



WHODOC

WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTÉ

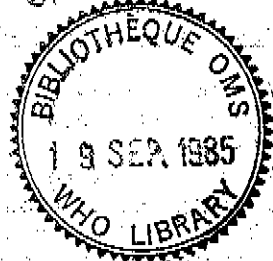
*416 Drugs. Sup. & des. sub
- at the end of the
Drugs list
Drugs list*

WHO/CONRAD/WP/RI

2 September 1985

CONFERENCE OF EXPERTS ON THE
RATIONAL USE OF DRUGS

25 - 29 November 1985, Nairobi, Kenya



466857

THE RATIONAL USE OF DRUGS: REVIEW OF MAJOR ISSUES

CONTENTS

| | <u>Page</u> |
|---|-------------|
| Drugs and health for all by the year 2000 | 2 |
| Criteria for rational drug use | 2 |
| National drug policies | 3 |
| Information, education and rational prescribing | 3 |
| Dispensing and consumption practices | 4 |
| Drug development | 4 |
| Drug manufacturing | 4 |
| Dosage forms, packaging and labelling | 5 |
| Drug distribution | 5 |
| Drug promotion | 5 |
| Costs and prices | 6 |
| National drug legislation | 6 |
| WHO's initiatives | 6 |

THE RATIONAL USE OF DRUGS: REVIEW OF MAJOR ISSUES

Drugs and health for all by the year 2000

1. One of the main aims in HEALTH FOR ALL BY THE YEAR 2000 is an equitable distribution of resources for health. Equity is certainly not a characteristic feature of the existing drug situation in the world. The most urgent need regarding drugs at this stage is to make it possible for the vast majority of the world's people who live in the developing countries to have access at a cost they can afford to those 30 to 40 drugs that are vital to them as part of their primary health care, and to ensure that these drugs are used rationally.
2. In the industrialized countries there are thousands and even tens of thousands of drugs on the market, many of them identical or highly similar but sold under different names, and many of them incorporating a variety of active ingredients. Moreover, the commercial exploitation of herbal and other remedies adds to the plethora of products on the market. In the developing countries, while the situation in the towns may resemble that in the industrialized world, the vast majority of people who live in the rural areas have little or no systematic access to allopathic drugs. They rely mainly on traditional medicines, and to obtain modern medicines they often have to travel far and pay prices that are far beyond their reach.
3. In the developed countries, there is no shortage of doctors. Doctors there face the problem of selecting the most appropriate preparation for each patient from the multitude of drugs available and the enormous amount of information available. When selecting drugs, they are thus liable to become influenced by drug promotion of various kinds, not all of which is based on complete and unbiased information. The role of pharmacists, too, has changed radically, and thanks to developed transport and communication systems, drugs now reach even those in the most remote areas. They make up few medicines nowadays, but rather sell ready-made drugs, both those for which prescriptions by a doctor are required and those which are available to the public without prescription. To fulfil that function properly, they too require access to complete and unbiased information.
4. In developing countries, particularly outside the main towns, the situation is vastly different. Doctors are few and far between and mostly concentrated in the cities. There they face the same problems as those of doctors in developed countries. In other areas people rely for health care mainly on other categories of health workers such as, in some instances, nurses and pharmacists, but more usually nonprofessional health workers with limited training or traditional practitioners. There are few, if any, pharmacies outside the towns, whether private or government-owned, and other arrangements have to be made to ensure the availability of drugs, in places such as hospital outpatient departments, drug corners in health centres, village drug cooperatives, and small village shops. The inadequacy of the health infrastructure and the weakness of distribution, transport and communication systems make it more difficult than ever for drugs to reach those who need them; and when they do reach them, people usually cannot afford to pay for them.
5. In both developing and developed countries, a comprehensive national drug policy forming an integral part of a well defined national health policy is the exception rather than the rule.

Criteria for rational drug use

6. The above describes in a nutshell the irrationality of the drug situation in the contemporary world. Sometimes the most appropriate therapy does not include

drugs. When it does the rational use of drugs demands that the appropriate drug be prescribed, that it be available at the right time at a price people can afford, that it be dispensed correctly, and that it be taken in the right dose at the right intervals and for the right length of time. The appropriate drug must be effective, and of acceptable quality and safety.

National drug policies

7. The formulation and implementation by governments of a national drug policy are fundamental to ensure rational drug use. In 1982 the Thirty-fifth World Health Assembly endorsed the major components of such a policy. It is first necessary to identify therapeutic needs, to select essential drugs accordingly and to estimate the quantities needed for each of them. A drug supply system has to be devised or strengthened, including procurement, storage, inventory control, distribution, logistic support and related training of personnel. Proper use of drugs has to be promoted by such measures as providing different categories of prescribers with objective information and training them to use it properly, as well as informing and educating the public. The technical and economic feasibility of local formulation and production of drugs has to be considered. Quality control has to be ensured. Provision has to be made for monitoring adverse reactions. Appropriate legislation may have to be introduced and existing legislation brought up to date. Manpower requirements to conceive and implement the national drug policy have to be decided on and appropriate training provided. Measures have to be adopted to ensure the coordinated action of all sectors involved, such as health, education, planning, finance, industry, trade and communication. Monitoring and evaluation procedures have to be adopted. And finally, a financial masterplan has to be worked out for all such activities.

Information, education, and rational prescribing

8. To prescribe rationally, it is necessary not only to have speedy access to objective information on drug efficacy, safety and quality but also to use that information correctly. Prescribers, therefore, have to be capable first of judging if the information available to them is objective, then of selecting an appropriate drug in the right dosage form in the light of that information. They also have to be aware of the price of drugs since, if their patients or the public health service cannot afford them, they will not be bought. In addition, they have to be aware of adverse effects and how to deal with them, as well as of the danger of drug dependence. They have to know when not to resort to drugs and how to convince their patients on those occasions that it is in their best interest to abstain from drugs.

9. To facilitate rational prescribing, therefore, prescribers have to be trained accordingly. This is a major responsibility of schools of medicine, pharmacy, nursing and other categories of health personnel. Training is particularly important for nonprofessional community health workers in developing countries, who require guidance, supervision, and continued in-service training, particularly from the first referral level.

10. It is the duty of manufacturers and the regulatory authorities to generate and make available the drug information required for rational drug use. To do so manufacturers have to provide regulatory authorities with full information on their products; and regulatory authorities have to be sure that sufficient data are available to permit the products to be marketed and that objective information on each registered product is available to prescribers. This is particularly difficult within countries that have no or only rudimentary drug regulatory authorities. For them international cooperation and support are required, and WHO has a major responsibility to provide it.

Dispensing and consumption practices

11. Even when drugs are available and can be afforded, other factors in their rational use have to be considered. Pharmacists have to dispense the right drug and should be able to advise patients on how to use it correctly. They have to be properly trained for this and have easy access to complete and objective information - difficult enough in developed countries but a major obstacle in most developing countries. Since in most of the latter there are very few pharmacists outside the main towns, pragmatic solutions have to be adopted for dispensing drugs by others, with all the risks attached to the performance of this function by inadequately trained people. Patients have to understand the purpose and effects of the drugs they are taking, how to comply with the instructions for use and how to recognize and report adverse reactions. Non-observance of these requirements is a major source of error in drug use.

12. Pharmacists, nurses and other providers of health care have to dispense the right drugs at the right times and recognize and report adverse reactions. Throughout the world mistakes in dispensing to patients abound. To remedy this requires proper understanding of the use of drugs by those who dispense and administer them as well as strict managerial control.

Drug development

13. To ensure the availability of drugs, a country has to either manufacture them or import them. But they first have to be discovered, developed and approved.

14. To discover and develop drugs requires large-scale research and development. For each new drug as many as 10 000 compounds may have to be tested. Screening these requires laboratory studies including pharmacological and toxicological testing, as well as clinical trials, over a time scale of 8-10 years and at a reputed cost of up to US\$ 100 million. Most of this research and development is undertaken by the pharmaceutical industry. The research-based industries consequently tend to develop new drugs for an existing profitable market, paying less attention to such problems as tropical diseases for which the potential market is less attractive. Recent international efforts, however, have stimulated research into new vaccines and new drugs for tropical diseases. The need to develop drugs for which there is no commercial incentive is evident in government initiatives in some countries to promote the development of "orphan drugs".

15. Control over the safety, efficacy and quality of drugs is not only the responsibility of drug manufacturers but has also to be subjected to regulation by governments, a burdensome responsibility for even the most affluent administrative system. Countries that do not develop their own drugs (even if they manufacture some) and countries that import all their drugs also need to institute some form of regulatory control. Counterfeiting of drugs also has to be taken into account. A drug registration system is necessary as a basis for such control, but is still lacking or only rudimentary in many developing countries. Helping them to establish drug control systems is another area for international cooperation and support, particularly by WHO.

Drug manufacturing

16. Once drugs are approved they can be manufactured for sale. Good manufacturing practices should be observed. The technology of large-scale drug manufacturing from raw materials to finished product has become highly sophisticated. Modern drug manufacturing is mostly carried out by automated equipment, and robotized control of the process is beginning to be introduced. Moreover, new drug production processes involving sophisticated biotechnology are already gaining

ground and will grow in importance. Under these circumstances the gap is growing between the capacity of the industrialized countries and that of developing countries to manufacture drugs of consistent high quality at an acceptable cost. Notwithstanding their legitimate desire for self-reliance in drug manufacturing, developing countries are having to take this situation into consideration.

Dosage forms, packaging and labelling

17. The same drug is often required in different dosage forms for different indications, different age-groups, and different degrees of severity of the conditions for which it is needed. There is a need for appropriate packaging for different requirements, including extremes of temperature and humidity. Drugs also have to be clearly labelled and accompanied by data sheets containing relevant information on the pharmacology of the drug, indications for its use, contraindications, warnings, precautions, adverse reactions etc.

Drug distribution

18. Once drugs are manufactured or imported and controlled for quality they have to be properly stored and distributed, either through the public health service or through private channels. Storage and distribution demand attention to proper conditions of temperature, for example the cold chain for vaccines. In the public sector in many developing countries there is a need to improve the management and logistics of distribution including inventory control. Weakness in these, coupled with the weakness of the health infrastructure, hampers the availability of drugs, particularly for primary health care in rural communities. Drugs channelled through intermediate health institutions such as hospitals often do not reach their destination because these institutions too are short of drugs and need them. Often, too, drugs for the public sector infiltrate into the private sector. The improvement of distribution systems in developing countries is, therefore, a major imperative for a more rational use of drugs. Moreover, in some countries unscrupulous dealings occur between the initial procurement of drugs and their final sale to the public, adding considerably to the price to the consumer, and placing them beyond the means of many who need them. In the private sector in market economy countries, drugs are distributed through a network of middlemen before they reach retailers, obviously adding to their price.

Drug promotion

19. It is not easy for prescribers to select drugs properly and use them wisely when they face a bewildering amount and variety of information and consumers believe that there is "a wonder pill for every ill". To inform and influence prescribers and the public, manufacturers and distributors resort to various forms of promotion such as advertising, offering samples, using sales representatives, sponsoring symposia, and even providing financial and other incentives. Some of this conforms to acceptable ethical standards; some does not.

20. Drug promotion by the pharmaceutical industry has been the subject of much criticism because of its alleged aggressivity and bias, and there is wide agreement on the need for recognized norms, even if the nature of such norms and ways of enforcing them have met with less consensus. The multinational industry, through the International Federation of Pharmaceutical Manufacturers Associations, has issued its own voluntary code of marketing practices. Nevertheless, there has been a vigorous campaign for international action to curb the unethical promotion of drugs, particularly those being sold to developing countries. Whatever the nature of such action, it is abundantly clear that no international body has supranational powers permitting it to infringe on national sovereignty. Governments are

responsible for the control of drugs and their promotion in their country, although that responsibility has to be shared by the pharmaceutical industry, prescribers, and consumers.

Costs and prices

21. The rise in drug costs and the consequent increase in their price to consumers are a source of worry in many industrialized countries and a very serious impediment to the purchase of drugs in most developing countries. Two interrelated aspects have to be considered - the cost to society as a whole and the price to the individual. A number of governments are attempting to control the cost to society by reducing the number of drugs available in the health service, requiring evidence that a proposed new product fulfils a perceived medical need, limiting distribution costs, restricting manufacturers' profit margin, and promoting the use of generic drugs wherever possible. The price of drugs is influenced by the cost of research and development for brand products, which research-based industries have to recoup through profits accruing during each drug's patent life. Profits are also required by these industries to enable them to pursue research on and the development of new drugs. Branded generic drugs, for which there are only limited research and development costs, are frequently sold at significantly lower prices than new drugs, and other products sold under a nonproprietary name, either by tender or directly, are frequently sold at even lower prices than branded generics.

22. The cost of drugs for developing countries gives rise to deep concern. In addition to lacking financial resources in general, these countries have severely limited amounts of convertible currency for drug procurement. Recent experience with international tenders for generic drugs in developing countries has been very encouraging; thanks to purchasing larger quantities required for a longer period of time and thus benefiting from the economies of scale, as well as to international market forces, good-quality drugs have been obtained at lower prices than ever before. But greater efforts are required to help developing countries overcome their convertible currency problems as they relate to drug imports.

National drug legislation

23. To control the distribution and marketing of drugs, national legislation is required in most countries relating to such matters as: the registration of drugs; the sale of brand and generic products; labelling and packaging; pricing; the right to prescribe, distribute, and sell drugs; promotion, including advertising and the use of sales representatives; post-marketing surveillance; and, last but not least, measures to ensure the enforcement of laws and regulations. For legislation to be effective it has to be appropriate to local circumstances, accessible, understood, and acceptable to all concerned - another formidable task requiring heavy investment in professional and public education. One particular bone of contention is regulation of the export of drugs that have not been approved for domestic use, with the rare but important exception of drugs that are required and requested by the importing country but not used in the exporting country, for example drugs for tropical diseases. If these are difficult issues to handle in developed countries, they are infinitely more so in developing countries. This is a further area for international cooperation and support, to which governments and WHO should pay particular attention.

WHO's initiatives

24. In response to the above situation, WHO has taken many initiatives, of which those in the paragraphs that follow are the most important.

25. The Organization is promoting and coordinating research, mainly through voluntary contributions, into the development of badly needed new drugs for tropical diseases and new vaccines.

26. To introduce rationality into the naming of drug substances, the Organization assigns internationally recognized generic names, or International Nonproprietary Names (INNs). It has established an International Drug Monitoring Scheme on the adverse effects of drugs. It provides specifications in the International pharmacopoeia for assuring the quality of drug substances. It promulgates standards for good pharmaceutical manufacturing practices as embodied within the Certification Scheme for the Quality of Pharmaceutical Products Moving in International Commerce. It plans and co-sponsors the biennial International Conferences of Drug Regulatory Authorities (ICDRA). Through a network of national information officers it disseminates details of restrictive national regulatory decisions taken in respect of marketed drugs, when necessary by telex. It provides evaluated information on national regulatory decisions through the WHO Drug information bulletin, and work is in hand to produce a WHO model formulary based on the model list of essential drugs. WHO has also developed a simplified system of drug quality control that could be applied by countries with even the most limited resources.

27. As a result, several countries have now disestablished their nomenclature commissions and automatically accept all recommended INNs; and, where other national commissions still exist, each has come to accept a common set of conventions for devising generic names, with the result that nationally assigned names now rarely differ from INNs. The International Conferences of Drug Regulatory Authorities are proving to be a useful mechanism for intergovernmental exchange of information on drug regulation, and there is a welcome increase in the number of developing countries participating. As part of its responsibility for disseminating information, WHO has developed a therapeutic classification of drugs and a comprehensive dictionary of adverse drug reactions within the context of its International Drug Monitoring Scheme. The International pharmacopoeia is now being radically revised with a view to bringing an effective measure of quality control within the grasp of virtually every country. In establishing global standards for good practices in the manufacture and quality control of drugs, which are now recognized by 110 Member States, WHO has created a basis for extending mutual recognition of inspection procedures to all countries. This is the essence of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce.

28. The WHO certification scheme deserves special attention. This scheme provides a simple administrative mechanism whereby importing countries can

- (1) ascertain whether a given product has been registered for marketing in the exporting country and, when appropriate, request an explanation of the reason why registration has not been accorded;
- (2) obtain assurance that the manufacturing plant in which the product is produced is subject to periodic inspection and conforms to requirements for good practices in the manufacture and quality control of drugs as recommended by WHO; and
- (3) obtain details of the inspection and control procedures exercised by the authority in the exporting country and request relevant inquiries to be instituted by the exporting authority should a certified product be found to be of unacceptable quality.

29. Although not a WHO initiative, WHO collaborates with the Secretary-General of the United Nations to implement United Nations resolution GA 37/137 which aims at ensuring that products banned from domestic consumption and/or sale on grounds of safety are sold abroad only upon the request of the importing country or when the consumption of such products is officially permitted in the importing country, and that full information is provided to the importing country on products that are either severely restricted or not approved for domestic consumption and/or sale. This collaboration includes the provision of information on drugs that have been banned, withdrawn, severely restricted or not approved by governments.

30. In 1968 the Twenty-first World Health Assembly, in resolution WHA24.41, adopted ethical and scientific criteria for pharmaceutical advertising. These include the need for all advertising to be truthful and reliable, without incorrect statements, half-truths or unverifiable assertions; stress should be laid on facts, and statements should be supported by adequate scientific evidence. It is stipulated that promotional material should not be exaggerated or misleading and should maintain a fair balance between effectiveness on the one hand and adverse reactions and contraindications on the other. It should provide a full designation of the nature and content of active ingredient(s) per dose using generic or nonproprietary names; action and uses, dosage, form of administration and mode of application; side-effects and adverse reactions; precautions and contraindications; treatment in case of poisoning; and references to the scientific or professional literature. It is further stipulated that advertisements to the public should not be permitted for prescription drugs, for the treatment of conditions which can be treated only by a doctor, or in a form that could provoke fear or distress or that claims infallibility or suggests that the drug is recommended by members of the medical profession.

31. To answer the pressing question of which basic drugs are necessary for the health needs of a population, a WHO expert committee meeting in 1977 reached the conclusion that about 220 drugs and vaccines - "essential drugs" - are sufficient to deal with the vast majority of health problems. The committee established a WHO model list of essential drugs which is periodically updated. This model list does not imply that no other drugs are useful but simply that, in a given situation, these drugs are those most needed for the health care of the majority of the population and those, therefore, that should be available at all times in adequate amounts and in the proper dosage forms. The number of countries with lists of essential drugs or national formularies containing chiefly essential drugs now exceeds 80.

32. A WHO Action Programme on Essential Drugs was formally established in 1981 as an operational programme to support countries in the establishment of essential drug policies. Its aim is to help ensure the regular availability of essential drugs of good quality and at the lowest possible price. In 1981 WHO also joined forces with UNICEF to support the provision of essential drugs for primary health care in developing countries. This includes supporting these countries to procure drugs at the lowest possible prices, through open international tenders and through the UNICEF Packing and Assembly Centre (UNIPAC).

33. In 1982 the Thirty-fifth World Health Assembly endorsed the principles of the WHO Action Programme on Essential Drugs and adopted a plan of action for the Programme. The plan of action includes the major components of a national drugs policy outlined in paragraph 7 above.

34. According to this plan of action WHO has two mutually supportive roles, coordination and technical cooperation. The Organization directly or indirectly coordinates international efforts in support of country programmes. It is also active in advocating the concept of essential drugs, which is gaining

ever-increasing recognition. WHO cooperates with countries and a number of bilateral agencies in setting up essential drugs programmes in line with the above mentioned Health Assembly decisions.

35. WHO's Member States therefore have at their disposal an effective array of measures for improving their drug situation, that have been initiated by their Organization. If they apply them properly, they could have better access to objective information on drugs, improve their manufacturing practices and quality control measures, ensure that the drugs they import conform to the standards of the exporting country, introduce sound drug policies and country-wide programmes to give effect to them with a view to ensuring that all their people have regular access to the essential drugs they need, and reduce the costs of importing drugs and the price to the consumer. In short, they could take significant steps towards a rational use of drugs.