



W H O

Annual Report 2001

Essential Drugs and Medicines Policy: Extending the Evidence Base

The *WHO Medicines Strategy 2000–2003* identifies policy, access, quality and safety, and rational use as its four major objectives. In 2001, our medicines activities focused on extending the evidence base in each of these four areas. We applied that evidence to help countries improve access to affordable medicines of good quality, and ensure that those medicines were used to secure maximum health impact.

Our support to countries and regions included significant capacity-building, with courses and training for health professionals all around the world. Training was often carried out with collaborating institutions. All support was carefully tailored to meet country and regional needs (Box 1).

In parallel to regional and country activities, we provided guidance in support of major new medicines initiatives. This included technical advice to the European Commission, and to the Global Fund to Fight Tuberculosis, AIDS and Malaria. Concurrently, we continued to work with the wider UN family, nongovernmental organizations and foundations.

In 2002, major impetus is on public financing of medicines and improving the capacity of supply systems to deliver medicines of assured quality. Efforts to further broaden our partnership base will also continue, so that medicines issues are tackled rapidly, using the full range of expertise available globally.

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Box 1

Principal areas of support to countries and regions

In 2001, support was provided to 132 countries, or 66% of WHO Member States. Top areas of assistance were:

- national drug policy development – 84 countries
- medicines regulation and quality assurance – 65 countries
- rational medicines use by health professionals – 62 countries.

The relative emphasis of support varied among the regions:

- African Region: national drug policy development and access
- Americas Region: information for medicines regulation
- Eastern Mediterranean Region: medicines regulation and quality assurance
- European Region: medicines financing mechanisms
- South-East Asia Region: rational use of medicines by health professionals
- Western Pacific Region: medicines regulation and quality assurance.

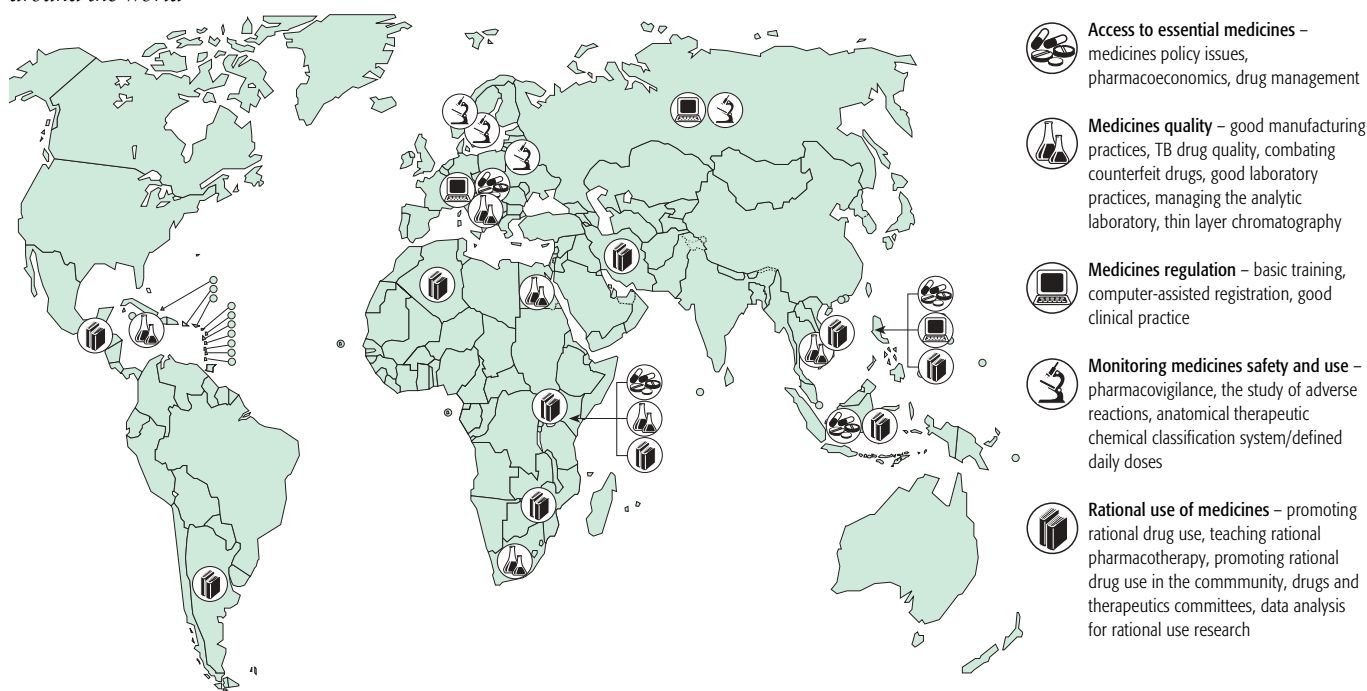
POLICY: CREATING A SHARED VISION FOR ACTION

A national drug policy (NDP) remains the most effective means of ensuring that a country can respond to a wide range of pharmaceutical challenges. In 2001, Argentina, the Dominican Republic, Panama and Venezuela started the process of updating their pharmaceuticals legislation – a key NDP implementation tool – while at regional level, country members of the MERCOSUR group (Argentina, Brazil, Paraguay and Uruguay) developed a common regional drug policy. Other countries such as Egypt officially adopted their NDP, while Morocco and the United Arab Emirates initiated the process of developing an NDP. Similarly both Oman and Pakistan worked on NDP implementation.

In Malaysia, a draft NDP was discussed during a national workshop, with the ratification process scheduled for early 2002. Likewise in Mongolia, a draft NDP was discussed at an NDP conference.

But NDP implementation has not been uniformly effective. This is partly due to the speed at which the pharmaceutical situation is changing. Globalization, the regrouping and redistribution of national and international pharmaceutical industries, the political implications of issues such as access to HIV/AIDS medicines, the growing threat posed by antimicrobial resistance, and the development of many new medicines, are complicating the elaboration of responses to pharmaceutical problems. For some countries, NDP

Figure 1 In 2001, training in a range of medicines areas was provided through 30 courses to more than 500 health professionals all around the world



implementation has not kept pace with such change.

In some countries, therefore, NDP components are failing to achieve maximum impact. This means that diseases which affect poor and marginalized populations the most, continue to exert a heavy toll, while national efforts to minimize the impact of noncommunicable diseases such as cancer, depression and diabetes could be undermined. WHO's international drug policy training course on drug policy issues in developing countries – which in 2001 took place in Yogyakarta, Indonesia – helps countries develop capacity to tackle these issues. (The 2001 course was organized by Boston University and Gadjah Mada University, Indonesia, in collaboration with WHO.)

But the most important means of ensuring effective NDP implementation are monitoring and evaluation. These provide the information needed to modify or update NDPs and NDP implementation plans. In 2001, Colombia and Guatemala updated their NDPs, to bring them closer in line with evolving pharmaceutical needs, while Ghana started reviewing

its NDP with a view to updating it, as did the Philippines. Namibia

carried out its third survey of medicines use in public health

Box 2

South Africa: laying the legal foundation to put national drug policy into action

WHO has worked closely with South Africa's new government to help formulate and implement South Africa's 1996 National Drug Policy. The policy aims to "ensure an adequate and reliable supply of safe, cost-effective drugs of acceptable quality to all citizens of South Africa and the rational use of medicines by prescribers, dispensers and consumers." Developed to operationalize key elements of this policy, the 1997 Medicines Act 90 embodies many of its key principles. These include: parallel importation; generic substitution; quality control of imported medicines; voluntary price reduction; international competitive tendering for the public sector; maintenance of an essential medicines list; and use of standard treatment guidelines.

Language within parts of the Act was considered unacceptable by some pharmaceutical companies and they initiated a court case to challenge the Act. They contended that it would lead to destruction of patent protections by giving the health minister overly broad powers to produce, or import more cheaply, versions of medicines still under patent. The South African Ministry of Health requested WHO to identify international legal expertise to support, and report, to the South African Government.

The case drew considerable media attention and became highly symbolic for both the AIDS community and for development with respect to globalization, international trade agreements and access to medicines.

On 18 April 2001, the 39 pharmaceutical companies involved dropped their case unconditionally. A joint statement of understanding issued by the Republic of South Africa and the Applicants – the 39 pharmaceutical companies – confirmed that, "the... applicants recognize and reaffirm that the Republic of South Africa may enact national laws or regulations, including regulations implementing Act 90 of 1997 or adopt measures necessary to protect public health, and broaden access to medicines in accordance with the South African Constitution and TRIPS."*

* TRIPS refers to the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights.

institutions, which included NDP monitoring.

Clearly, monitoring and evaluation should be built into an NDP right from the start. This is what is being done in China. A first consultative meeting of Chinese Government agencies involved in pharmaceuticals was held in September 2001, to lay the groundwork for developing China's first NDP. Following the meeting, baseline monitoring in four key cities was started. This focuses on rational medicines use and will generate data for use in stakeholder discussions of NDP development (see Box 10). The experience of NDP development in China will itself be used to create a methodology for formulating NDPs in other countries.

ACCESS: MORE MEDICINES FOR LESS MONEY

Essential medicines must be both available and affordable. Much has been done in recent years to ensure that they are. Price information for medicines is more widely available through WHO and other organizations (Box 3). Local production of some key pharmaceuticals has increased price-lowering competition. Experiences with improved public sector medicines management, contracting out of supply services, and growth of nongovernmental organizations' (NGO) medicines supply services, have shown that access to essential medicines can be improved. In 2001, progress continued, but especially in terms of helping governments to optimize use of financing for medicines.

To help governments investigate and respond to price variations for medicines, a manual for collecting data on drug prices and price composition in low- and middle-income countries was developed jointly by WHO and Health Action International. It will help governments in pharmaceutical policy-making,

Box 3

WHO medicines price information services (<http://www.who.int/medicines/organization/par/ipc/drugpriceinfo.shtml>)

WHO works with several partners to make price information easily accessible to governments, nongovernmental organizations, donor agencies and any institution involved in medicines procurement.

International Drug Price Indicator Guide: Details 252 active ingredients in 448 dosage forms. Indicative prices of generic products on the international market and selected tender prices. Produced by Management Sciences for Health and WHO.

Sources and Prices of Selected Drugs and Diagnostics for People Living With HIV/AIDS: Details 73 active ingredients in 110 dosage forms. Issued by UNICEF, UNAIDS, Médecins Sans Frontières and WHO. Covers antiretroviral (ARV) medicines, HIV/AIDS test kits for diagnosis and ongoing monitoring, and medicines for treating opportunistic infections, for pain relief, for use in palliative care, for the treatment of HIV/AIDS-related cancers, and for managing drug dependence.

Pharmaceutical Starting Materials/Essential Drugs Report: Details over 262 active ingredients. Issued by WHO and the International Trade Centre, a joint WTO–UNCTAD centre.

AFRO Essential Drugs Price Indicator: Nearly 300 essential medicines and dosage forms listed – details provided by 24 Member States and 2 international low-cost essential drugs suppliers. Published by the Regional Office for Africa and the WHO Collaborating Centre for the Quality Assurance of Medicines, University of Potchefstroom, South Africa.

Average Prices of a One Year Treatment with Antiretrovirals in Countries of Latin America and the Caribbean: Survey by Pan American Health Organization of ARV therapy in Latin American countries.

Antiretrovirals in Latin America and the Caribbean: Details of prices and uses of ARV treatments, and access policies for these medicines. Also covers prices by country and by groups of countries.

and offer a standard basis for developing more and better-quality information on drug price variation and trends across countries. Field-testing was completed in Armenia, Brazil, Kenya, South Africa and Sri Lanka. Further country studies, and publication and distribution of the manual, will take place in 2002.

While prices are important, calculating cost-benefit is also crucial since it can help policy-makers and clinicians to make the best use of available resources. An international course on pharmacoeconomic analysis and medicines selection (organized by WHO and the University of Newcastle, Australia) teaches how well-established cost-effectiveness and biostatistical methods can be adapted to help make better choices in medicines selection. Bringing together scientific evidence on

clinical outcomes with information on cost, participants learn how to compare the potential health gain from any drug with the next best alternatives. In 2001, the course was held in Hungary, India and Latvia.

New research into cost-effectiveness was also initiated, including an analysis of the cost-effectiveness of HIV-related interventions in Africa. This demonstrated the large variation in cost per life-year gained for various preventive and therapeutic interventions. In other words, cost-effectiveness analysis is an essential component of informed debate about priority setting for HIV/AIDS.¹ Systematic examination of the evidence on cost-effectiveness of non-communicable disease interventions was undertaken too, with the focus on specific treatments for certain cardiovascular conditions, risk

¹ See: Creese A et al. Cost-effectiveness of HIV/AIDS interventions in Africa: a systematic review of the evidence. *The Lancet*, 2002, May 11, Vol 359(9262): 1635–1642.

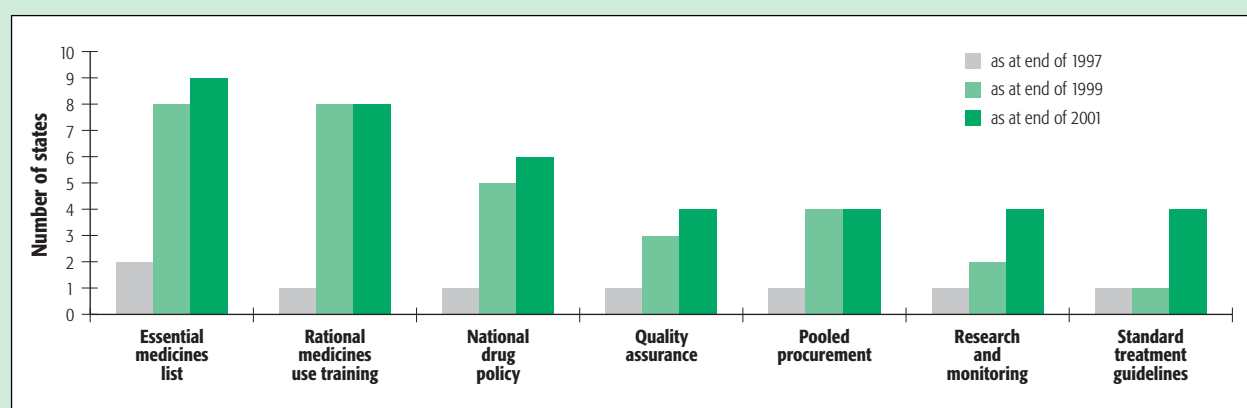
Expanding access to essential medicines in India

India's population – in 6 territories and 26 states – is around 1200 million. Many of the states are larger than most other countries in Asia. So the potential for creating positive pharmaceutical impact is immense. All the more so given that most health care spending is out of pocket and mostly for medicines. (Only a few states, such as Delhi and Himachal Pradesh, distribute the majority of essential medicines free of charge in public facilities. And health insurance coverage is very low at about 3%.)

In 1997, WHO expanded its support to the WHO India Essential Drugs Programme. This was so that the Programme could replicate the success of its Delhi Capital Territory essential drugs programme, largely operated by the Delhi Society for the Promotion of Rational Use of Drugs (DSPRUD), in other states. Evidence shows that Delhi's essential drugs programme has had substantial impacts, including a 30–40% reduction in drug prices, as a result of central bulk procurement for 31 hospitals and 150 primary health care centres.

By the end of 2001, the WHO India Essential Drugs Programme was operating comprehensive programmes in 6 states and partial programmes in a further 8 states. Combined, these 11 states have 580 million inhabitants. The bar graphs summarize progress up to the end of 2001 in nine states (Delhi, Maharashtra, Andhra Pradesh, Himachal Pradesh, Karnataka, Punjab, Rajasthan, Uttar Pradesh, West Bengal).

Progress in the WHO-India Essential Drugs Programme 1997–2001: number of states implementing specific components of an essential drugs programme



As a result of success at state level, changes are now occurring at national level. For the first time, the National Health Policy for India (2001) incorporated rational drug use principles – to promote more equitable access to health care needs – and clinical guidelines for the conduct of clinical practice and delivery of medical services. The Tenth National Five Year Plan, and several national policy-making bodies (the Planning Commission of India, the National Commission on Population and the Indian Council for Research on International Economic Relations) have recognized the value of the Delhi model, and recommended that similar models be adopted by every state government and the national government.

Additionally, DSPRUD has advised on preparation of an essential medicines list, preparation of standard treatment guidelines, and quantification of drug needs for the Uttar Pradesh Health Systems Development Project, funded by the World Bank. Meanwhile, in Delhi, over 70 senior prescribers from the public sector are collaborating on developing standard treatment guidelines for all levels of health care. Many more initiatives for further expansion to other states are planned.

factors such as high blood lipids, chronic diseases such as diabetes, and cancer.

Other work focused on developing medicines financing strategies as part of overall health financing. In 2000–2001 this included work undertaken in more than 35 countries, contribution to a publication on medicines benefits in Latin American social security systems (see Box 6), a regional workshop on medicines reimbursement in the European Region, and country support for quantification of medicines needs

and managing medicines benefits in health insurance programmes.

Additionally, a regional consultation was held in the Eastern Mediterranean Region to consider how best its middle-income countries can make the transition from out-of-pocket expenditure to public health insurance. In Kathmandu, a workshop for Indonesia, Myanmar, Nepal and Thailand examined prepayment schemes, particularly in light of the South-East Asian financial crisis of 1997. Myanmar and Nepal have relatively little in the way of public

health insurance. But as a result of this workshop, Nepal is now actively exploring the possibility of significantly extending such insurance.

In the Americas, a strategic fund for purchasing medicines and insecticides for targeted diseases (HIV/AIDS, leishmaniasis, malaria and tuberculosis) was established with WHO assistance. It provides for supplier prequalification, standardized criteria for inspection, harmonized medicines specifications, medicines quality surveillance and technical cooperation with countries. These

are helping to strengthen medicines selection, distribution and rational use. Eight countries participate in the fund, and many others are expected to participate once they have reviewed and met administrative requirements. In the Caribbean,

development of bulk procurement capacity facilitated development of regional antiretroviral (ARV) treatment and care plans.

In the Western Pacific Region, WHO supported collaborative pharmaceu-

tical procurement involving small Pacific island countries through a pharmaceutical bulk purchasing scheme based in Fiji. In 2001, the scheme was extended to include the Cook Islands, Kiribati and the Marshall Islands.

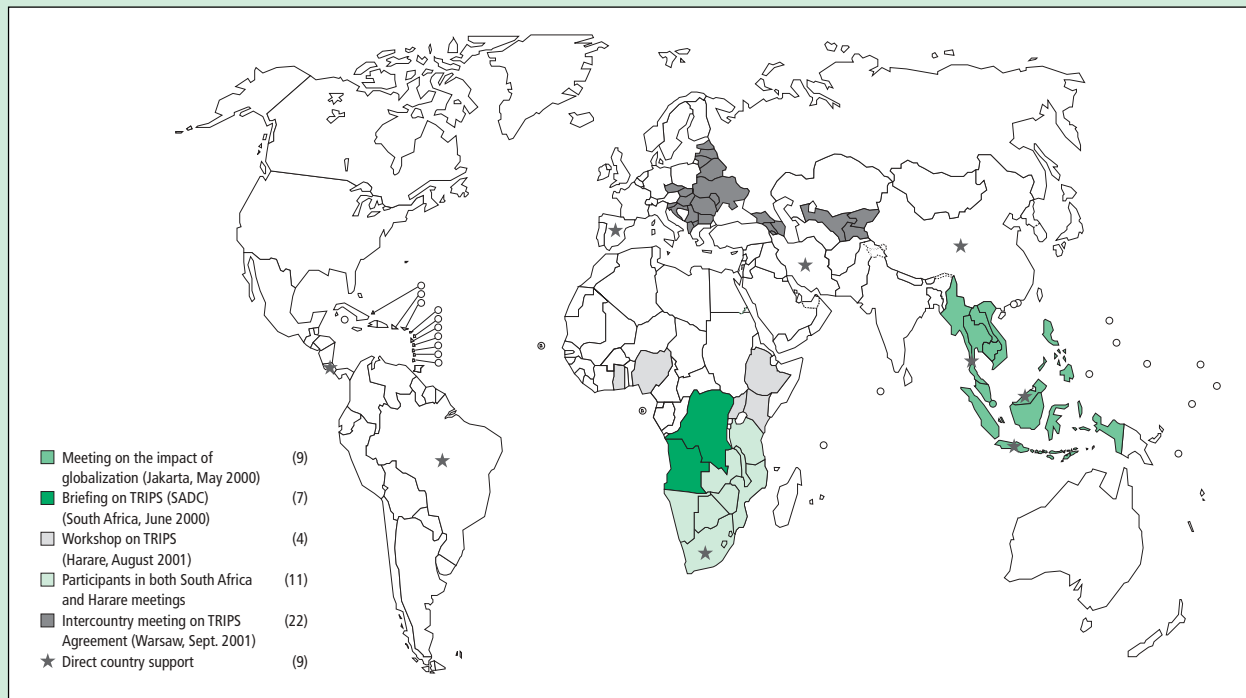
Box 5

Public health after Doha: understanding the implications of trade issues

The *Doha Declaration on the Agreement on Trade-Related Aspects of Intellectual Property Rights and Public Health*, adopted by the World Trade Organization (WTO) Ministerial Conference, in November 2001, affirmed that the Agreement (known as TRIPS) should be interpreted and implemented so as to protect public health and promote access to medicines for all. This was the first time in the 50-year history of the multilateral trading system that a separate Ministerial Declaration was considered on intellectual property and public health issues.

The declaration enshrines the principle publicly advocated and advanced by WHO over the last four years: namely, that WTO Members have the right to make full use of the safeguard provisions of the TRIPS Agreement, so as to protect public health and promote access to medicines.

Countries receiving technical support 2000–2001 from WHO on how international trade agreements can influence access to medicines



WHO will continue to assess the public health implications of the Doha Declaration and advise Member States on how to implement the declaration through national legislation. In parallel, the Network for Monitoring the Impact of Globalization and TRIPS on Access to Essential Drugs (consisting of WHO Collaborating Centres in Brazil, Spain, Thailand and the United Kingdom, is measuring the impact of TRIPS on access to essential medicines. Indicators used cover: changes in pricing; generic competition; investment in research and development; and technology transfer. They also cover use of TRIPS safeguards, such as: provision for use of transitional period; parallel imports; compulsory licensing; and early workings of generics (“Bolar” provisions).

“Ministers of trade, economy, industry and foreign affairs gave a great deal of attention to the issue of access to essential medicines in Doha. This demonstrates the growing appreciation of the importance of international trade agreements for people’s lives and well-being.”

Director-General Dr Gro Harlem Brundtland, statement after World Trade Organization’s Doha Ministerial Conference, November 2001.

Towards equitable medicines financing in the Americas

6

Health system reform, including pharmaceutical reform has been in progress throughout the Americas since the 1980s. Pharmaceutical reform has aimed at improving medicines selection, procurement and use. At the same time, more and more health insurance systems have been created in response to populations' health needs. They range from private for-profit organizations, to social security organizations financed with public resources. Between these two extremes, a large number of alternative arrangements have evolved – within the context of managed competition – including private, non-profit insurance companies and public insurance plans.

A WHO study* compared the health reform process and health insurance systems in Argentina, Colombia, Chile, Costa Rica, Guatemala and the United States. Data collected showed that:

- In **Argentina**, medicines prescribing has been rationalized and positive changes in consumption patterns achieved, resulting in improved control of expenditures and improved quality control.
- In **Colombia**, a medicines list has been included in the Compulsory Health Plan, experience with bulk purchasing schemes by cooperatives and groups of health service providers has been positive, and generic medicines have been introduced successfully.
- In **Costa Rica**, a universal health insurance system, based on solidarity, equity and obligation, has been established, together with a pharmaceuticals policy based on the essential medicines concept. Additionally, a centralized purchasing system has been put in place leading to considerable savings on medicines purchases.
- In **Chile**, use of generic medicines has been a great success.
- In the **USA**, the pharmaceuticals market is regulated effectively. Selective formularies which favour generic medicines are used by many US public health services and major private insurance programmes to establish which medicines must be available. Nevertheless, millions of people lack coverage for their medicines costs and patient co-payments may limit the access of some low-income patients who find it difficult to make the necessary immediate payment.
- In **Guatemala**, single-dose packaging and specification of dosage by therapeutic committees has been key to successful medicines management in hospitals. As in Costa Rica, centralized purchasing has enabled medicines to be bought at much lower prices than on the general market.

These country examples indicate that a combination of equitable financing arrangements, risk sharing through insurance and reimbursement schemes, wise medicines selection, reliable medicines management and rational medicines use, are all needed to ensure access to essential medicines.

“A health system is not good because of what it spends or because of who spends it. It is good because of the health results that it generates for each unit of money invested.”

* Reported in: Zerda A et al. *Sistemas de Seguros de Salud y Acceso a Medicamentos (Health Insurance Systems and Access to Medicines)*. Buenos Aires, ISALUD, 2001, ISBN 92 75 32353 4 (ISBN 92 75 12353 5).

capacity to regulate not only medicines, but also vaccines.² The tool enables realistic assessment of a country's medicines and vaccines regulation needs (i.e. its priorities), and what it can reasonably be expected to develop and implement (i.e. what it can plan).

Reviews of medicines and vaccines regulatory capacity were carried out in Indonesia, Morocco, Nepal, the Philippines, Tunisia and Viet Nam, and led to rapid improvements in regulatory capacity. For example, in Viet Nam, assessment showed an absence of written procedures, slowing staff performance of day-to-day regulatory tasks. Also, staff lacked capacity to assess new medicines and access to reliable technical literature. Six months later, Tunisia's procedures for DRA staff had been revised, freeing up their time for other technical work. And DRA staff had received tailor-made training on assessing new medicines and accessing technical literature. The outcome of 2001 activities confirmed that joint medicines and vaccines regulatory assessments are useful and cost-effective.

Other training for DRAs included an international training course on assessing applications for marketing authorizations. Organized by WHO and the Philippine Bureau of Food and Drugs, the course was attended by representatives of ASEAN (Association of South-East Asian Nations) countries and China.

Harmonization of medicines regulation requirements is another means of improving the cost-effectiveness of regulatory activities – by minimizing their duplication between countries and accelerating access to medicines, particularly new medicines. In the Americas, such harmonization has supported harmonization within the region's various economic integration groups in a number of related technical areas. These include

QUALITY AND SAFETY: REDUCING RISK AND PROMOTING EFFECTIVENESS

Around one-third of WHO's Member States have either no drug regulatory authority (DRA) or very limited regulation capacity. Work to increase regulatory capacity is thus a high

priority. Evidence shows, however, that interventions to improve regulation that have been successful in one country, work best if customized, rather than being imported “wholesale”.

In 2001, WHO finalized a data collection tool for reviewing regulatory

² It is supported by an assessment recently undertaken in the Americas of different DRA models by PAHO and Temple University, USA. The results suggest that integrated regulatory agencies – covering medicines, technical devices and food – and financially independent agencies, operate the most effectively.

bioequivalence, good manufacturing practice, good clinical practice, defining counterfeits and development of pharmacopoeias.

In Asia, an ASEAN-WHO project was set up to improve the public health impact of medicines regulation, especially harmonization. Activities included developing a common set of requirements for new chemical entities and multisource medicines, and creating a common technical dossier for applications. Sharing of expertise was also actively promoted, principally through use of resource centres within ASEAN to support weaker DRAs.

Harmonization of medicines registration and quality control also continued within the Southern African Development Community. Common technical documents for both registration and quality control were drafted, and will be finalized in 2003.

In terms of medicines quality, WHO's Good Manufacturing Practices (GMP) Project is having an impact worldwide. During 2000–2001, more than 400 people from 50 countries were trained in GMP implementation. In 2001 alone, courses were held in Bosnia Herzegovina, China, Egypt, India,

Jamaica and Uganda. Additionally, national GMP seminars were held in Colombia, Costa Rica, Cyprus, the Dominican Republic, Honduras, Oman, the Philippines and Syria, at which more than 180 people from the public and private sectors were trained.

The GMP training modules are now backed up with a video and a CD-ROM, so that after attending workshops participants can continue to learn about and also guide others on GMP implementation. Progress in China has been particularly rapid – only around 800 of the country's 6300 pharmaceutical manufacturers met GMP standards in 2000. But thanks to increasing collaboration between China's State Drug Administration and WHO, all pharmaceutical manufacturers are projected to become GMP-compliant by 2004 (Figure 3).

Strengthening official medicines control laboratories is another major element of quality assurance. WHO's external quality control programme counted 36 participating laboratories by the end of 2001. International Chemical Reference Materials were provided to all participating laboratories in order to enhance their capacity to carry out pharmacopoeial tests for essential medicines.

Work carried out in 2001 showed that counterfeit and substandard medicines continue to be a major concern globally, with a number of specific problems, such as no active ingredient, or wrong level of active ingredient observed. For example, a survey completed in 2001 in Cambodia showed that of the samples of 24 pharmaceutical products collected from the market, about 50% (115/230) were unregistered. Laboratory tests based on registration status showed that of 98 imported registered products, 6 (6.1%) failed the laboratory test. Results of tests on 112 imported but unregistered products showed that the active ingredients in 22.3% of the samples were lower than the amount indicated by the label. The overall failure rate for the total of 230 samples was 13%. Studies such as these serve as a starting point for formulating national strategies for fighting counterfeit drugs.

Another counterfeits survey was carried out by the WHO-Industry-NGO Working Group on Counterfeits in a Western Pacific country. Samples have been analysed by an independent laboratory and the survey results will be made available in 2002.

Activities to combat counterfeits included an intercountry workshop organized by WHO in Phnom Penh, Cambodia, to enable South-East Asian and Western Pacific countries to share experience and information, to identify areas of collaboration and draw up an anti-counterfeits workplan. A similar workshop was held in Nairobi, Kenya for African drug regulatory authorities.

Other quality-related activities focused on improving the quality of medicines for treating specific diseases. Malaria was one of these. Between 800 and 900 thousand people die every year of malaria in Africa – not simply because antimalarials are unavailable but also because the quality of antimalarials is often poor. In 2001, specifications for testing antimalarial agents promoted for use by the Roll

Box 7

Ensuring access to quality HIV/AIDS medicines

Dramatic decreases in supplier prices for medicines for HIV/AIDS – particularly antiretroviral (ARV) medicines – has brought with it the need to ensure the quality of these products. In March 2001, WHO launched a project to prequalify manufacturers of ARVs, including generic producers. Working closely with the International Pharmaceutical Coordination (IPC) group (WHO, UNICEF, UNAIDS, UNFPA and the World Bank), WHO established consensus on standards that products submitted by suppliers must attain for prequalification status, and on the need for a list of prequalified HIV/AIDS medicines and their suppliers.

Other elements in a comprehensive programme to promote access to quality medicines for HIV/AIDS and other priority health problems included:

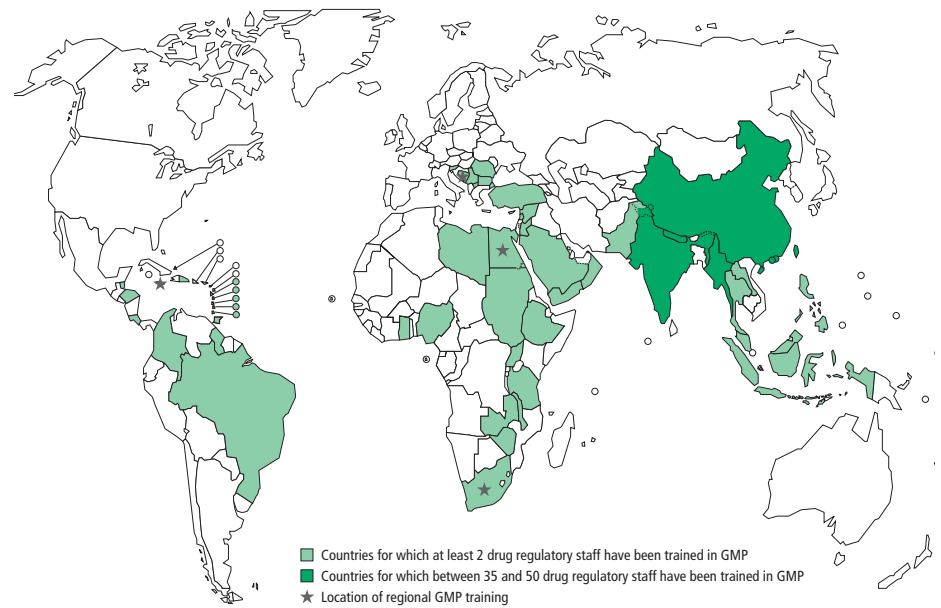
- creating a WHO Model Quality Assurance System for procurement
- development of quality specifications for nine priority ARV agents, in collaboration with national and regional pharmacopoeial authorities
- expansion to include a prequalification process for antituberculosis and antimalarial medicines
- feedback to regulators regarding information collected during assessments, to increase their capacity to ensure the quality of ARVs on their national market
- regional workshops for drug regulators on registration of generic ARVs.

Back Malaria initiative were finalized, including full pharmacopoeial monographs.

Suspecting that the problem of poor-quality antimalarials is widespread, WHO initiated a pilot project to collect data at country level on the quality of antimalarials. Six countries, from the African and Eastern Mediterranean regions, each representing a different geographical area, were selected for inclusion in the project. Evaluation focused on the antimalarial products most widely used (chloroquine tablets and syrup, and sulfadoxine/pyrimethamine (SP) tablets) in those countries. It also included sampling from various levels of the distribution chain (i.e. household, private sector pharmacy, peripheral health units, district hospitals, teaching/referral hospitals and district and/or medical stores). Samples were examined using a screening test tool (known as a “mini-lab”) and, if results were significant, they were verified at a central laboratory (using pharmacopoeial tests) in South Africa.

Results showed that the biggest problem is with SP tablets – for more than 60% of samples, for all countries, the dissolution rate was unacceptably slow (see Figure 4). The countries’ DRAs are now being encouraged to continue post-marketing surveillance of antimalarials in order to detect substandard products, to stipulate a dissolution rate that an antimalarial must attain if it is to be approved,

Figure 2 More than 400 professionals in 50 countries received training in good manufacturing practice (GMP) during 2000–2001



and to develop capacity in ensuring GMP compliance. Two more African countries are scheduled for similar investigations in 2002. The technical “sensitivity” of the mini-lab and pharmacopoeial tests for antimalarials will also be harmonized to ensure data comparability.

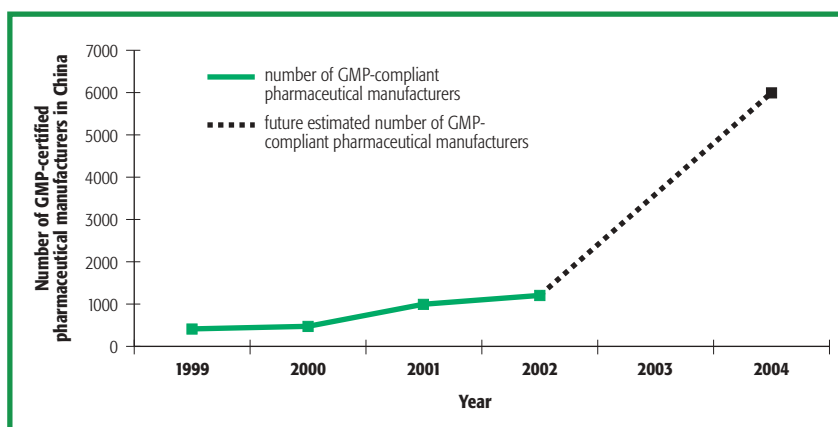
Tuberculosis (TB) is another disease which afflicts poor countries disproportionately. In 2001, WHO medicines support to the Stop TB Partnership for operation of the Global TB Drug Facility included development of application materials, product selection and development of quality specifications for TB medicines (in

cooperation with the US Pharmacopoeia).

Other work on promoting quality of medicines resulted in the adoption, by the WHO Expert Committee on Specifications for Pharmaceutical Preparations, of nine new WHO guidance texts. These were on topics such as the certification scheme for pharmaceutical starting materials, GMP-related issues and storage practices. Work on proposing international nonproprietary names also continued.

Drug safety was also actively promoted. The *WHO Drug Dictionary* provides information on all medicines that have been entered into the WHO database since 1968. National drug monitoring centres and many pharmaceutical companies around the world use it as the standard reference tool for coding drugs. In 2001, WHO strengthened its efforts to improve the database. In 1995, the European Union (EU) commissioned the European Agency for the Evaluation of Medicinal Products to set up an adverse drug reactions database for the EU. The first version of the EudraVigilance database was launched in December 2001. Concern has been raised over

Figure 3 Enhancing local pharmaceutical production in China – increasing and projected increase in GMP-certified pharmaceutical manufacturers



problems that could arise due to the existence of two levels of monitoring: international WHO monitoring and European regional monitoring.

Access to WHO's international adverse drug reaction (ADR) monitoring database was simplified during 2001. The database will become available as a website for national pharmacovigilance centres in 2002. It is the cornerstone of the WHO International Programme on International Drug Monitoring (in which 68 countries participate), operated by the Uppsala Monitoring Centre in Sweden.

“The global epidemics of HIV/AIDS, tuberculosis, and malaria continue to spread. Yet, there is a growing recognition of the vulnerability faced by poor and marginalized communities, and of the impact such vulnerability has on global stability and growth. We know now, more than ever, that there is no wall between the wealthy and poor nations of the world.”

James D. Wolfensohn, President of the World Bank in foreword to *Global Plan to Stop TB. Phase 1: 2001–2005*.

Additionally, growing awareness of the need to ensure the safety of herbal medicines stimulated efforts to increase safety monitoring and pharmacovigilance for this type of health care. WHO worked with the Uppsala Monitoring Centre to

incorporate monitoring of herbal medicines in the Programme on International Drug Monitoring.

RATIONAL SELECTION AND USE: KNOWING WHEN TO USE WHAT

The evidence on rational medicines use is clear: multiple interventions reinforce each other and must be repeated over time. WHO therefore continues to provide considerable training in promoting rational medicines use. In 2001, national and international training was provided to countries in the African, Eastern Mediterranean, European and Western Pacific regions.

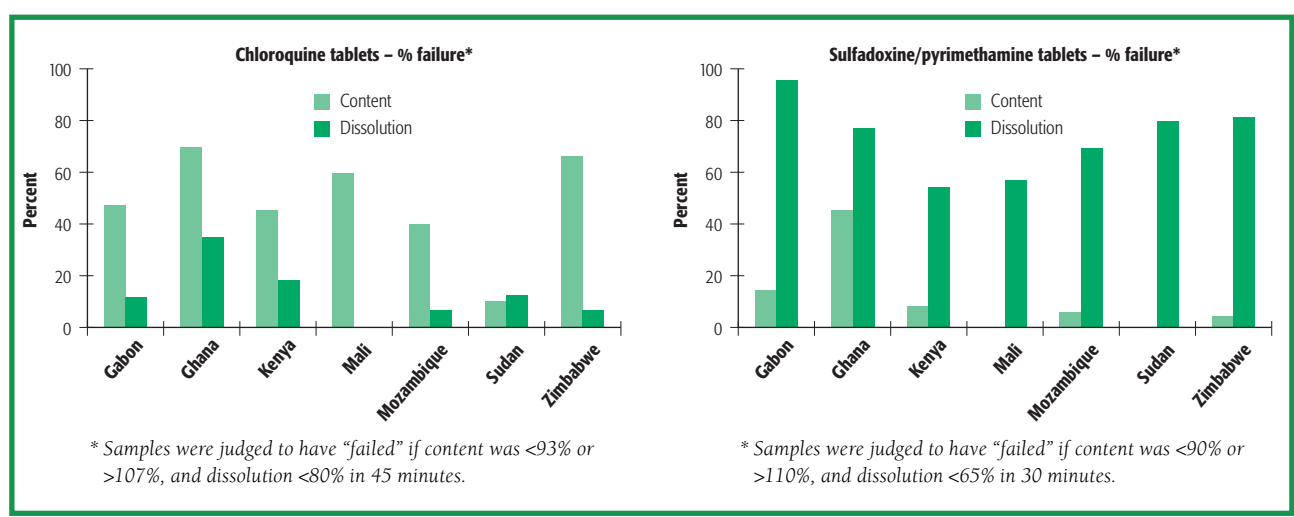
The first Asian international training course on problem-based pharmacotherapy (organized jointly by the Philippine Society of Experimental and Clinical Pharmacology, and the WHO Collaborating Centre for Training in Pharmacology and Rational Drug Use at the University of Newcastle, Australia) was held in Manila. National workshops and courses on problem-based pharmacotherapy teaching were also held in China, Japan, Malaysia and Viet Nam. In the European region, the American International Health Alliance and Zdraveform-plus joined the Regional Office for Europe in providing rational medicines use training.

Efforts to promote hospital drugs and therapeutics committees (DTCs) also continued, especially in the Western Pacific, where the need for more effective DTCs had become evident. A meeting for hospital DTC members in the region was held in Penang, Malaysia. Organized by the WHO Collaborating Centre on Drug Information of the Universiti Sains Malaysia, with support from WHO, it was attended by 30 participants from 13 countries. Following the meeting, innovative rational medicines use strategies are now being implemented in a number of countries. Additionally, an international course on drugs therapeutics committees was organized in Yogyakarta, Indonesia, by Management Sciences for Health and the WHO Collaborating Centre for Research and Training on Rational Drug Use (at Gadjah Mada University).

Elsewhere, in the African, South-East Asian and Western Pacific Regions, courses on medicines and therapeutics committees were organized in collaboration with Management Sciences for Health.

Other rational medicines use efforts focused on community medicines use. The international course on promoting rational medicines use in the community (held in Uganda), was particularly well received. Developed and first tested in 2000, participants

Figure 4 Too little too late: in six African countries 10–65% of sampled chloroquine tablets failed on content and 50–90% of sampled sulfadoxine/pyrimethamine tablets failed to dissolve

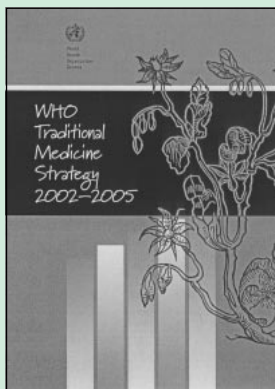


Traditional, and complementary and alternative medicine: does it work and is it safe?

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Populations throughout Africa, Asia, and Central and South America, use traditional medicine (TM) to help meet their primary health care needs. As well as being accessible and affordable, it is also often part of a wider belief system, and as such considered integral to everyday life and well-being. At the same time, in Australia, Europe and North America, “complementary and alternative medicine” (CAM) is increasingly used in parallel to modern medicine, particularly for treating and managing chronic disease and conditions. Such widespread and growing use of TM/CAM is creating public health challenges, however, with respect to: policy; safety, efficacy and quality; access; and rational use.

In 2001, WHO responded to these challenges by developing a *WHO Traditional Medicine Strategy* for 2002–2005 (document reference: WHO/EDM/TRM/2002.1). It reviews the status of TM/CAM globally, and outlines WHO’s own role and activities in TM/CAM. But



more importantly, it provides a framework for action for WHO and its partners, to enable TM/CAM to play a far greater role in reducing excess mortality and morbidity, especially among impoverished populations. The strategy focuses on integrating TM/CAM with national health systems, as appropriate, by developing TM/CAM policies and programmes, and promoting the safety, efficacy and quality of TM/CAM by expanding the knowledge base on TM/CAM, and by providing guidance on regulatory and quality assurance standards.

Also in 2001, the *Legal Status of Traditional Medicine and Complementary/Alternative Medicine* (document reference: WHO/EDM/TRM/2001.2) was published and

Volume III of the *WHO Monographs on Selected Medicinal Plants* finalized. Summarizing the legal status of TM/CAM in 123 countries, the former is a valuable guide for policy-makers and legislators working to develop a legal framework in their country covering both the practice of TM/CAM and the quality assurance and appropriate use of TM/CAM products.

“...effective integration strategies will promote communication and mutual understanding among different medical systems, evaluate traditional medicine in its totality, integrate at both theoretical and clinical levels, ensure equitable distribution of resources between complementary and alternative medicine, provide a training and educational programme for both traditional and conventional medicine, and generate a drug policy that includes herbal medicines.”

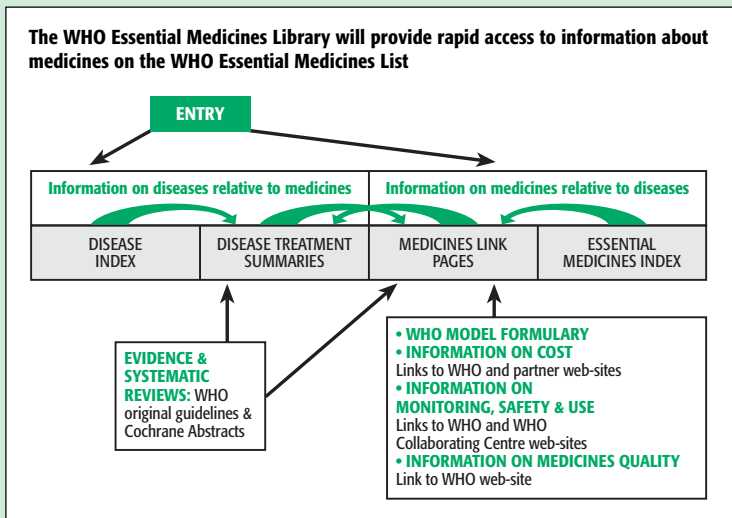
G. Bodeker. Lessons on integration from the developing world’s experience. *British Medical Journal*, 2001, 322:164–167 (20 January).

Making the medicines evidence base more accessible

The concept of essential medicines was initiated by the World Health Assembly in 1975. It requested WHO to assist Member States by, “advising on the selection and procurement, at reasonable cost, of essential medicines of established quality corresponding to their national health needs.” A WHO Expert Committee developed the first WHO Model List of Essential Medicines in 1977. Since then, the list has been revised every two years. Numerous studies have documented the impact of clinical guidelines and essential medicines lists on the availability and proper use of medicines within health care systems. A careful selection of a limited range of essential medicines results in a higher quality of care, better management of medicines, and more cost-effective use of health finance.

But in 1999, the relevant WHO Expert Committee recommended that the methods for updating and disseminating the Model List be revised. This was a response to advances in evidence-based decision making, the increased need to link use of essential medicines to clinical guidelines, and the high cost of many new and effective medicines. An extensive consultation process followed. Revisions proposed ranged from development of a more transparent process for selecting medicines, to creation of a WHO Essential Medicines Library.

The WHO Essential Medicines Library is now being created and will contain not only information about how and why medicines are selected for the List, and links to WHO clinical guidelines, but also links to the WHO Model Formulary, price information services, and information on international nomenclature and quality standards.



learned how to assess and remedy inappropriate medicines use in the community, including an analysis of what shapes medicines demand.

Rational use efforts are also being targeted at pharmacists, given the considerable influence they can have on community medicines demand and use. The EuroPharm Forum Network of pharmaceutical associations and the Regional Office for Europe developed guidelines and model programmes for improving the performance of pharmacists in the areas of health

promotion and management of chronic illness. Its Pharmacy-based Hypertension Management Model has now been tested and implemented in Estonia, Latvia, Lithuania, Portugal, Slovenia and Spain. Care provided by pharmacists includes screening for high blood pressure, regular blood pressure measurement and patient counselling. In Slovenia, Estonia, Lithuania and Spain, 10%, 27%, 57% and 64% respectively of individuals referred by their pharmacist to a doctor for investigation of elevated blood pressure were

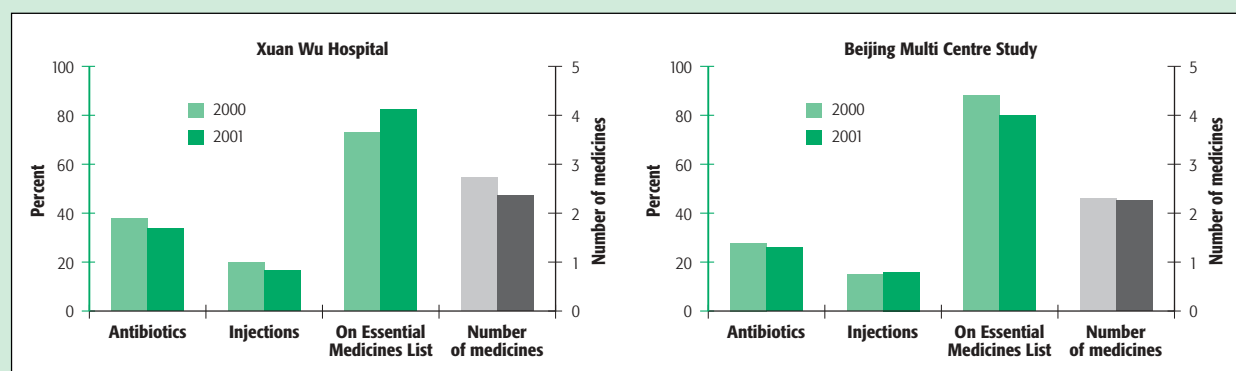
diagnosed with hypertension.

The Europharm Form Network also initiated an education campaign for patients – *Questions to ask about your medicines* – in Croatia, Estonia and Latvia through twinning arrangements with countries that are already implementing a similar campaign.

Other rational use activities focused on fighting the development of antimicrobial resistance (AMR). 2001 saw the launch of the *WHO Global Strategy for the Containment of Antimicrobial Resistance*. Summarizing evidence on

Box 10

Promoting rational medicines use in China: when evidence leads to policy change and impact



In 2000, as part of the groundwork for developing a national drug policy, baseline data on rational medicines use were collected from a number of health facilities in Beijing, including Xuan Wu Hospital. Following analysis of the baseline data, intervention strategies involving printed materials on rational medicines use (particularly rational use of antibiotics), reference materials and poster displays on appropriate medicines use were identified. Additionally, since antibiotic use at Xuan Wu Hospital was notably high, active promotion of applications of guidelines on rational use of antibiotics was also recommended.

In 2001, after the above recommendations had been implemented, monitoring indicated that:

- specific strategies for facility-level interventions, targeting specific prescribing practices, are most appropriate since their impact can be measured accurately
- interventions are more effective if targeted at a clearly defined group and the facility can implement managerial interventions to improve medicines availability and use.

Following further collection of baseline data in 2001, WHO recommended that:

- the Chinese Ministry of Health develop and promote educational, supervisory and managerial strategies to improve medicines use
- the medicines reimbursement list and use of China's Essential Medicines List be synchronized in order to promote rational medicines use among prescribers
- the impact of rational medicines use interventions be monitored regularly.

Activities carried out in 2001 to implement the above recommendations included:

- a national course on promoting rational medicines use
- local courses on promoting rational medicines use
- development and implementation of research proposals
- pilot-testing of national antimicrobial standard treatment guidelines
- consultative meeting with the Ministry of Health, the State Drug Administration, the State Planning Commission and other stakeholders to review and synchronize the medicines reimbursement list and China's Essential Medicines List.

The results of all the above activities indicate that national policies for improving rational medicines use in China can be:

- readily developed if data and evidence are presented to stakeholders
- readily adopted or adapted, and enforced, through directives from national level.

Box 11

Improving rational medicines use in Laos

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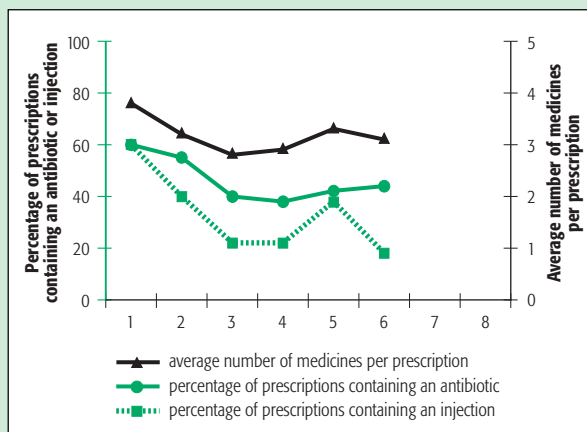
Monitoring, Training and Planning (MTP) is a simple managerial tool that can be used to make cumulative improvements to prescribing practices. The strategy covers:

- monitoring: identifying and measuring problems
- training: identifying the underlying causes of the problems and finding solutions (i.e. searching for relevant information or providing training)
- planning: targeting the levels of improvement after implementing a solution.

The idea is that a group (such as a group of providers, prescribers or dispensers) meets to identify specific medicines use problems. Medicines use indicators are then used to measure their extent. The group then explores possible underlying factors and agrees on how to tackle them. The level of improvement for the next period is agreed upon. Before the next meeting, information is collected using the indicators to see whether the targeted improvement has been achieved. The group again discusses the problem and how further improvements can be achieved.

The figure – based on average data from 5 regional hospitals – shows the impact of MTP implementation on rational medicines use in Laos. Use of antibiotics and injections declined. By the 4th month, however, a trend towards pre-MTP levels can be seen, indicating the need to further reinforce and sustain the MTP programme.

Source: Presentation of Dr Bouathong Sisounthone at intercountry meeting for hospital drugs and therapeutics committees, Penang, Malaysia, October 2001.



interventions to promote rational use of antimicrobials, it aims to both persuade governments to take urgent action and to guide this action with expert technical and practical advice. A special issue of the *Essential Drugs Monitor* (Vol 28/29) in English, French, Spanish and Russian also raised awareness of the problem and what policy-makers, health care professionals, health advocates and members of the public can do to help tackle it.

Work to promote use of four-drug fixed-dose combination (4FDC) anti-TB medicines also aims in part at reducing AMR. Widespread use of these medicines would not only reduce the risk of the emergence of drug-resistant TB, however. It would also simplify TB treatment, minimize TB prescription errors, and increase patient adherence to treatment regimens. Inadvertent medication errors and adverse medicines reactions would also decrease. Medicines management would improve, too, since procurement, distribution and dispensing/handling are all easier with fewer

Table 1 Principal impediments to ensuring availability of opioid analgesics for palliative care

- Concern about addiction to opioids
- Insufficient training about opioids for health-care providers
- Restrictive laws relating to manufacture, prescribing and dispensing
- Reluctance of health care providers to use opioids due to concerns about legal sanctions
- Reluctance of health care providers to stock opioids due to concerns about theft or robbery
- Burden of regulatory requirements
- Potential for diversion

Source: *Assuring Availability of Opioid Analgesics for Palliative Care. Report on a WHO Workshop, Budapest, Hungary 25–27 February 2002.* Document reference: EUR/02/5037079.

items, that share a single expiry date. Clinical evidence to support use of 4FDC anti-TB medicines was collected. And guidance for national TB programme managers on use of these medicines was developed.

Conversely, other rational use activities focused on how to increase use of a medicine. WHO launched a report, *Achieving Balance in National Opioids Control Policy* (document reference: WHO/EDM/QSM/2000.4) in 2000, to advocate balanced control

approaches. This was in response to concern that overemphasis of the dependence-producing characteristics of opioid analgesics was leading to excessive fear of addiction, under-use for legitimate medical purposes, and unduly restrictive regulations on distribution and use of these medicines (see Table 1). Regulatory barriers to access to opioid analgesics have since been lowered in several countries, including China, India, Italy and Mexico.