Importation		Pharma registration		
Date	DRA registers drug	List of registered drugs maintained	Law on manufacturing	Date	DRA inspects manufacturers	Law on importation	Date	Law on distribution	Date	DRA inspects drug outlets
	1=yes	1=yes	1=yes		1=yes	1=yes		1=yes		1=yes
	0	0	1	1991	1	1	1991	1	1991	1
		0	0			0		0		0
1998	1	1	1	1998	1	1	1998	1	1998	1
1974	1	1	1	1974	1	1	1974	1	1998	1
1994	1	1	1	1981	1	1	1994	1	1997	1
1959	1	1	1	1959	1	1	1959	1	1959	1
	0		0			1	1991	1	1991	1
1993	0	0	1	1993	1	1	1993	1	1993	1
1992	1	1	1	1996	1	1	1991	1	1993	1
	0	0	1	1985	1	1	1985	1	1985	1
1987	1	1	1	1987	1	1	1987	1	1987	1
1994	1	1	1	1998	1	1	1998	1	1998	0
1995	1	1	0		1	1	1995	1	1995	1
1984	1	0	1	1984	0	1	1984	1	1984	1
1992	1	1	1	1996	1	1	1996	1	1996	1
	1	1	1		1	1		1		1
1995	1	1	1	1992	1	1	1987	1	1995	1
	0	0	0		0	0		0		1
1997	1	1	1	1997	1	1	1997	1	1997	1
1984	1	1	1	1994	0	1	1984	1	1984	
	1	1	1	1999	1	1	1999	1	1999	1
1994	1	1	0		0	1	1994	1	1994	1
1998	1	1	1	1998	1	1	1998	1	1998	1
1997	1	1	1	1996	1	1	1996	1	1997	1
	1	1	1		1	0		1		1
1971	1	1	1	1965	1	1	1965	1	1964	1
1988	1	1	1	1988	1	1	1988	1	1988	1
1996	1	1	1	1992	1	1	1998	0		1
1964	1	1	1	1964	1	1	1964	1	1965	1
1996	1	1	1	1996	1	1	1996	1	1994	1
	1	1	1		1	1		1		1
1983	1	1	1	1983	1	1	1983	1	1983	1
	0	0	0		0	1	1981	1	1981	0
1995	1	1	1	1990	1	1	1991	1	1989	1
1998	1	1	1	1994	1	1	1996	1	1995	1
1994	1	0	1	1994	1	1	1994	1	1994	1
		0	0			0		0		1
1999	1	0	0		0	1	1998	1	1998	
1973	1	1	1	1973	1	1	1972	1	1972	1

Annex Table 3: 1999 World drug survey – access, national medicines policies

Country	DATA FROM 1999 WORLD DRUG SURVEY							
	Questionnaire response – % with access to EMs	% with access to EMs	Status of NMP	Date of latest EM policy document	NMP implementation		Drug registration	
	1997 int $				Date	Less than five years of NMP	There is DRA	Law on registration
	Med Strat comp 3 indicator	Med Strat comp 3 indicator	1=NMP official <10yrs; 2=NMP official >10yrs; 3=draft NMP; 4=no NMP; 5=no response		Col H regional policy	(use yes or no from col I in regional policy)	1=yes	1=yes
Lithuania	88	81–95	5					
Luxembourg	99	>95	5					
Madagascar	65	50–80	3	1998	1997	Yes	1	0
Malawi	44	<50	1	1991				
Malaysia	70	50–80	1	1991			1	1
Maldives	50	50–80	3	1995			1	0
Mali	60	50–80	3	1998	1998	Yes	0	1
Malta	–		5					
Marshall Islands	90	81–95	4				0	0
Mauritania	66	50–80	5					
Mauritius	100	>95	3	1996	1997	Yes	1	1
Mexico	92	81–95	3	1982			1	1
Micronesia, Federated States of	95	81–95	3				0	0
Monaco	–		4				1	0
Mongolia	60	50–80	3	1992			0	1
Morocco	66	50–80	5					
Mozambique	50	50–80	2	1985			1	1
Myanmar	60	50–80	1	1993	1993		1	1
Namibia	80	50–80	1	1998			1	1
Nauru	100	50–80	4		1999	Yes		0
Nepal	20	<50	1	1995			1	1
Netherlands	100	>95	1	1994			1	1
New Zealand	100	>95	4				1	1
Nicaragua	46	<50	1	1996	1998	Yes	1	1
Niger	66	50–80	1	1995				
Nigeria	10	<50	1	1990			1	1
Niue	95	81–95	3				1	1
Norway	100	>95	4				1	1
Oman	90	81–95	3	1997	1999	Yes	1	1
Pakistan	65	50-80	1	1997	1998	Yes	1	1
Palau	100	>95	4				0	0
Panama	80	50–80	4				1	1
Papua New Guinea	90	81–95	1	1998	1998	Yes	0	0
Paraguay	44	<50	1	1997			1	1
Peru	60	50–80	1	1997			1	1
Philippines	66	50–80	2	1987	1998		1	1
Poland	–		5					
Portugal	100	>95	1	1997			1	1
Qatar	99	>95	5					
Republic of Korea	99	81–95	3					
Republic of Moldova	66	50–80	3	1997			1	1
Romania	85	81–95	3	1998			1	1
Russian Federation	66	50–80	5					
Rwanda	44	<50	4		1997		1	1
Saint Kitts and Nevis	66	50–80	4				0	0
Saint Lucia	66	50–80	5					
Saint Vincent and the Grenadines	85	81–95	4				1	0
Samoa	100	>95	3				1	0
San Marino	–		5					
São Tomé and Principe	44	<50	5					

			Manufacturing			Importation		Pharma registration		
Date	DRA registers drug	List of registered drugs maintained	Law on manufacturing	Date	DRA inspects manufacturers	Law on importation	Date	Law on distribution	Date	DRA inspects drug outlets
	1=yes	1=yes	1=yes		1=yes	1=yes		1=yes		1=yes
	1	1	0		1	0		0		1
1984	1	1	1	1984	1	1	1984	1	1984	1
	0	1	0		0	1	1993	1	1993	1
1995	1	1	1	1991	1	1	1994	1	1991	1
	0	0	0		0	0		0		0
1985	1	1	1	1985	1	1	1985	1	1985	1
1998	1	1	1	1997	1	1	1998	1	1998	1
	0	0	0			0		0		
	0	0	1	1997	1	0		1	1997	1
1994	0	1	1	1998	0	1	1992	0		1
1997	0	0	1	1997	1	1	1997	1	1997	1
1958	1	1	1	1954	1	1	1958	1	1958	1
1965	1	1	1	1965	1	1	1965	1	1965	1
	0	0	0		0	0		0		1
1981	1	1	1	1981	1	1	1981	1	1981	1
1963	1	1	1	1963	1	1	1963	1	1963	1
1984	1	0	1	1984	1	1	1984	1	1984	1
1998	1	1	1	1998	1	1	1998	1	1998	1
1993	1	1	1	1958	1	1	1958	1	1958	1
	1	1	1		1	1		1		1
1994	1	1	1	1994	1	1	1994	1	1994	1
1987	1	0	0		1	1	1973	1	1973	1
1976	1	1	1	1976	1	1	1976	1	1976	1
		0	0			0		1	1984	
1993	1	1	1	1997	1	1	1963	1	1963	
	0	0	0		0	0		0		0
1997	1	1	1	1994	1	1	1990	1	1995	1
1997	1	1	1	1997	1	1	1997	1	1997	1
	1	1	1		1	1		0		1
1995	1	1	1	1992	1	1	1991	1	1991	1
1997	1	1	1	1997	1	1	1997	1	1997	1
1991	1	1	1	1995	1	1	1992	1	1995	1
1998	1	0	1	1998	1	1	1998	1	1998	1
	0	0	0			0		0		
	0	0	0			0		0		1
	0	0	0		0	0		0		0

Annex Table 3: 1999 World drug survey – access, national medicines policies

Country	DATA FROM 1999 WORLD DRUG SURVEY							
	Questionnaire response – % with access to EMs	% with access to EMs	Status of NMP	Date of latest EM policy document	NMP implementation		Drug registration	
	1997 int $				Date	Less than five years of NMP	There is DRA	Law on registration
	Med Strat comp 3 indicator	Med Strat comp 3 indicator	1=NMP official <10yrs; 2=NMP official >10yrs; 3=draft NMP; 4=no NMP; 5=no response		Col H regional policy	(use yes or no from col I in regional policy)	1=yes	1=yes
Saudi Arabia	99	>95	5					
Senegal	66	50–80	1	1995	1998	Yes	1	1
Seychelles	88	81–95	5					
Sierra Leone	44	<50	1	1993				
Singapore	100	>95	4				1	1
Slovakia (Slovak republic)	100	>95	1	1997	1997	Yes	1	1
Slovenia	100	>95	5				1	1
Solomon Islands	80	50–80	4				1	0
Somalia	44	<50	3	1990				
South Africa	80	50–80	1	1996	1998	Yes	1	1
Spain	100	>95	4				1	1
Sri Lanka	95	81–95	1	1994			1	1
Sudan	15	<50	1	1997			1	1
Suriname	100	>95	1	1997			1	1
Swaziland	100	>95	3	1998			0	1
Sweden	99	>95	4				1	1
Switzerland	100	>95	4				1	1
Syrian Arab Republic	80	50–80	1	1995			1	0
Tajikistan	44	<50	1					
Thailand	95	81–95	1	1993	1996	Yes	1	1
Macedonia, The former Yugoslav Republic of	66	50–80	4				1	1
Togo	70	50–80	1	1997			1	1
Tonga	98	>95	4					0
Trinidad and Tobago	77	50–80	1	1998	1998	Yes	1	1
Tunisia	51	50–80	4		1992		1	1
Turkey	99	>95	4				1	1
Turkmenistan	66	50–80	1	1997				
Tuvalu	90	81–95	4				0	0
Uganda	70	50–80	1	1993	1994	Yes	1	1
Ukraine	66	50–80	5					
United Arab Emirates	99	>95	5					
United Kingdom	99	>95	5					
United Republic of Tanzania	66	50–80	1	1993				
United States of America	99	>95	5				1	1
Uruguay	66	50–80	5					
Uzbekistan	66	50–80	5					
Vanuatu	–		5					
Venezuela, Bolivarian Republic of	90	81–95	3	1995			1	1
Viet Nam	85	81–95	1	1996	1996		1	1
Yemen	50	50–80	1	1998			1	1
Yugoslavia	80	50–80	3	1998	1998	Yes	1	1
Zambia	66	50–80	1	1996				
Zimbabwe	70	50–80	1	1995			1	1

			Manufacturing			Importation		Pharma registration		
Date	DRA registers drug	List of registered drugs maintained	Law on manufacturing	Date	DRA inspects manufacturers	Law on importation	Date	Law on distribution	Date	DRA inspects drug outlets
	1=yes	1=yes	1=yes		1=yes	1=yes		1=yes		1=yes
1954	1	1	1	1954	1	1	1954	1	1954	1
1985	1	1	1	1985	1	1	1985	1	1985	1
1997	1	1	1	1997	1	1	1997	1	1997	1
1996	1	1	1	1996	1	1	1996	1	1996	1
	0	0	0		0	1	1960	1	1960	1
1998	1	1	1	1998	1	1	1998	1	1998	0
1990	1	1	1	1990	1	1	1990	1	1990	1
	1	1	1		1	1		1		1
1974	1	1	1	1974	1	1	1974	1	1963	0
1973	1	1	0		0	0		0		0
1998	0	0	1	1998	0	1	1998	1	1998	0
1995	1	1	1	1995	1	1	1997	1	1997	1
1995	1	1	1	1995	1	1	1976	1	1976	0
	1	1	1	1952	1	1	1965	0		
1987	1	1	1	1987	1	1	1987	1	1987	1
1998	1	1	1	1998	1	1	1998	1	1998	1
1993	1	1	1		1	1	1996	1	1996	1
	0	0	0		0	0		0		0
	1	1	1		1	1		1		1
1990	1	1	1	1985	1	1	1961	1	1960	0
1995	1	1	1	1995	1	1	1984	1	1928	1
	0	0	0		0	0		0		0
1993	1	1	1	1993	1	1	1993	1	1993	1
1997	1	1	1	1998	1	1		1	1997	0
1998	1	1	1	1997	1	0		0		1
1996	1	1	1	1996	1	1	1989	1	1992	1
1999	1	1	1	1999	1	1	1999	1	1999	1
1993	1	1	1	1993	1	1	1993	1	1993	1
1997	1	1	1	1997	1	1	1998	1	1991	1

Annex Table 4: 1999 World drug survey – quality control, essential medicines lists, procurement

Country	DATA FROM 1999 WORLD DRUG SURVEY						
	Regulation of promotion		Quality control of medicines			Public finance	
	Law on promotion	Date	Requirements for registration	Samples for testing taken during:	Testing at:	Drugs are covered in public insurance	Generic substitution public (1)
	1=yes		Proof GMP (1); Proof of registration in other country (2); Others (3)	Inspection of manuf (1); Public proc (2); Drug registration (3); Inspection of retail outlet (4); No sampling (5)	Nat'l lab (1); academic inst. (2); priv. lab (3); other country (4)	1=yes; 0=no	public (1); private (2)
Afghanistan	1	1980		1	1		12
Albania	1	1998	123	134	14	1	12
Algeria	1	1992	12	3	1		12
Andorra							
Angola	0			0	4	0	
Antigua and Barbuda							
Argentina	1	1964	12	134	1	1	3
Armenia	0		12	1234	1	0	12
Australia	1	1998	13	12	13	1	12
Austria	0		12	34	1		3
Azerbaijan							
Bahamas	0		12	2		1	12
Bahrain	1	1997	123	134	1	1	1
Bangladesh	1	1982	2	1234	4	0	12
Barbados	1	1969	123	24	4	0	12
Belarus	1	1997	123	3	1	0	12
Belgium							
Belize	0		3	2			12
Benin	1	1975	12	123	4	0	1
Bhutan	0		12	2		0	12
Bolivia	1	1997	12	134	14	1	12
Bosnia and Herzegovina							
Botswana	1	1992	123	1234	14	1	12
Brazil	1	1999	12		1		
Brunei Darussalam							
Bulgaria	1	1995	123	1234	1	1	12
Burkina Faso	1	1998	123		4		12
Burundi	0			0		1	12
Cambodia	1	1994	13	234	1	0	12
Cameroon							
Canada	1		1			1	12
Cape Verde	1	1993	12		1	0	12
Central African Republic	0		123	3	4	0	12
Central America							
Chad	1	1965	3	2		0	3
Chile							
China	1	1985	123	1234	1	1	1
Colombia							
Comoros	0					0	3
Congo	1	1933	123	1234	234	0	3
Cook Islands	0		3	0	4		12
Costa Rica	1	1994	1	234	1	1	2
Côte d'Ivoire	1	1998	12	23	124	1	12
Croatia	1	1997	123	1234	1	1	3
Cuba	0		12		1	1	3
Cyprus	1	1960	123	234	14	0	1
Czech Republic	0		1	124	1	1	3
Democratic People's Republic of Korea							
Democratic Republic of the Congo							
Denmark							

EML last update	Av no. medicines on EML	% total purchases by competitive tender					Price regulation	National list of registered drugs
		International tender	National tender	Public proc. Limited to drugs in EML	STG last year of update	Prescribers and dispensers		
				1=yes		Essential drug part of curricula: medicine (1), nursing (2), pharmacy (3); Pharm aides (4)	Regulate manuf. ex.fact.price (1); Max retail markup (2); Max wholesale markup (3); None (4)	1=yes; 2=no
1995	356			0	1996	1	2	1
2000	295			0		123	23	
1997	1100			1	1986	1	23	
1977				0	1986	12	23	2
1994								
1988		70	50	0	1989		4	1
1998	278			1	1998	13		
1999	531	0	100	1	1999	1234	123	1
						13	123	1
1995								
1998	807		100	0		1234	4	2
1997	1800	45	60	1			123	1
1982	150			1	1987	1234	2	1
1998	1200	95	5	1		123	3	2
1998	400			0		1234	123	1
1997		70	30	1		3	4	2
1997	220	100		0		12	123	1
1997	337	90		1	1998	24	2	2
1998	252	20	80	0	1996	13	4	1
1995								
1992	520	100		1	1998	234	4	1
1999	305				1989	3	2	1
1997	241			1	1995	13	123	1
1997	227	50	50	1	1984	1234	1	1
1994	500	100		1	1989		4	2
1997	274	100		1	1994	3	4	1
1995					1993			
2000				0			1	1
1998	641	12	42	1	1993	24	2	2
1996	222			1		12	4	1
1996	270	100	2	1	1998	2	4	1
1996								
1998	1842	15	85	0		13	123	1
1990					1991			
1998				0			2	1
1982	186			0		123	123	1
1997	344	100		0		123	4	
1997	583		100	1	1997	3	4	1
1997	137	80	10	1	1997	13	123	1
1998	1366	100		0	1998	13	3	1
1994	904			1	1994		123	1
1996	1000	100		0			123	1
2000				0			123	1
1991								
1979								

Annex Table 4: 1999 World drug survey – quality control, essential medicines lists, procurement

Country	DATA FROM 1999 WORLD DRUG SURVEY						
	Regulation of promotion		Quality control of medicines			Public finance	
	Law on promotion	Date	Requirements for registration	Samples for testing taken during:	Testing at:	Drugs are covered in public insurance	Generic substitution public (1)
	1=yes		Proof GMP (1); Proof of registration in other country (2); Others (3)	Inspection of manuf (1); Public proc (2); Drug registration (3); Inspection of retail outlet (4); No sampling (5)	Nat'l lab (1); academic inst. (2); priv. lab (3); other country (4)	1=yes; 0=no	public (1); private (2)
Djibouti	0						12
Dominica	0			0	4	1	12
Dominican Republic	1	1998	13	23	13	0	12
Ecuador	1	1974	23	0	1	1	12
Egypt	1	1994	12	134	12	1	12
El Salvador	1	1988	12	1234	134	1	2
Equatorial Guinea	1	1991		24		1	12
Eritrea	1	1993	123	24	14	0	12
Estonia	1	1994	12	134	1	1	2
Ethiopia							
Fiji	1	1985		2		0	1
Finland	1	1998	1	14	1	1	3
France	1	1994	13	1234	1	1	
French West Africa							
Gabon	1	1995	123	234	4		3
Gambia	1	1984	2	0			1
Georgia	1	1996	123	3	1	0	12
Germany	1		13	124	1	1	3
Ghana							
Greece	1	1993	12	1234	123	1	3
Grenada	1	1986					1
Guatemala	1	1997	123	123	1	1	3
Guinea	1	1984	123	3	12	0	12
Guinea-Bissau							
Guyana							
Haiti	1	1999	3	0		0	1
Honduras	1	1994	123	23	34	1	12
Hungary	1	1997	1	134	1	1	2
Iceland	1	1995	123	134	24	1	12
India	1		1	3	1	1	3
Indonesia	1	1971	12	1234	1	1	1
Iran, Islamic Republic of	0		123	14	1	1	
Iraq	1	1998	123	123	1		12
Ireland							
Israel							
Italy							
Jamaica	1	1964	12	1234	14	0	12
Japan	1	1983	1	1234	1	1	3
Jordan	0		123	1234	1	1	1
Kazakhstan							
Kenya	1	1983	23	2		0	12
Kiribati	0		12	2			1
Kuwait							
Kyrgyzstan							
Lao People's Democratic Republic	1	1997	12	1234	1	0	12
Latvia	1	1995	12	1234	1	1	12
Lebanon	0		3	1234	1	1	
Lesotho	0		3	124	4		12
Liberia	1	1998	123	34	4		1
Libyan Arab Jamahiriya	1	1972	12	234	124	1	12

EML last update	Av no. medicines on EML	% total purchases by competitive tender					Price regulation	National list of registered drugs
		International tender	National tender	Public proc. Limited to drugs in EML	STG last year of update	Prescribers and dispensers		
				1=yes		Essential drug part of curricula: medicine (1), nursing (2), pharmacy (3); Pharm aides (4)	Regulate manuf. ex.fact.price (1); Max retail markup (2); Max wholesale markup (3); None (4)	1=yes; 2=no
1977	412					2	4	2
1998	350	80		1		3	4	
1997			100	0	1998	3	12	1
1996	306	20	80	0	1996	123	12	1
1998	35			0		13	3	1
1991		5	95	0	1993	1	4	1
1996	134			1			23	2
1996	313	99	1	1	1999	24	23	2
2000	179	1			1998			1
1989					1998			
1996	450	100		1		123	23	2
				0	1998			1
					1994			1
1997	184	80	20	0			12	1
1997	250	100		1	1998	2	4	1
1999	253	3		0	1995		4	1
				0			4	1
1996					1995			
1998	3280			1	1995	1	123	1
1998	271	90		0			4	2
1994	470		100	0	1994	3	4	1
1996	165	70	30	1		13	123	1
1990					1990			
1997								
1996	155	90	10	0	1998		4	1
1997	365		100	1	1998	13	23	1
1997	750		1	0	1997		23	1
			40	0	1997		23	1
1998	350			0		1	2	1
1998	487		100	1	1997	1	12	1
1998	1483	7	93	1			23	1
1996	1773	80	20	1	1990	1234	2	1
1998	494	98		1			4	1
				0		1234	1	1
1998	325	42	58	0		1234	23	1
1995								
1993	330	91	8	1	1994	1234		1
1998	240	80		1		123	4	2
1996					1993			
2000								
1997	365		100	1	1998	34	4	1
1994	257		100	0	1996	13	23	1
1992	370	3	96	0		13	23	1
1990	256			0	1986	23	4	
1998	149			1	1993	34	4	1
1997	911	100		1		1234	12	1

Annex Table 4: 1999 World drug survey – quality control, essential medicines lists, procurement

Country	DATA FROM 1999 WORLD DRUG SURVEY						
	Regulation of promotion		Quality control of medicines			Public finance	
	Law on promotion	Date	Requirements for registration	Samples for testing taken during:	Testing at:	Drugs are covered in public insurance	Generic substitution public (1)
	1=yes		Proof GMP (1); Proof of registration in other country (2); Others (3)	Inspection of manuf (1); Public proc (2); Drug registration (3); Inspection of retail outlet (4); No sampling (5)	Nat'l lab (1); academic inst. (2); priv. lab (3); other country (4)	1=yes; 0=no	public (1); private (2)
Lithuania							
Luxembourg							
Madagascar	0		123	23	4		12
Malawi							
Malaysia	1	1953	123	1234	12	2	1
Maldives	1	1993	12	4	4	0	3
Mali	1	1986	12	134	1		2
Malta							
Marshall Islands	0			0	4	1	12
Mauritania							
Mauritius	1	1985	123	1234	234	0	1
Mexico	1	1993	123	124	123	1	2
Micronesia, Federated States of	0			4	4	0	12
Monaco	1	1997	12	12	4		3
Mongolia	1	1998	12	134	1	1	12
Morocco							
Mozambique	1	1997	12	12	1	0	12
Myanmar	1	1954	12	3		1	12
Namibia	1	1965	123	0	4	1	1
Nauru	0		2	0	34	0	12
Nepal	1	1978	13	134	14		1
Netherlands	1	1963	3	14	1	1	12
New Zealand	1	1984	13	12346	3	1	12
Nicaragua	1	1998	123	1234	12	0	12
Niger							
Nigeria	1	1993	123	1234	1		12
Niue	1		2	1	4	0	1
Norway	1	1994	13		1	1	3
Oman	0		123	1234	14	0	1
Pakistan	1	1976	123	124	1	1	12
Palau	0		2	0	4	1	1
Panama	1	1992	12	1234	1	1	1
Papua New Guinea	0		12	2		0	12
Paraguay	1	1997	2	3	2	0	3
Peru	1	1997	12	124	13	1	12
Philippines	1		12	1234	12	1	12
Poland							
Portugal	1	1994	13		12	1	3
Qatar							
Republic of Korea							
Republic of Moldova	1	1997	12	1234	1	1	12
Romania	1	1994	12	1234	1	1	12
Russian Federation							
Rwanda	1	1998	23	14	34	0	12
Saint Kitts and Nevis	0		12	2			12
Saint Lucia							
Saint Vincent and the Grenadines	0			2	4		12
Samoa	0		3	0	4	0	1
San Marino							
São Tomé and Principe							

EML last update	Av no. medicines on EML	% total purchases by competitive tender					Price regulation	National list of registered drugs
		International tender	National tender	Public proc. Limited to drugs in EML	STG last year of update	Prescribers and dispensers		
				1=yes		Essential drug part of curricula: medicine (1), nursing (2), pharmacy (3); Pharm aides (4)	Regulate manuf. ex.fact.price (1); Max retail markup (2); Max wholesale markup (3); None (4)	1=yes; 2=no
2000								
1995	245	100		1	1994	1	1	1
1995								
1989	450			0			4	1
1998	247			0		24	2	2
1997	333	80		1	1995	2	4	1
		100		0		13	4	2
1992	650	95	5	1	1997	1234	123	1
1998	776			1			123	1
1995		10	90	1		1234	4	2
				0			3	2
1996	6000			0	1994	3	4	2
1991								
1984	480	100		1	1987	1234	2	2
1998	184			1	1998	1234	4	1
1996	585	100		1	1994	4	4	1
				0		3	4	2
1997	262		85	1	1996	3	4	1
					1998	1234	3	1
1994			100	0	1998		1	1
1998	348	100	100	1	1998	13	23	1
1994					1994			
1996	448	10	90	1	1989	34	4	1
1998	277	100		1		123	2	1
2000				0	1998		12	1
1995	870	58	42	1		4	4	1
1996	470		80	0	1993		2	1
1998	400	10		1		24	4	
1993	216		100	0			4	1
1996	379	100		1		1234	1	2
				0			2	1
1998	459			1			4	1
1997	517			1	1989	1	4	1
1995								
				0	1998	13	123	1
1996	209			1	1997	1234	23	1
1994	2348	40	60	0		13	123	1
2000								
1998	134		100	1		23	4	1
1998	250	90		1				2
1994								
1994		100		0		3	4	2
1998				1		123	1	2

Annex Table 4: 1999 World drug survey – quality control, essential medicines lists, procurement

Country	DATA FROM 1999 WORLD DRUG SURVEY						
	Regulation of promotion		Quality control of medicines			Public finance	
	Law on promotion	Date	Requirements for registration	Samples for testing taken during:	Testing at:	Drugs are covered in public insurance	Generic substitution public (1)
	1=yes		Proof GMP (1); Proof of registration in other country (2); Others (3)	Inspection of manuf (1); Public proc (2); Drug registration (3); Inspection of retail outlet (4); No sampling (5)	Nat'l lab (1); academic inst. (2); priv. lab (3); other country (4)	1=yes; 0=no	public (1); private (2)
Saudi Arabia							
Senegal	1	1954	1	3	1		12
Seychelles							
Sierra Leone							
Singapore	1	1985	123	1234	13	1	12
Slovakia	1	1997	1	134	1	1	3
Slovenia	1	1997	123	234	1	1	12
Solomon Islands	1	1960			34	1	1
Somalia							
South Africa	1	1998	1	1234	2	1	12
Spain	1	1990	12	1234	1	1	12
Sri Lanka	1		13	23	1	1	
Sudan	1	1978	123	1234	1	1	12
Suriname	0		23	3	1	1	12
Swaziland	1	1998		2		0	1
Sweden	1	1993	1	123	134		1
Switzerland	1	1995	13	123	13	1	12
Syrian Arab Republic	1	1965	12	1234	1		3
Tajikistan							
Thailand	1	1987	123	1234	1	1	12
Macedonia, The former Yugoslav Republic of	1	1998	123	134	4	1	12
Togo	1	1996	1	3	1	0	1
Tonga	0		1			0	12
Trinidad and Tobago	1		12	3	14		1
Tunisia	1	1990	12	1234	1	1	1
Turkey	1	1990	12	23	1	1	
Turkmenistan							
Tuvalu	0			0			3
Uganda	1	1993	123	347	12	0	12
Ukraine							
United Arab Emirates							
United Kingdom							
United Republic of Tanzania							
United States of America	1	1997	3	12	12		12
Uruguay							
Uzbekistan							
Vanuatu							
Venezuela, Bolivarian Republic of	1	1998	1	13	1	1	3
Viet Nam	1	1997	12	1234	1	1	12
Yemen	1	1999	12	1234	14	0	12
Yugoslavia	1	1993	12	134	12	1	12
Zambia							
Zimbabwe	1	1998	123	1234	1		12

EML last update	Av no. medicines on EML	% total purchases by competitive tender					Price regulation	National list of registered drugs
		International tender	National tender	Public proc. Limited to drugs in EML	STG last year of update	Prescribers and dispensers		
				1=yes		Essential drug part of curricula: medicine (1), nursing (2), pharmacy (3); Pharm aides (4)	Regulate manuf. ex.fact.price (1); Max retail markup (2); Max wholesale markup (3); None (4)	1=yes; 2=no
1989								
1998		100		1	1992		123	1
1988					1988			
1992								
1998	603	8	92	0	1998	123	4	1
1994	800	70	30	1	1997	13	1	1
1996				0			3	1
1996	350	100		1	1988	234	4	2
1998	750		95	0	1998	1234	4	1
						13	123	1
1998		90		0	1994	123	2	1
1995	792	52	48	1	1991		23	1
1997	300	90	10	0	1998	4	4	1
1998	350	100		1	1989	2	4	2
2000				0	1998	12	1	1
				0	1998		23	1
1998	750			1	1998	1234		1
2000								
1993	377			0	1998	1234	1	1
2000				0		3	123	1
1995	155	90	10	1	1993	123	23	1
1996	420	100		1			4	2
1998	988		100	1			23	1
1991		40		0			123	1
1995							123	1
2000								
		100		0			4	2
1996	335	90	10	1	1993	1234	4	1
1996								
1991					1991			
					1998		4	1
1980								
1996								
1981								
1993	896		100	0	1993	3	23	1
1998	325			1	1995	1234	4	1
1996	280			1	1996	1234	2	1
1998	535		100	0		1	123	1
1990					1990			
1994	592	40	60	1	1998	1234	4	1

*6/2/03