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THE USE OF ESSENTIAL DRUGS

Seventh report of the
WHO Expert Committee

(including the revised Model List of Essential Drugs)

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Geneva, 4–8 December 1995

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1. Introduction

The WHO Expert Committee on the Use of Essential Drugs met in Geneva from 4 to 8 December 1995. The meeting was opened on behalf of the Director-General by Dr F.S. Antezana, Assistant Director-General, who emphasized that the concept of essential drugs was fundamental both to WHO's revised drug strategy (*1*), as endorsed by the World Health Assembly in resolution WHA39.27 in 1986 (*2*), and to the development of comprehensive national drug policies. Regular updating of WHO's Model List of Essential Drugs sustained the momentum of the revised drug strategy and was a basic element of the validated information required by most of WHO's Member States for optimal rationalization of drug procurement and supply. Dr Antezana also emphasized the importance of the emergence of resistance to antimicrobials that, in many cases, is dangerously eroding their effectiveness. This is leading to a situation whereby it will be increasingly difficult to combat serious infections. He requested the Committee to explore mechanisms whereby WHO could maintain a leadership role in this area in countries where the concept of having reserve antimicrobials runs counter to commercial interests.

The Committee decided to prepare its report as a self-contained document and to incorporate into it those parts of the previous report (*3*) that required no modification or merely bringing up to date. The ninth Model List of Essential Drugs will be found in section 16 of this report, and explanations of the changes in section 17.

In a report (*4*) to the Twenty-eighth World Health Assembly in 1975, the Director-General reviewed the main drug problems facing the developing countries and outlined possible new drug policies. The Director-General also referred to the experience gained in some countries where schemes of basic or essential drugs had been implemented. Such schemes were intended to extend the accessibility and rational use of the most necessary drugs to populations whose basic health needs could not be met by the existing supply system. The Director-General pointed out that the selection of these essential drugs would depend on the health needs and on the structure and development of the health services of each country. Lists of essential drugs should be drawn up locally, and periodically updated, with the advice of experts in public health, medicine, pharmacology, pharmacy and drug management. He also considered that adequate information on the properties, indications and use of the drugs listed should be provided. By resolution WHA28.66 (*5*), the Health Assembly requested the Director-General to implement the proposals contained in his report and, in particular, to advise Member States on

the selection and procurement, at reasonable cost, of essential drugs of established quality corresponding to their national health needs.

Following wide consultation, an initial Model List of Essential Drugs was included in the first report of the Expert Committee on the Selection of Essential Drugs (*6*). This has subsequently been revised and updated in seven further reports (*3*, *7–12*).

In undertaking a further review of the list at its present meeting, the Expert Committee was guided throughout by the following statement contained in the previous reports:

> Because of the great differences between countries, the preparation of a drug list of uniform, general applicability is not feasible or possible. Therefore, each country has the direct responsibility of evaluating and adopting a list of essential drugs, according to its own policy in the field of health.
>
> The list of essential drugs based on the guidelines put forward in this report is a model which can furnish a basis for countries to identify their own priorities and to make their own selection.

The Committee also drew attention to the following guidelines set out in the initial report:

1. The extent to which countries implement schemes or establish lists of essential drugs is a national policy decision of each country.
2. As far as health services in developing countries are concerned, the organized procurement and use of essential drugs have many advantages in terms of economy and effectiveness. However, the concept of "essential drug lists" must accommodate a variety of local situations if the lists are ever to meet the real health needs of the majority of the population.
3. There are convincing justifications for WHO to propose "model" or "guiding" lists of essential drugs as a contribution to solving the problems of Member States whose health needs far exceed their resources and who may find it difficult to initiate such an endeavour on their own.
4. Such "guiding" or "model" lists should be understood as a tentative identification of a "common core" of basic needs which has universal relevance and applicability. In certain situations, there is a need to make available additional drugs essential for rare diseases. The further local needs move away from the core, the more the health authorities or specific sectors of the health services will have to adjust the lists. However, any list proposed by WHO should set out to

indicate priorities in drug needs, with the full understanding that exclusion does not imply rejection. A list of essential drugs does not imply that no other drugs are useful, but simply that in a given situation these drugs are the most needed for the health care of the majority of the population and, therefore, should be available at all times in adequate amounts and in the proper dosage forms.

5. The selection of essential drugs is a continuing process, which should take into account changing priorities for public health action and epidemiological conditions, as well as progress in pharmacological and pharmaceutical knowledge. It should be accompanied by a concomitant effort to supply information and give education and training to health personnel in the proper use of the drugs.
6. Finally, the WHO Action Programme on Essential Drugs (*13*) should be a focal point for organized and systematic investigation of this approach. Thus it will identify plans of action and research at the national and international level to meet unsatisfied basic health needs of populations which, at present, are denied access to the most essential prophylactic and therapeutic substances.

At its present meeting, the Committee also reviewed and endorsed the independent report of a workshop on essential drugs and the WHO Model List (*14*) whose purpose was to determine how the list has evolved, to what extent it still responds to the original objectives, and whether those objectives need to be reconsidered. Committee members and workshop participants were unanimous in their opinion that the concept of essential drugs retains its original relevance. There are now over 120 countries with essential drugs lists. These lists are used, *inter alia*, for the procurement of needed drugs, for training of health workers, for developing standard treatment guidelines, for encouraging local pharmaceutical production of drugs of adequate quality and for reimbursement of costs in health insurance schemes.

2. Guidelines for establishing a national programme for essential drugs

Since the first report on the selection of essential drugs was published in 1977, the concept of essential drugs has been widely applied. It has provided a rational basis not only for drug procurement at national level but also for establishing drug requirements at various levels within the health care system. In fact, many developing countries have already selected essential drugs according to their needs and the

related programmes are, in some cases, at an advanced stage of implementation. The Committee was informed that a WHO Expert Committee on National Drug Policies had been convened in 1995 to review and contribute to updating WHO's guidelines for developing national drug policies (*15*).

In order to ensure that an essential drugs programme is adequately instituted at national level, several steps are recommended:

1. A standing committee of health care professionals should be appointed to give technical advice to the national programme. The committee should include individuals competent in the fields of medicine, pharmacology and pharmacy, as well as peripheral health workers. Where individuals with adequate training are not available within the country, cooperation from WHO could be sought until such individuals can be trained. The first task of the committee should be to recommend a list of essential drugs for the national programme. The committee should remain a part of the national programme for essential drugs, continually advising on matters of technical importance.
2. The international nonproprietary (generic) names for drugs or pharmaceutical substances (*16*) should be used whenever available, and prescribers should be provided with a cross-index of nonproprietary and proprietary names.
3. Concise, accurate and comprehensive drug information should be prepared to accompany the list of essential drugs, in the form of a prescriber's formulary to serve as a pocket guide to rational drug use. More detailed information about drugs should be made available at drug and poison information centres, pharmacies and all educational institutes concerned with training health professionals.
4. Quality, including drug content, stability and bioavailability, should be assured through testing or regulation, as discussed in section 5. Where national resources are not available for this type of control, the suppliers should provide documentation of the product's compliance with the required specifications.
5. Competent health authorities should decide on the level of expertise required to prescribe individual drugs or a group of drugs in a therapeutic category. Consideration should be given, in particular, to the competence of the personnel to make a correct diagnosis. In some instances, while individuals with advanced training are necessary to prescribe initial therapy, individuals with less training could be responsible for maintenance therapy.
6. The success of the entire essential drugs programme is dependent upon the efficient administration of supply, storage and distribution at every point from the manufacturer to the end-user. Government

intervention may be necessary to ensure the availability of some drugs in the formulations listed, and special arrangements may need to be instituted for the storage and distribution of drugs that have a short shelf-life or require refrigeration.

7. Efficient management of stocks is necessary to eliminate waste and to ensure continuity of supplies. Procurement policy should be based upon detailed records of turnover. In some instances, drug utilization studies may contribute to a better understanding of true requirements.
8. Research, both clinical and pharmaceutical, is sometimes required to settle the choice of a particular drug product under local conditions. Facilities and trained personnel for such research must be provided. Clinical trials of pharmaceutical products should follow the Guidelines for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products presented in Annex 3 of the Committee's previous report (*3*).
9. A national drug regulatory authority should be established along the lines recommended in the guiding principles for small national drug regulatory authorities presented in Annex 1 of the fifth report of the Expert Committee (*12*). The authority should interact with other interested bodies, including organizations responsible for drug procurement in the public and private sectors and the committee referred to in item 1.

3. Criteria for the selection of essential drugs

Essential drugs are those that satisfy the health care needs of the majority of the population; they should therefore be available at all times in adequate amounts and in the appropriate dosage forms.

The choice of such drugs depends on many factors, such as the pattern of prevalent diseases; the treatment facilities; the training and experience of the available personnel; the financial resources; and genetic, demographic and environmental factors.

Because of differing views on the definition of an essential drug in terms of what is meant by the "health care needs of the majority" of the population, the model list has been gradually expanded since its introduction. Some drugs are included that are essential only if a therapeutic programme is planned to address the diseases for which these drugs are used. For example, the cytotoxic drugs (section 8.2 of the model list) are essential only if a comprehensive cancer treatment programme is planned. Such a programme requires adequate hospital, diagnostic and clinical laboratory facilities for its implementation.

In contrast, the drugs used in palliative care (section 8.4) are always essential, even when a comprehensive cancer treatment programme does not exist.

Only those drugs should be selected for which sound and adequate data on efficacy and safety are available from clinical studies and for which evidence of performance in general use in a variety of medical settings has been obtained.

Each selected drug must be available in a form in which adequate quality, including bioavailability, can be assured; its stability under the anticipated conditions of storage and use must be established.

Where two or more drugs appear to be similar in the above respects, the choice between them should be made on the basis of a careful evaluation of their relative efficacy, safety, quality, price and availability.

In cost comparisons between drugs, the cost of the total treatment, and not only the unit cost of the drug, must be considered. The cost/benefit ratio is a major consideration in the choice of some drugs for the list. In some cases the choice may also be influenced by other factors, such as comparative pharmacokinetic properties, or by local considerations such as the availability of facilities for manufacture or storage.

Most essential drugs should be formulated as single compounds. Fixed-ratio combination products are acceptable only when the dosage of each ingredient meets the requirements of a defined population group and when the combination has a proven advantage over single compounds administered separately in therapeutic effect, safety or compliance.

4. Guidelines for the selection of pharmaceutical dosage forms

The purpose of selecting dosage forms and strengths for the drugs in the model list is to provide guidance to countries wishing to standardize or minimize the number of preparations in their own drug lists. As a general rule, pharmaceutical forms are selected on the basis of their general utility and their wide availability internationally. In many instances, a choice of preparations is provided, particularly in relation to solid dosage forms. Tablets are usually less expensive than capsules, but, while cost should be taken into account, the selection should also be based on a consideration of pharmacokinetics,

bioavailability, stability under ambient climatic conditions, availability of excipients, and established local preference.

In a few instances where there is no uniformity of tablet strength, for example acetylsalicylic acid and paracetamol, a dosage range is provided from within which suitable tablet strengths should be selected on the basis of local availability and need. When precise dosage is not mandatory, the use of scored tablets is recommended as a simple method of making dosage more flexible if so required and, in some instances, to provide a convenient paediatric dose. Specific paediatric dosages and formulations are included in the list only when indicated by special circumstances. In many instances, dosage is specified in terms of a selected salt or ester, but in others – for example chloroquine – it is calculated, in accordance with common practice, in terms of the active moiety.

For certain drugs with short half-lives that are rapidly metabolized, such as carbamazepine, calcium-channel blockers and theophylline, conventional-release dosage forms must often be taken three or four times a day to maintain drug levels in the required narrow range. Sustained-release dosage forms can reduce the frequency of drug administration, thereby improving compliance and, often, the therapeutic effectiveness of the drug by maintaining a more constant drug level than can be obtained using traditional dosage forms. Because the preparation of sustained-release products is difficult and requires special expertise, a proposal to include such a product in a national list of essential drugs should be justified by adequate documentation.

5. Quality assurance

Quality assurance of drugs, as embodied in product development, good manufacturing practice and subsequent monitoring of quality throughout the distribution chain to utilization, is a crucial element in any essential drugs programme. All aspects of these procedures have been dealt with at length in the twenty-sixth to thirty-fourth reports of the WHO Expert Committee on Specifications for Pharmaceutical Preparations (*17–25*).

Priority should be given to ensuring that the available drugs have been made according to good manufacturing practices (*23*, Annex 1) and are of generally recognized quality. This requires knowledge of and confidence in the origin of the product. The risks of procuring drugs from anonymous sources cannot be overstressed. It is recommended that drugs are purchased directly from known

manufacturers, their duly accredited agents or recognized international agencies known to apply high standards in selecting their suppliers.

5.1 WHO's Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce

The Committee emphasized the importance of WHO's Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce, particularly in countries with inadequate laboratory facilities for drug analysis which may be unable to carry out the process of quality control. This scheme has been available since 1975 as a means of exchanging information between regulatory authorities in importing and exporting countries. Its purposes are:

1. To provide assurance that a given product has been authorized to be placed on the market in the exporting country, and, if not, to explain why authorization has been withheld, or has not been requested.
2. To provide assurance that the plant in which the product is manufactured is subject to inspections at suitable intervals and conforms to the requirements for good practices in the manufacture and quality control of drugs, as recommended by WHO.
3. To provide for exchange of information on the implementation of inspections and controls by the authorities in the exporting country. In the case of serious quality defects inquiries may also be made.

In 1988 the scope of the certification scheme was extended, in accordance with World Health Assembly resolution WHA41.18, to provide for a more comprehensive exchange of information between governments (*26*). Drug substances as well as finished dosage forms intended for administration to human beings or to food-producing animals were included within the scheme. The revised scheme also required the competent authority in the exporting country to provide copies of all approved product information, including labelling, as determined by the product licence issued by the regulatory authority in the country of manufacture.

In 1992 the Forty-fifth World Health Assembly, by resolution WHA45.29 (*27*), endorsed the "Guidelines for implementation of the WHO Certification Scheme", which include models for a Certificate of a Pharmaceutical Product, a Statement of Licensing Status of Pharmaceutical Product(s), and a Batch Certificate of a Pharmaceutical Product. In this resolution the Health Assembly established a period of 5 years to evaluate and revise the proposed forms for these certificates. The evaluation was done on the basis of field trials and

subsequent discussions were held during the Seventh International Conference of Drug Regulatory Authorities (ICDRA). The revised text was adopted by the WHO Expert Committee on Specifications for Pharmaceutical Preparations at its thirty-fourth meeting, and is included in its report (*25*).

It is important that the model certificates in the Guidelines are followed when certificates are issued and that they are clearly identified as conforming to the format recommended by WHO, since they may differ from other certificates issued by countries. This, however, does not mean that WHO issues the model certificates. These are issued by the competent authority in the exporting country. Importing countries are also urged to use the scheme and request certificates from the exporting countries in the format recommended by WHO.

5.2 Bioavailability

Poor bioavailability of a pharmaceutical product can result in treatment failure just as readily as can a deficiency of active ingredients. The bioavailability of essential drugs should therefore continue to receive consideration since it is a key factor in the efficacy of multisource products.

5.3 *The international pharmacopoeia*

The Committee appreciates that the development of the Model List of Essential Drugs has provided a natural focus for the third edition of *The international pharmacopoeia* (*28*), thus enhancing its potential value to developing countries. Essential drugs are accorded priority and all quality specifications are supported by classical methods of testing and analysis. A plan for a small quality-control laboratory in which most of these tests can be performed has been available since 1984 (*20*). Since quality assurance of essential drugs is so important, the Committee recommends to national governments the setting up of such laboratories and the adoption of *The international pharmacopoeia* by those currently lacking the means to confirm independently the quality of the supplies they procure. Where national capacity is lacking, a regional effort involving several countries may be useful. In this context, attention is also drawn to the WHO publication *Basic tests for pharmaceutical substances* (*29*), which enables the identity of drug substances to be verified and gross degradation to be excluded when laboratory facilities for full pharmacopoeial analyses are not available.

The Committee emphasizes the need to extend the coverage of *The international pharmacopoeia* to include not only essential drug substances, but also the dosage forms (*30*) specified in the Model List of Essential Drugs, together with additional information on bioavailability, stability and recommended packaging and storage conditions.

5.4 Counterfeit drugs

Concern has been expressed about the export, import and smuggling of falsely labelled, spurious, counterfeited or substandard pharmaceutical preparations. Some products contain little or no active ingredient and may even contain a different active substance from that on the label. A workshop on counterfeit drugs cosponsored by WHO and the International Federation of Pharmaceutical Manufacturers Associations was held in 1992 (*31*), which emphasized the need for a comprehensive strategy to detect and deter the manufacture and distribution of counterfeited and substandard medicines. In response to this recommendation, WHO has established a database for reports of counterfeited drugs and developed methodologies for determining the prevalence of both counterfeited and substandard products. The Committee strongly endorsed these activities and recommended that they be continued by WHO and its Member States.

6. Reserve anti-infective agents and monitoring of resistance

The increasing prevalence of strains of common pathogenic bacteria resistant to widely available, relatively cheap antimicrobials included in the model list is, in many cases, dangerously eroding their effectiveness.

6.1 Need for surveillance of resistance

The need for more systematic and coordinated international approaches to laboratory monitoring of antimicrobial sensitivity is important and urgent. It has already been emphasized that reference laboratories need to be established in developing as well as developed countries in order to monitor the resistance of important bacterial pathogens (*32, 33*). Knowledge of prevailing sensitivity patterns is vital to the selection and use of antimicrobials and to the development of appropriate prescribing policies. Without these data the health of seriously ill patients could be jeopardized. Knowledge of sensitivity patterns should come from proper laboratory investigations. In some

countries, decisions on drug use are taken on the basis of standardized therapeutic efficacy testing.

The exchange of information on patterns of antimicrobial sensitivity via the WHONET[1] and other sources of data should assist in the selection of the most appropriate antimicrobial agent. Such information should be collected for bacterial and fungal pathogens, as well as for protozoal infections including malaria.

6.2 Reserve antimicrobials

It is becoming increasingly common for important pathogens to emerge in a country or locality that are shown, on sensitivity testing, to have developed resistance to all normally appropriate essential drugs. In these circumstances a reserve antimicrobial is needed. A reserve antimicrobial is an antimicrobial that is useful for a wide range of infections but, because of the need to reduce the risk of development of resistance and because of its relatively high cost, it would be inappropriate to recommend its unrestricted use.

The concept of reserve antimicrobials is of practical relevance only when information is available on the prevailing sensitivities of important bacterial pathogens. Within this context the second- and third-generation cefalosporins, the fluoroquinolones and vancomycin are most important.

There are many third-generation cefalosporins. Cefalosporins should be used only to treat specific infections that are resistant to antimicrobials on the main list; for this purpose, they are considered essential. Some are suitable for the treatment of *Haemophilus influenzae* type b meningitis, where strains are resistant to chloramphenicol and benzylpenicillin, or pneumococcal meningitis, where penicillin-resistant pneumococci are common. Ceftazidime is an example of a cefalosporin that is used for the treatment of *Pseudomonas aeruginosa* infections resistant to gentamicin. Ceftriaxone is included in the model list because the Committee recognized the need for a β-lactam antibiotic that reaches high levels in the cerebrospinal fluid following parenteral administration. Ceftriaxone is considered to be effective for the treatment of meningitis caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria meningitidis*.

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[1] For further information, contact the Division of Emerging and other Communicable Diseases Surveillance and Control, World Health Organization, 1211 Geneva 27, Switzerland.

Ciprofloxacin is a member of the fluoroquinolone family of antimicrobials. Although this is now listed as an essential drug, the comparative costs of alternative broad-spectrum products will be an important determinant of selection. Ciprofloxacin and certain other fluoroquinolones may still be considered of value as reserve agents. Their use may need to be restricted to the following circumstances:

- For typhoid fever and other systemic salmonella infections where there are strains of *Salmonella* resistant to chloramphenicol, amoxicillin and trimethoprim/sulfamethoxazole.
- For severe shigellosis where *Shigella* spp. strains exist that are resistant to ampicillin, chloramphenicol, sulfamethoxazole/trimethoprim, tetracyclines and nalidixic acid.
- For gonorrhoea and chancroid, as alternatives to cefalosporins, when oral administration is appropriate.
- For hospital-acquired infections due to Gram-negative bacilli, including *Escherichia coli, Klebsiella* spp. and *Pseudomonas aeruginosa*, that are resistant to essential drugs such as amoxicillin, chloramphenicol and gentamicin.

Meticillin-resistant *Staphylococcus aureus* strains are usually resistant to all β-lactam antimicrobials and also to unrelated drugs such as erythromycin, clindamycin, chloramphenicol, the tetracyclines and the aminoglycosides. The only effective reserve drug for infections due to these multiresistant organisms is vancomycin, which is expensive and must be administered intravenously.

In some countries, strains of *Plasmodium falciparum* have developed resistance to all of the antimalarial drugs except for artemisinin and its derivatives. For patients with falciparum malaria resistant to chloroquine, sulfadoxine/pyrimethamine, mefloquine or quinine with tetracycline, the use of artemisinin and its derivatives appears essential. In order to limit the development of resistance to these drugs and keep them effective for as long as possible, their use should be restricted to areas in which multidrug-resistant falciparum malaria exists. In such countries artemisinin and its derivatives should be used for the treatment of uncomplicated infections resistant to all other antimalarials, or for severe falciparum malaria where quinine is ineffective.

The need for the development of new anti-infective drugs, especially for those diseases mainly prevalent in developing countries, continues to be of high priority. The pharmaceutical industry should be encouraged to engage in this research.

7. Antiviral drugs

Antiviral drugs were considered because the Committee recognizes the importance of viral illnesses and the need for effective antiviral drugs. Every effort should be made to promote the development of antiviral agents against important viral pathogens including human immunodeficiency virus (HIV), papillomaviruses, hepatitis B and C, respiratory syncytial viruses, adenoviruses and haemorrhagic fever viruses. However, because of their limited efficacy, toxicity and cost, none of those currently available was considered to qualify for inclusion in the model list at this time. Aciclovir was, none the less, accepted as being of value in the treatment of severe herpes infections. Similarly, zidovudine was acknowledged to suppress the progression of HIV infection temporarily. Data from preliminary studies also suggested that administration of zidovudine to pregnant women may reduce the risk of HIV infection in infants (*34*, *35*). Neither aciclovir nor zidovudine was considered essential, however, for the reasons given above.

8. Applications of the essential drugs concept

The concept of essential drugs has been endorsed unanimously by the World Health Assembly. It is intended to be flexible and adaptable to many different situations; exactly which drugs are regarded as essential remains a national responsibility.

The concept of essential drugs has been disseminated and promoted extensively at the country level by WHO's Action Programme on Essential Drugs, as well as by disease control programmes in WHO, international and nongovernmental organizations throughout the world and bilateral agencies. The wide applicability of the concept is now evident from experience gained in many countries. Most national lists of essential drugs are stratified to reflect requirements at different levels within the health care infrastructure. Typically, a very short list has been compiled for community health workers while the most comprehensive lists have been reserved for large urban and regional hospitals. Many countries have also successfully applied the concept to teaching hospitals and facilities providing specialized care. The concept has also been applied in the dissemination of drug information.

The model list has been adopted by numerous international and bilateral agencies that now include drug supply and the rationalization of drug use in their health care programmes. Adoption of the list

has resulted in greater international coordination in health care development, and it is also being used to evaluate whether drug donations are appropriate in a given situation.

A shorter, adapted list has proved to be of particular value in emergency situations. It is contained in an emergency health kit (*36*), designed to cover the basic needs of a population of 10000 for a period of about 3 months, which has been developed and updated by WHO, the Office of the United Nations High Commissioner for Refugees, UNICEF, *Médecins sans frontières*, the International Federation of Red Cross and Red Crescent Societies, the Christian Medical Commission and several other nongovernmental organizations. Many non-profit suppliers maintain a stock of most of the drugs on the list, which allows a rapid response to demand. In addition, the same interagency group is currently drawing up a slightly longer list of essential drugs for use in emergency situations, which will be included in a United Nations catalogue of items for emergency relief (*37*).

The concept of essential drugs has also been applied to the integrated management of childhood illness (*38*), which the Committee considered an important aspect of WHO's work.

9. Essential drugs and primary health care

The selection of drugs for primary health care must be determined nationally since the training and responsibilities of the personnel charged to administer this care vary considerably. Highly trained workers are able to use a wide range of drugs, while workers with limited training should use only those drugs appropriate to their diagnostic skills, knowledge and experience. For this reason, a shorter, adapted list of essential drugs is often adequate for primary health care. Decisions about which specific drugs should be made available in this shorter list can be made only when all relevant local factors have been taken into account. The following considerations will inevitably influence the compilation of such drug lists.

9.1 Existing systems of medicine

The establishment of primary health care services in developing countries should not result in abrupt disruption of prevailing cultural patterns in rural communities. The work of traditional healers, for example, should be adapted and supplemented so as to ensure that innovation is successfully integrated into existing systems of care.

9.2 The national health infrastructure

The type of primary health care service that a country requires is dependent upon the proximity and nature of the first referral facilities. It is still not unusual in some countries for the nearest permanently staffed health post to be a day's travelling time or more from isolated villages in its catchment area.

9.3 The pattern of endemic disease

The prevalence of major endemic infections and parasitic diseases may vary from region to region within a country in conformity with climatic, geographical, topographical, social, economic and occupational factors. Careful planning and, in some cases, epidemiological surveys are required to ensure that the most effective drugs are provided and to obtain full benefit from limited resources.

9.4 Supplies

Continuity of essential supplies and information must be assured. It is especially important that drugs be distributed and stored correctly. For example, the cold chain must be maintained for drugs requiring this type of care, such as insulin and vaccines.

9.5 Medicinal drug promotion

Medicinal drug promotional and marketing activities can strongly influence prescribing practices. Methods of evaluating new drugs based on their comparative safety, efficacy, availability and cost should form part of the training of primary health care workers. In addition, the WHO ethical criteria for medicinal drug promotion (*39*) should continue to be widely distributed and followed. This is particularly important for drugs used to treat infections so that inappropriate use is kept to a minimum, thereby limiting both the development of resistance to new antimicrobial drugs and unwarranted expense.

10. Drug donations

General principles for drug donations were listed in the previous report of this Committee (*3*). These principles are now being updated through a global consultation process in collaboration with the major international relief organizations.[1]

[1] *Guidelines for drug donations*. Geneva, World Health Organization, 1996 (unpublished document WHO/DAP/96.2; available on request from Action Programme on Essential Drugs, World Health Organization, 1211 Geneva 27, Switzerland).

11. Post-registration drug studies

Clinical studies for the development of new drugs take place, for the most part, in major medical centres with extensive facilities and highly trained staff. The patients entering the clinical trials in these centres will usually have received full medical evaluations.

Often, certain groups of patients such as pregnant women, young children and old people will have been excluded from the trials. For this reason, the patients receiving the new drug prior to registration will not represent the full range of patients who will be receiving the drug after registration. In addition, the genetic and environmental factors influencing populations in other parts of the world may differ from those that characterize the populations in which the drug was studied and cause differences in population dose–response relationships.

Little is known about the clinical consequences of different prescribing patterns between countries or between regions within a country. There are few systematic and comprehensive data on the utilization of drugs after they have been marketed, but it is recognized that they are frequently not used to their full potential or in accordance with generally accepted criteria. Moreover, data on overdose effects and uncommon or longer-term adverse effects are usually not available at the time of registration. It is important, whenever feasible, to quantify these risks in order to identify the safest available products and to remove from the market those that are unacceptably dangerous. Such information is essential if drug selection committees are to function optimally.

Other information that can be obtained when a drug is used in practice relates to unanticipated uses discovered when the drug is given to patients who have both the accepted indication and another illness. Furthermore, when used in practice, a drug may fail to produce the benefit that was expected on the basis of the pre-registration studies. This may be because the results of the pre-registration clinical trials cannot be applied to the entire population of patients with the indication for the drug or because the dosage form being used contains less than the labelled amount of the drug or contains the labelled amount, but not in a bioavailable form. These latter factors could result from poor manufacturing practices or from intentional counterfeiting of legitimate dosage forms.

In order to obtain all the additional information needed for the fully rational use of essential drugs, post-registration drug surveillance or surveys are needed.

Depending on their purpose and the facilities available, drug surveys can be carried out at various levels. Their value is enhanced by using standard procedures (common drug classification systems and units of measurement) in different regions and countries. These procedures should be used to provide data on all relevant drugs in a particular therapeutic class, paying attention to both cost and quantities prescribed, and taking differences in therapeutic practice into consideration.

The main purpose of drug surveys is to quantify present usage and estimate future demands. Studies can be designed simply to quantify the drug inventory only or to evaluate drug utilization. Data can also be used: (a) to measure the effects of informational and regulatory measures, price policy, etc.; (b) to define areas for further investigation of the absolute and relative efficacy and safety of drug therapy; (c) to aid in the determination of benefit/risk ratios and cost-effectiveness; and (d) when properly interpreted, to indicate the over-use, underuse or misuse of individual drugs or therapeutic classes of drugs.

Many drug regulatory authorities have recognized the value of post-marketing drug surveillance and the need for sustained international surveillance schemes. For many years the WHO Collaborating Centre on International Drug Monitoring has collated the reports of national monitoring schemes based on spontaneous notification by health professionals. Originally the programme included only countries with highly evolved regulatory agencies, where its main use was for generating signals of possible adverse drug reactions and for confirming cases. Currently the Collaborating Centre is attracting many developing countries which are in the process of establishing national drug policies. WHO is collaborating closely with the Council for International Organizations of Medical Sciences to promote epidemiologically based methods of monitoring.

The ability of most developing countries to carry out studies using such methods is limited by cost. Nevertheless, when concern arises over the safety of a drug used exclusively for a tropical disease, the need for post-marketing surveillance is as great as in any other situation. Such a matter is already being addressed by WHO in the instance of the use of ivermectin in community-based mass treatment programmes for onchocerciasis. Such surveillance may also require the establishment of special reporting facilities and, exceptionally, small follow-up studies of people exposed to specific drugs may be necessary.

If the detection of longer-term adverse sequelae to drug use is to become more efficient, reliable methods of linking prescribing

information to hospital records will need to be more widely introduced. This, in turn, will require a means of assuring the confidentiality and privacy of personal information. Until these methods are developed, the application of epidemiological principles to the assessment of drug-induced effects will remain difficult to explore. WHO possesses the appropriate consultative capacity to promote debate of the issues, to promote the most suitable methods, and to monitor the results of their application.

These general principles apply not only to the detection and assessment of adverse drug effects but to all other indicators of drug performance. In particular, the Committee emphasized the need for access to microbiological reference laboratories as a mandatory prerequisite for the rational use of the expensive reserve antimicrobials.

The opportunities to advance therapeutics through post-registration drug studies will be only partially utilized until all health care professionals accept their responsibility to report on the effects of drugs in actual use.

12. Research and development

If the establishment of a list of essential drugs is to succeed in improving health and in reducing drug costs in developing countries, use of the list should be either preceded by, or developed together with, adequate supply and distribution systems and procurement procedures. To hasten the self-reliance of countries, research and development should be undertaken in the following broad areas.

12.1 Pharmaceutical aspects

1. Development of local or regional capability in quality assurance in order to ensure that drug quality is maintained.
2. Development of procurement procedures to take advantage of the benefits of purchasing large quantities of drugs.
3. Development of facilities for processing and packaging simple dosage forms, and ensuring the quality of the product.
4. Development of an efficient countrywide distribution system with suitably trained personnel.

12.2 Clinical and epidemiological aspects

1. Development of facilities and expertise to carry out clinical trials according to the guidelines presented in Annex 3 of the Committee's previous report (*3*) in order to assess:
   - the relative efficacy and safety of new candidate compounds for inclusion in an essential drugs list;

- the benefits and safety of traditional medicines, including medicinal plants;
- the effects of genetic and environmental differences among populations on pharmacokinetic, pharmacodynamic and therapeutic parameters.

2. Development of expertise to carry out drug utilization studies and to assess therapeutic practice.

12.3 Educational aspects

1. Development of simple, concise labels for each dosage form.
2. Development of training programmes in policy formulation, quality control, pharmaceutical information systems, and drug procurement, production, storage and distribution procedures.
3. Development of educational and training programmes for prescribers and other health care professionals.
4. Development of appropriate public education and information programmes in diagnosis and self-medication for conditions for which early recognition of symptoms and prompt self-medication are crucial.

13. Nomenclature

The need to identify each pharmaceutical substance by a unique, globally recognized generic name is of critical importance in facilitating communication as well as in the labelling and advertising of medicinal products in international commerce.

This is the objective of the WHO programme on the selection of international nonproprietary names (INNs), whose activities have led to the publication of names for roughly 6600 new pharmaceutical products since 1950. Its role is to coordinate and harmonize the activities of existing national drug nomenclature commissions, which now follow a common set of conventions for devising generic names. Officially assigned generic names now rarely differ from the INNs, and some countries have disestablished their national commissions and automatically accept all recommended INNs.

The procedure for selecting INNs allows manufacturers to contest names that are either identical or similar to their licensed trade marks. In contrast, trade-mark applications are disallowed, in accordance with the present procedure, only when they are identical to an INN. A case for increased protection of INNs is now apparent as a result of competitive promotion of products no longer protected by patents. Rather than marketing these products under the generic name, many companies apply for a trade mark derived from an INN

and, in particular, including the INN common stem. This practice endangers the principle that INNs are public property; it can frustrate the rational selection of further INNs for related substances, and it will ultimately compromise the safety of patients by promoting confusion in drug nomenclature.

On the basis of the Committee's previous recommendations concerning trade marks derived from INNs, a resolution on nonproprietary names for pharmaceuticals (WHA46.19) was adopted by the World Health Assembly in 1993 (*40*). The resolution requested Member States:

(1) to enact rules or regulations, as necessary, to ensure that international nonproprietary names (or the equivalent nationally approved generic names) used in the labelling and advertising of pharmaceutical products are always displayed prominently;
(2) to encourage manufacturers to rely on their corporate name and the international nonproprietary names, rather than on trade marks, to promote and market multisource products introduced after the expiry of a patent;
(3) to develop policy guidelines on the use and protection of international nonproprietary names, and to discourage the use of names derived from them, and particularly names including established stems, as trade marks.

The resolution called upon the Director-General to intensify his consultations with governments and representatives of the pharmaceutical industry on ways of reducing to a minimum the problems arising from drug nomenclatures that may create confusion and jeopardize the safety of patients.

While INNs are widely used in reference books and journals, they are not always identified as such or even accorded preference, particularly in the case of older substances that may have several different generic names. Editors are urged to give preference to INNs in reference works, journals and data banks and to allow the use of a code for a new substance (pending the assignment of an INN) rather than an unofficial name.

14. Drug information and educational activities

For the safe, effective and prudent use of essential drugs, relevant and reliable drug information should be available. In order to provide this, a series of publications entitled *WHO model prescribing information* is being prepared. The first four titles in this series, *Drugs used in*

anaesthesia (*41*), *Drugs used in parasitic diseases* (*42*), *Drugs used in mycobacterial diseases* (*43*) and *Drugs used in sexually transmitted diseases and HIV infection* (*44*) have already been published. The fifth title, *Drugs used in skin diseases* (*45*), is in press, and further titles are in preparation. The Committee supports with great enthusiasm the provision of model prescribing information and considers that the documents published to date are clear, useful and well written.

In addition, the Committee urged that a Model Formulary should be developed to complement the Model List of Essential Drugs. The purpose of such a formulary, which could be updated periodically, would be to provide general information and information on prototype drugs in the Model List of Essential Drugs according to the specifications as shown in the sample drug information sheet overleaf. This information could then be adapted by countries according to their own needs and would be a key element in rational drug use.

Health care professionals should receive education about the use of drugs not only during their initial professional training but throughout their professional careers. The more highly trained individuals should assume a responsibility to educate those with less training. Pharmacists and other health care workers responsible for dispensing drugs should accept every opportunity to inform consumers about the rational use of these products, including those for self-medication, at the time they are dispensed.

The Committee recommended that comprehensive educational programmes for health care professionals include:

- accurate and understandable drug information and information on all aspects of medical care in which they are involved;
- information about patterns of disease in the community, especially prevailing sensitivity patterns, to aid in the selection of antimicrobial drugs;
- diagnostic and therapeutic guidelines for conditions recognized as important.

Governments, universities and professional associations have a major responsibility to collaborate on improving undergraduate, postgraduate and continuing education in clinical pharmacology, therapeutics and drug information issues.

Appropriate drug information that is well presented is cost-effective in that it ensures that drugs are used properly and decreases inappropriate drug use; drug information activities should be financed from the national budget for the provision of drugs.

Drug information sheets

The following is an example of a format for supplying information to prescribers to facilitate the safe and effective use of drugs. The content should be adjusted to the needs, knowledge and responsibilities of the prescriber.

1. INN of each active substance.

2. Pharmacological data: a brief description of pharmacological properties and mechanism of action.

3. Clinical information:
   (a) Indications: whenever appropriate, simple diagnostic criteria should be provided.
   (b) Dosage regimen and relevant pharmacokinetic data:
      - average and range for adults and children;
      - dosing interval;
      - average duration of treatment;
      - special situations, e.g. renal, hepatic, cardiac or nutritional insufficiencies that require either an increased or a reduced dosage.
   (c) Contraindications.
   (d) Precautions and warnings (reference to pregnancy, lactation, etc.).
   (e) Adverse effects (quantify by category, if possible).
   (f) Drug interactions (include only if clinically relevant; drugs used for self-medication should be included).
   (g) Overdosage:
      - brief clinical description of symptoms;
      - non-drug treatment and supportive therapy;
      - specific antidotes.

4. Pharmaceutical information:
   (a) Dosage forms.
   (b) Strength of dosage form.
   (c) Excipients.
   (d) Storage conditions and shelf-life (expiry date).
   (e) Pack sizes.
   (f) Description of the product and package.
   (g) Legal category (narcotic or other controlled drug, prescription or non-prescription).
   (h) Name and address of manufacturer(s) and importer(s).

The Committee also recognized the need to develop appropriate drug information sheets for consumers.

15. Updating of lists of essential drugs

An essential drug list must be flexible enough to accommodate, as necessary, new drugs, new information on established drugs and changes in the status of internationally controlled substances. Experience with the original model list and the subsequent revisions, as well as with regional and national lists of essential drugs, has confirmed the need for regular review and updating. Revision is necessary not only because of advances in drug therapy but also in order to meet the needs of practice in the light of experience. Frequent and extensive changes are clearly undesirable since they result in disruption of channels of procurement and distribution and may have implications for the training of health personnel. For this reason a number of drugs have been retained on the model list that have been largely superseded in countries where there is a more extensive range of new medicaments but that are still used widely and successfully elsewhere.

Applications for the addition of drugs to the model list will always receive full consideration by WHO. An application form can be found in Annex 1.

16. Model List of Essential Drugs (ninth list)

Explanatory notes[1]

Many drugs included in the list are preceded by a square symbol (□) to indicate that they represent an *example of a therapeutic group* and that various drugs could serve as alternatives. It is imperative that this is understood when drugs are selected at national level, since choice is then influenced by the comparative cost and availability of equivalent products. Examples of acceptable substitutions include:

- □ Codeine: other drugs for the symptomatic treatment of diarrhoea in adults, such as loperamide or, when indicated for cough relief, dextromethorphan.
- □ Hydrochlorothiazide: any other thiazide-type diuretic currently in broad clinical use.
- □ Hydralazine: any other peripheral vasodilator having an antihypertensive effect.
- □ Senna: any mild stimulant laxative (either synthetic or of plant origin).
- □ Sulfadimidine: any other short-acting, systemically active sulfonamide unlikely to cause crystalluria.

[1] The numbers preceding the drug sections and subsections in the model list have, in general, been allocated in accordance with English alphabetical order; they have no formal significance.

Numbers in parentheses following the drug names indicate:

(1) Drugs subject to international control under: (a) the Single Convention on Narcotic Drugs, 1961 (*46*); (b) the Convention on Psychotropic Substances, 1971 (*47*); or (c) the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances, 1988 (*48*).
(2) Specific expertise, diagnostic precision, individualization of dosage or special equipment required for proper use.
(3) Greater potency or efficacy.
(4) In renal insufficiency, contraindicated or dosage adjustments necessary.
(5) To improve compliance.
(6) Special pharmacokinetic properties.
(7) Adverse effects diminish benefit/risk ratio.
(8) Limited indications or narrow spectrum of activity.
(9) For epidural anaesthesia.
(10) Sustained-release preparations available. A proposal to include such a product in a national list of essential drugs should be justified by adequate documentation.

Letters in parentheses after the drug names indicate the reasons for the inclusion of *complementary drugs*:

(A) When drugs in the main list cannot be made available.
(B) When drugs in the main list are known to be ineffective or inappropriate for a given individual.
(C) For use in rare disorders or in exceptional circumstances.

Certain pharmacological effects have many therapeutic uses. Drugs with these effects could be listed in many different therapeutic categories in the model list. However, the inclusion of such drugs in more than one therapeutic category has been limited to circumstances that the Committee wished to emphasize. Drugs in the model list are therefore not necessarily listed in each of the therapeutic categories in which they are of value. Information on therapeutic use is available in the *WHO model prescribing information* publications (*41–45*), and several other WHO publications (*49–52*). In addition, essential drugs could be categorized by whether their use is to treat a life-threatening illness, to minimize or prevent a disability, or to improve the quality of life. This system is not used here, however, since the Committee considered all of these uses to be essential for proper therapeutics. It is necessary for individual countries to specify which drugs have priority in their country.

Drug	*Route of administration, dosage forms and strengths*[a]
1. Anaesthetics	
1.1 *General anaesthetics and oxygen*	
ether, anaesthetic (1c, 2)	inhalation
halothane (2)	inhalation
ketamine (2)	injection, 50mg (as hydrochloride)/ml in 10-ml vial
nitrous oxide (2)	inhalation
oxygen	inhalation (medicinal gas)
□thiopental (2)	powder for injection, 0.5g, 1.0g (sodium salt) in ampoule
1.2 *Local anaesthetics*	
□bupivacaine (2, 9)	injection, 0.25%, 0.5% (hydrochloride) in vial
	injection for spinal anaesthesia, 0.5% (hydrochloride) in 4-ml ampoule to be mixed with 7.5% glucose solution
□lidocaine	injection, 1%, 2% (hydrochloride) in vial
	injection, 1%, 2% (hydrochloride) + epinephrine 1:200000 in vial
	injection for spinal anaesthesia, 5% (hydrochloride) in 2-ml ampoule to be mixed with 7.5% glucose solution
	topical forms, 2–4% (hydrochloride)
	dental cartridge, 2% (hydrochloride) + epinephrine 1:80000
1.3 *Preoperative medication and sedation for short-term procedures*	
atropine	injection, 1mg (sulfate) in 1-ml ampoule
chloral hydrate	syrup, 200mg/5ml
□diazepam (1b)	injection, 5mg/ml in 2-ml ampoule
	tablet, 5mg
□morphine (1a)	injection, 10mg (sulfate or hydrochloride) in 1-ml ampoule
□promethazine	elixir or syrup, 5mg (hydrochloride)/5ml

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
2. Analgesics, antipyretics, non-steroidal anti-inflammatory drugs and drugs used to treat gout	
2.1 *Non-opioids*	
acetylsalicylic acid	tablet, 100–500mg
	suppository, 50–150mg
allopurinol (4)	tablet, 100mg
colchicine (7)	tablet, 500µg
□ibuprofen	tablet, 200mg, 400mg
paracetamol	tablet, 100–500mg
	suppository, 100mg
	syrup, 125mg/5ml
2.2 *Opioid analgesics*	
□codeine (1a)	tablet, 30mg (phosphate)
□morphine (1a)	injection, 10mg (sulfate or hydrochloride) in 1-ml ampoule
	oral solution, 10mg (hydrochloride or sulfate)/5ml
	tablet, 10mg (sulfate)
Complementary drug	
□pethidine (A) (1a, 4)	injection, 50mg (hydrochloride) in 1-ml ampoule
	tablet, 50mg, 100mg (hydrochloride)
3. Antiallergics and drugs used in anaphylaxis	
□chlorphenamine	tablet, 4mg (hydrogen maleate)
	injection, 10mg (hydrogen maleate) in 1-ml ampoule
□dexamethasone	tablet, 500µg, 4mg
	injection, 4mg (as sodium phosphate) in 1-ml ampoule
epinephrine	injection, 1mg (as hydrochloride or hydrogen tartrate) in 1-ml ampoule

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
3. Antiallergics and drugs used in anaphylaxis *(continued)*	
hydrocortisone	powder for injection, 100mg (as sodium succinate) in vial
□prednisolone	tablet, 5mg
4. Antidotes and other substances used in poisonings	
4.1 ***Non-specific***	
□charcoal, activated	powder
ipecacuanha	syrup, containing 0.14% ipecacuanha alkaloids calculated as emetine
4.2 ***Specific***	
atropine	injection, 1mg (sulfate) in 1-ml ampoule
deferoxamine	powder for injection, 500mg (mesilate) in vial
dimercaprol (2)	injection in oil, 50mg/ml in 2-ml ampoule
□DL-methionine	tablet, 250mg
methylthioninium chloride (methylene blue)	injection, 10mg/ml in 10-ml ampoule
naloxone	injection, 400µg (hydrochloride) in 1-ml ampoule
penicillamine (2)	capsule or tablet, 250mg
potassium ferric hexacyanoferrate(II)·$2H_2O$ (Prussian blue)	powder for oral administration
sodium calcium edetate (2)	injection, 200mg/ml in 5-ml ampoule
sodium nitrite	injection, 30mg/ml in 10-ml ampoule
sodium thiosulfate	injection, 250mg/ml in 50-ml ampoule
5. Anticonvulsants	
carbamazepine (10)	scored tablet, 100mg, 200mg
□diazepam (1b)	injection, 5mg/ml in 2-ml ampoule (intravenous or rectal)

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
5. Anticonvulsants *(continued)*	
ethosuximide	capsule, 250mg
	syrup, 250mg/5ml
magnesium sulfate	injection, 500mg/ml in 2-ml ampoule
phenobarbital (1b)	tablet, 15–100mg
	elixir, 15mg/5ml
phenytoin	capsule or tablet, 25mg, 50mg, 100mg (sodium salt)
	injection, 50mg (sodium salt)/ml in 5-ml vial
valproic acid (7)	enteric coated tablet, 200mg, 500mg (sodium salt)
Complementary drug	
□clonazepam	scored tablet, 500µg
6. Anti-infective drugs	
6.1 *Anthelminthics*	
6.1.1 Intestinal anthelminthics	
albendazole	chewable tablet, 400mg
levamisole (8)	tablet, 50mg, 150mg (as hydrochloride)
□mebendazole	chewable tablet, 100mg, 500mg
niclosamide	chewable tablet, 500mg
praziquantel	tablet, 150mg, 600mg
pyrantel	chewable tablet, 250mg (as embonate)
	oral suspension, 50mg (as embonate)/ml
6.1.2 Antifilarials	
diethylcarbamazine	tablet, 50mg (dihydrogen citrate)
ivermectin	scored tablet, 6mg
Complementary drug	
suramin sodium (B) (2, 7)	powder for injection, 1g in vial

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
6. Anti-infective drugs *(continued)*	
6.1 ***Anthelminthics*** (continued)	
6.1.3 Antischistosomals	
metrifonate	tablet, 100mg
oxamniquine	capsule, 250mg
	syrup, 250mg/5ml
praziquantel	tablet, 600mg
6.2 ***Antibacterials***	
6.2.1 Penicillins	
□amoxicillin (4)	capsule or tablet, 250mg, 500mg (anhydrous)
	powder for oral suspension, 125mg (anhydrous)/5ml
ampicillin (4)	powder for injection, 500mg (as sodium salt) in vial
benzathine benzylpenicillin	powder for injection, 1.44g benzylpenicillin (= 2.4 million IU) in 5-ml vial
benzylpenicillin	powder for injection, 600mg (= 1 million IU), 3g (= 5 million IU) (as sodium or potassium salt) in vial
□cloxacillin	capsule, 500mg (as sodium salt)
	powder for oral solution, 125mg (as sodium salt)/5ml
	powder for injection, 500mg (as sodium salt) in vial
phenoxymethylpenicillin	tablet, 250mg (as potassium salt)
	powder for oral suspension, 250mg (as potassium salt)/5ml
procaine benzylpenicillin	powder for injection, 1g (= 1 million IU), 3g (= 3 million IU)

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
6. Anti-infective drugs *(continued)*	
6.2 *Antibacterials* (continued)	
6.2.2 Other antibacterials	
□chloramphenicol (7)	capsule, 250mg
	oral suspension, 150mg (as palmitate)/5ml
	powder for injection, 1g (as sodium succinate) in vial
□ciprofloxacin	tablet, 250mg (as hydrochloride)
□doxycycline (5, 6)	capsule or tablet, 100mg (as hyclate)
□erythromycin	capsule or tablet, 250mg (as stearate or ethyl succinate)
	powder for oral suspension, 125mg (as stearate or ethyl succinate)
	powder for injection, 500mg (as lactobionate) in vial
□gentamicin (2, 4, 7)	injection, 10mg, 40mg (as sulfate)/ml in 2-ml vial
□metronidazole	tablet, 200–500mg
	injection, 500mg in 100-ml vial
	suppository, 500mg, 1g
	oral suspension, 200mg (as benzoate)/5ml
nalidixic acid (8)	tablet, 250mg, 500mg
nitrofurantoin (4, 7, 8)	tablet, 100mg
spectinomycin (8)	powder for injection, 2g (as hydrochloride) in vial
□sulfadimidine (4)	tablet, 500mg
	oral suspension, 500mg/5ml
	injection, 1g (sodium salt) in 3-ml ampoule

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
6. Anti-infective drugs *(continued)*	
6.2 ***Antibacterials*** (continued)	
6.2.2 Other antibacterials (continued)	
□sulfamethoxazole + trimethoprim (4)	tablet, 100mg + 20mg, 400mg + 80mg
	oral suspension, 200mg + 40mg/5ml
trimethoprim (8)	tablet, 100mg, 200mg
Complementary drugs	
chloramphenicol (C)	oily suspension, 0.5g (as sodium succinate)/ml in 2-ml ampoule
clindamycin (B)	injection, 150mg (as phosphate)/ml
Restricted indications	
ceftazidime	powder for injection, 250mg (as pentahydrate) in vial
ceftriaxone	powder for injection, 250mg (as sodium salt) in vial
vancomycin	powder for injection, 250mg (as hydrochloride) in vial
6.2.3 Antileprosy drugs	
clofazimine	capsule, 50mg, 100mg
dapsone	tablet, 50mg, 100mg
rifampicin	capsule or tablet, 150mg, 300mg
6.2.4 Antituberculosis drugs	
ethambutol (4)	tablet, 100–400mg (hydrochloride)
isoniazid	tablet, 100–300mg
isoniazid + ethambutol	tablet, 150mg + 400mg
pyrazinamide	tablet, 400mg
rifampicin	capsule or tablet, 150mg, 300mg
rifampicin + isoniazid	tablet, 150mg + 75mg, 300mg + 150mg, 150mg + 150mg[b]

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

[b] For intermittent use three times weekly

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
6. Anti-infective drugs *(continued)*	
6.2 *Antibacterials* (continued)	
6.2.4 Antituberculosis drugs (continued)	
rifampicin + isoniazid + pyrazinamide	tablet, 150mg + 75mg + 400mg, 150mg + 150mg + 500mg[b]
streptomycin (4)	powder for injection, 1g (as sulfate) in vial
Complementary drug	
thioacetazone + isoniazid (A) (7)	tablet, 50mg + 100mg, 150mg + 300mg
6.3 *Antifungal drugs*	
amphotericin B (4)	powder for injection, 50mg in vial
griseofulvin (7)	capsule or tablet, 125mg, 250mg
□ ketoconazole (2)	tablet, 200mg
	oral suspension, 100mg/5ml
nystatin	tablet, 100000IU, 500000IU
	lozenge, 100000IU
	pessary, 100000IU
Complementary drugs	
flucytosine (B) (4, 8)	capsule, 250mg
	infusion, 2.5g in 250ml
potassium iodide (A)	saturated solution
6.4 *Antiprotozoal drugs*	
6.4.1 Antiamoebic and antigiardiasis drugs	
□ diloxanide	tablet, 500mg (furoate)
□ metronidazole	tablet, 200–500mg
	injection, 500mg in 100-ml vial
	oral suspension, 200mg (as benzoate)/5ml

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

[b] For intermittent use three times weekly.

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
6. Anti-infective drugs *(continued)*	
6.4 ***Antiprotozoal drugs*** (continued)	
6.4.2 Antileishmaniasis drugs	
□meglumine antimoniate	injection, 30%, equivalent to approx. 8.5% antimony, in 5-ml ampoule
pentamidine (5)	powder for injection, 200mg (isetionate) in vial
Complementary drug	
amphotericin B (4) (B)	powder for injection, 50mg in vial
6.4.3 Antimalarial drugs	
(a) For curative treatment	
□chloroquine	tablet, 100mg, 150mg (as phosphate or sulfate)
	syrup, 50mg (as phosphate or sulfate)/5ml
	injection, 40mg (as hydrochloride, phosphate or sulfate)/ml in 5-ml ampoule
primaquine	tablet, 7.5mg, 15mg (as diphosphate)
□quinine	tablet, 300mg (as bisulfate or sulfate)
	injection, 300mg (as dihydrochloride)/ml in 2-ml ampoule
Complementary drugs	
□doxycycline (B)[b]	capsule or tablet, 100mg (hyclate)
mefloquine (B)	tablet, 250mg (as hydrochloride)
□sulfadoxine + pyrimethamine (B)	tablet, 500mg + 25mg
Restricted indications	
artemether	injection, 80mg/ml in 1-ml ampoule

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

[b] For use only in combination with quinine.

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
6. Anti-infective drugs *(continued)*	
6.4 *Antiprotozoal drugs* (continued)	
6.4.3 Antimalarial drugs (continued)	
(b) For prophylaxis	
chloroquine	tablet, 150mg (as phosphate or sulfate)
	syrup, 50mg (as phosphate or sulfate)/5ml
mefloquine	tablet, 250mg (as hydrochloride)
proguanil[b]	tablet, 100mg (hydrochloride)
6.4.4 Antitrypanosomal drugs	
(a) African trypanosomiasis	
melarsoprol (5)	injection, 3.6% solution
pentamidine (5)	powder for injection, 200mg (isetionate) in vial
suramin sodium	powder for injection, 1g in vial
Complementary drug	
eflornithine (C)	injection, 200mg (hydrochloride)/ml in 100-ml bottles
(b) American trypanosomiasis	
benznidazole (7)	tablet, 100mg
nifurtimox (2, 8)	tablet, 30mg, 120mg, 250mg
6.5 *Insect repellents*	
diethyltoluamide	topical solution, 50%, 75%
7. Antimigraine drugs	
7.1 *For treatment of acute attack*	
acetylsalicylic acid	tablet, 300–500mg
ergotamine (1c, 7)	tablet, 1mg (tartrate)
paracetamol	tablet, 300–500mg

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

[b] For use only in combination with chloroquine.

Drug	*Route of administration, dosage forms and strengths*[a]
7. Antimigraine drugs *(continued)*	
7.2 ***For prophylaxis***	
□propranolol	tablet, 20mg, 40mg (hydrochloride)
8. Antineoplastic and immunosuppressant drugs and drugs used in palliative care	
8.1 ***Immunosuppressant drugs***	
□azathioprine (2)	tablet, 50mg
	powder for injection, 100mg (as sodium salt) in vial
ciclosporin (2)[b]	capsule, 25mg
	concentrate for injection, 50mg/ml in 1-ml ampoule
8.2 ***Cytotoxic drugs***	
asparaginase (2)	powder for injection, 10000IU in vial
bleomycin (2)	powder for injection, 15mg (as sulfate) in vial
calcium folinate (2)	tablet, 15mg
	injection, 3mg/ml in 10-ml ampoule
chlormethine (2)	powder for injection, 10mg (hydrochloride) in vial
cisplatin (2)	powder for injection, 10mg, 50mg in vial
cyclophosphamide (2)	tablet, 25mg
	powder for injection, 500mg in vial
cytarabine (2)	powder for injection, 100mg in vial
dacarbazine (2)	powder for injection, 100mg in vial
dactinomycin (2)	powder for injection, 500µg in vial
□doxorubicin (2)	powder for injection, 10mg, 50mg (hydrochloride) in vial
etoposide (2)	capsule, 100mg
	injection, 20mg/ml in 5-ml ampoule

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

[b] For organ transplantation.

□ Example of a therapeutic group

Drug	*Route of administration, dosage forms and strengths*[a]
8. Antineoplastic and immunosuppressant drugs and drugs used in palliative care *(continued)*	
8.2 *Cytotoxic drugs* (continued)	
fluorouracil (2)	injection, 50mg/ml in 5-ml ampoule
levamisole (2)	tablet, 50mg (as hydrochloride)
mercaptopurine (2)	tablet, 50mg
methotrexate (2)	tablet, 2.5mg (as sodium salt)
	powder for injection, 50mg (as sodium salt) in vial
procarbazine	capsule, 50mg (as hydrochloride)
vinblastine (2)	powder for injection, 10mg (sulfate) in vial
vincristine (2)	powder for injection, 1mg, 5mg (sulfate) in vial
8.3 *Hormones and antihormones*	
□prednisolone	tablet, 5mg
	powder for injection, 20mg, 25mg (as sodium phosphate or sodium succinate) in vial
tamoxifen	tablet, 10mg, 20mg (as citrate)
8.4 *Drugs used in palliative care*	
The Committee recommended that all the drugs mentioned in the WHO publication *Cancer pain relief: with a guide to opioid availability*, second ed. (*52*) be considered essential. The drugs are included in the relevant sections of the model list, according to their therapeutic use, e.g. analgesics.	
9. Antiparkinsonism drugs	
□biperiden	tablet, 2mg (hydrochloride)
	injection, 5mg (lactate) in 1-ml ampoule
levodopa + □carbidopa (5, 6)	tablet, 100mg + 10mg, 250mg + 25mg

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
10. Drugs affecting the blood	
10.1 *Antianaemia drugs*	
ferrous salt	tablet, equivalent to 60mg iron
	oral solution, equivalent to 25mg iron (as sulfate)/ml
ferrous salt + folic acid[b]	tablet, 60mg + 250µg
folic acid (2)	tablet, 1mg, 5mg
	injection, 1mg (as sodium salt) in 1-ml ampoule
hydroxocobalamin (2)	injection, 1mg in 1-ml ampoule
Complementary drug	
□iron dextran (B) (5)	injection, equivalent to 50mg iron/ml in 2-ml ampoule
10.2 *Drugs affecting coagulation*	
desmopressin (8)	injection 4µg (acetate)/ml in 1-ml ampoule
	nasal spray, 10µg (acetate)/metered dose
heparin sodium	injection, 1000IU/ml, 5000IU/ml, 20000IU/ml in 1-ml ampoule
phytomenadione	injection, 10mg/ml in 5-ml ampoule
	tablet, 10mg
protamine sulfate	injection, 10mg/ml in 5-ml ampoule
□warfarin (2, 6)	tablet, 1mg, 2mg, 5mg (sodium salt)
11. Blood products and plasma substitutes	
11.1 *Plasma substitutes*	
□dextran 70	injectable solution, 6%
□polygeline	injectable solution, 3.5%

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

[b] Nutritional supplement for use during pregnancy.

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
11. Blood products and plasma substitutes *(continued)*	
11.2 *Plasma fractions for specific uses*[b]	
□albumin, human (2, 8)	injectable solution, 5%, 25%
Complementary drugs	
□factor VIII concentrate (C) (2, 8)	dried
□factor IX complex (coagulation factors II, VII, IX, X) concentrate (C) (2, 8)	dried
12. Cardiovascular drugs	
12.1 *Antianginal drugs*	
□atenolol	tablet, 50mg, 100mg
glyceryl trinitrate	tablet (sublingual), 500μg
□isosorbide dinitrate	tablet (sublingual), 5mg
□verapamil (10)	tablet, 40mg, 80mg (hydrochloride)
12.2 *Antidysrhythmic drugs*	
□atenolol	tablet, 50mg, 100mg
lidocaine	injection, 20mg (hydrochloride)/ml in 5-ml ampoule
verapamil (8, 10)	tablet, 40mg, 80mg (hydrochloride)
	injection, 2.5mg (hydrochloride)/ml in 2-ml ampoule
Complementary drugs	
isoprenaline (C)	injection, 1mg (hydrochloride)/ml
□procainamide (B)	tablet, 250mg, 500mg (hydrochloride)
	injection, 100mg (hydrochloride)/ml in 10-ml ampoule
□quinidine (A) (7)	tablet, 200mg (sulfate)

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

[b] All plasma fractions should comply with the Requirements for the Collection, Processing and Quality Control of Blood, Blood Components and Plasma Derivatives (Revised 1992). *WHO Expert Committee on Biological Standardization. Forty-third report* (WHO Technical Report Series, No. 840, 1994, Annex 2).

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
12. Cardiovascular drugs *(continued)*	
12.3 ***Antihypertensive drugs***	
□atenolol	tablet, 50mg, 100mg
□captopril	scored tablet, 25mg
□hydralazine	tablet, 25mg, 50mg (hydrochloride)
	powder for injection, 20mg (hydrochloride) in ampoule
□hydrochlorothiazide	scored tablet, 25mg
□nifedipine (10)	capsule or tablet, 10mg
Complementary drugs	
doxazosin (B)	tablet, 1mg, 2mg, 4mg (mesilate)
methyldopa (B) (7)	tablet, 250mg
□reserpine (A)	tablet, 100µg, 250µg
	injection, 1mg in 1-ml ampoule
□sodium nitroprusside (C) (2, 8)	powder for infusion, 50mg in ampoule
12.4 ***Cardiac glycosides***	
digoxin (4)	tablet, 62.5µg, 250µg
	oral solution, 50µg/ml
	injection, 250µg/ml in 2-ml ampoule
Complementary drug	
digitoxin (B) (6)	tablet, 50µg, 100µg
	injection, 200µg in 1-ml ampoule
12.5 ***Drugs used in vascular shock***	
dopamine	injection, 40mg (hydrochloride)/ml in 5-ml vial
12.6 ***Antithrombotic drugs***	
acetylsalicylic acid	tablet, 100mg
Complementary drug	
streptokinase (C)	powder for injection, 100000IU, 750000IU in vial

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

' Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
13. Dermatological drugs (topical)	
13.1 *Antifungal drugs*	
benzoic acid + salicylic acid	ointment or cream, 6% + 3%
□miconazole	ointment or cream, 2% (nitrate)
sodium thiosulfate	solution, 15%
Complementary drug	
selenium sulfide (C)	detergent-based suspension, 2%
13.2 *Anti-infective drugs*	
□methylrosanilinium chloride (gentian violet)	aqueous solution, 0.5% tincture, 0.5%
neomycin (7)	ointment, 5mg neomycin sulfate
neomycin + □bacitracin (7)	ointment, 5mg neomycin sulfate + 500IU bacitracin zinc/g
potassium permanganate	aqueous solution, 1:10000
silver sulfadiazine	cream, 1%, in 500-g container
13.3 *Anti-inflammatory and antipruritic drugs*	
□betamethasone (3)	ointment or cream, 0.1% (as valerate)
□calamine lotion	lotion
□hydrocortisone	ointment or cream, 1% (acetate)
13.4 *Astringent drugs*	
aluminium diacetate	solution, 13% for dilution
13.5 *Keratoplastic and keratolytic agents*	
benzoyl peroxide	lotion or cream, 5%
coal tar	solution, 5%
dithranol	ointment, 0.1–2%
fluorouracil	ointment, 5%
□podophyllum resin (7)	solution, 10–25%
salicylic acid	solution, 5%
urea	ointment or cream, 10%

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
13. Dermatological drugs (topical) *(continued)*	
13.6 *Scabicides and pediculicides*	
benzyl benzoate	lotion, 25%
permethrin	cream, 5%
	lotion, 1%
13.7 *Ultraviolet-blocking agents*	
Complementary drugs	
□benzophenones, sun protection factor 15 (C)	cream, lotion or gel
□zinc oxide (C)	cream or ointment
14. Diagnostic agents	
14.1 *Ophthalmic drugs*	
fluorescein	eye drops, 1% (sodium salt)
□tropicamide	eye drops, 0.5%
14.2 *Radiocontrast media*	
□amidotrizoate	injection, 140–420mg iodine (as sodium or meglumine)/ml in 20-ml ampoule
barium sulfate	aqueous suspension
□iopanoic acid	tablet, 500mg
□propyliodone	oily suspension, 500–600mg/ml in 20-ml ampoule[b]
Complementary drug	
□meglumine iotroxate (C)	solution, 5–8g iodine in 100–250ml
15. Disinfectants and antiseptics	
15.1 *Antiseptics*	
□chlorhexidine	solution, 5% (digluconate) for dilution
hydrogen peroxide	solution, 3%
□polyvidone iodine	solution, 10%

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

[b] For administration only into the bronchial tree.

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
15. Disinfectants and antiseptics *(continued)*	
15.2 *Disinfectants*	
□calcium hypochlorite	powder (70% available chlorine) for solution
glutaral	solution, 2%
□phenolic disinfectants	solution
16. Diuretics	
□amiloride (4, 7, 8)	tablet, 5mg (hydrochloride)
□furosemide	tablet, 40mg
	injection, 10mg/ml in 2-ml ampoule
□hydrochlorothiazide	tablet, 25mg, 50mg
Complementary drugs	
□mannitol (C)	injectable solution, 10%, 20%
spironolactone (C)	tablet, 25mg
17. Gastrointestinal drugs	
17.1 *Antacids and other antiulcer drugs*	
aluminium hydroxide	tablet, 500mg
	oral suspension, 320mg/5ml
□cimetidine	tablet, 200mg
	injection, 200mg in 2-ml ampoule
magnesium hydroxide	oral suspension, equivalent to 550mg magnesium oxide/10ml
17.2 *Antiemetic drugs*	
metoclopramide	tablet, 10mg (as hydrochloride)
	injection, 5mg (as hydrochloride)/ml in 2-ml ampoule
□promethazine	tablet, 10mg, 25mg (hydrochloride)
	elixir or syrup, 5mg (hydrochloride)/5ml
	injection, 25mg (hydrochloride)/ml in 2-ml ampoule

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
17. Gastrointestinal drugs *(continued)*	
17.3 *Antihaemorrhoidal drugs*	
□local anaesthetic, astringent and anti-inflammatory drug	ointment or suppository
17.4 *Anti-inflammatory drugs*	
hydrocortisone	suppository, 25 mg (acetate)
□sulfasalazine (2)	tablet, 500 mg
17.5 *Antispasmodic drugs*	
□atropine	tablet, 1 mg (sulfate)
	injection, 1 mg (sulfate) in 1-ml ampoule
17.6 *Cathartic drugs*	
□senna	tablet, 7.5 mg (sennosides) (or traditional dosage forms)
17.7 *Drugs used in diarrhoea*	
17.7.1 Oral rehydration	
oral rehydration salts (for glucose–electrolyte solution)	powder, 27.9 g/l
Components — *g/litre*: sodium chloride 3.5; trisodium citrate dihydrate[b] 2.9; potassium chloride 1.5; glucose 20.0	
17.7.2 Antidiarrhoeal (symptomatic) drugs	
□codeine (1a)	tablet, 30 mg (phosphate)
18. Hormones, other endocrine drugs and contraceptives	
18.1 *Adrenal hormones and synthetic substitutes*	
□dexamethasone	tablet, 500 µg, 4 mg
	injection, 4 mg (as sodium phosphate) in 1-ml ampoule

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

[b] Trisodium citrate dihydrate may be replaced by sodium hydrogen carbonate (sodium bicarbonate) 2.5 g/l. However, as the stability of this latter formulation is very poor under tropical conditions, it is only recommended when manufactured for immediate use.

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
18. Hormones, other endocrine drugs and contraceptives *(continued)*	
18.1 *Adrenal hormones and synthetic substitutes* (continued)	
hydrocortisone	powder for injection, 100mg (as sodium succinate) in vial
□prednisolone	tablet, 1mg, 5mg
Complementary drug	
fludrocortisone (C)	tablet, 100µg (acetate)
18.2 *Androgens*	
Complementary drug	
testosterone (C) (2)	injection, 200mg (enantate) in 1-ml ampoule
18.3 *Contraceptives*	
18.3.1 Hormonal contraceptives	
□ethinylestradiol + □levonorgestrel	tablet, 30µg + 150µg, 30µg + 250µg
□ethinylestradiol + □norethisterone	tablet, 35µg + 1.0mg
Complementary drugs	
□ethinylestradiol + □levonorgestrel (C)	50µg + 250µg (pack of four)
□levonorgestrel	tablet, 30µg
medroxyprogesterone acetate (B) (7, 8)	depot injection, 150mg/ml in 1-ml vial
norethisterone enantate (B) (7, 8)	oily solution, 200mg/ml in 1-ml ampoule
18.3.2 Intrauterine devices	
copper-containing device	
18.3.3 Barrier methods	
condoms with or without spermicide (nonoxinol)	
diaphragms with spermicide (nonoxinol)	
18.4 *Estrogens*	
□ethinylestradiol	tablet, 10µg, 50µg

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
18. Hormones, other endocrine drugs and contraceptives *(continued)*	
18.5 *Insulins and other antidiabetic agents*	
insulin injection (soluble)	injection, 40 IU/ml in 10-ml vial, 80 IU/ml in 10-ml vial, 100 IU/ml in 10-ml vial
intermediate-acting insulin	injection, 40 IU/ml in 10-ml vial, 80 IU/ml in 10-ml vial, 100 IU/ml in 10-ml vial (as compound insulin zinc suspension or isophane insulin)
□ tolbutamide	tablet, 500 mg
18.6 *Ovulation inducers*	
□ clomifene (2, 8)	tablet, 50 mg (citrate)
18.7 *Progestogens*	
norethisterone	tablet, 5 mg
Complementary drug	
medroxyprogesterone acetate (B)	tablet, 5 mg
18.8 *Thyroid hormones and antithyroid drugs*	
levothyroxine	tablet, 50 µg, 100 µg (sodium salt)
potassium iodide	tablet, 60 mg
□ propylthiouracil	tablet, 50 mg
19. Immunologicals	
19.1 *Diagnostic agents*	
tuberculin,[b] purified protein derivative (PPD)	injection
19.2 *Sera and immunoglobulins*[c]	
anti-D immunoglobulin (human)	injection, 250 µg in single-dose vial
antiscorpion sera	injection

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

[b] All tuberculins should comply with the Requirements for Tuberculins (Revised 1985). *WHO Expert Committee on Biological Standardization. Thirty-sixth report* (WHO Technical Report Series, No. 745, 1987, Annex 1).

[c] All plasma fractions should comply with the Requirements for the Collection, Processing and Quality Control of Blood, Blood Components and Plasma Derivatives (Revised 1992). *WHO Expert Committee on Biological Standardization. Forty-third report* (WHO Technical Report Series, No. 840, 1994, Annex 2).

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
19. Immunologicals *(continued)*	
19.2 *Sera and immunoglobulins*[b] (continued)	
□antitetanus immunoglobulin (human)	injection, 500 IU in vial
antivenom serum	injection
diphtheria antitoxin	injection, 10 000 IU, 20 000 IU in vial
immunoglobulin, human normal (2)	injection (intramuscular)
immunoglobulin, human normal (2, 8)	injection (intravenous)
□rabies immunoglobulin	injection, 150 IU/ml in vial
19.3 *Vaccines*[c]	
19.3.1 For universal immunization	
BCG vaccine (dried)	injection

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

[b] All plasma fractions should comply with the Requirements for the Collection, Processing and Quality Control of Blood, Blood Components and Plasma Derivatives (Revised 1992). *WHO Expert Committee on Biological Standardization. Forty-third report* (WHO Technical Report Series, No. 840, 1994, Annex 2).

[c] All vaccines should comply with the following Requirements for Biological Substances, as published in the reports of the WHO Expert Committee on Biological Standardization. Dried BCG vaccine (Revised 1985) (WHO Technical Report Series, No. 745, 1987) and Amendment 1987 (WHO Technical Report Series, No. 771, 1988); Diphtheria, Tetanus, Pertussis and Combined Vaccines (Revised 1989) (WHO Technical Report Series, No. 800, 1990); Measles, Mumps and Rubella Vaccines and Combined Vaccine (Live) (Revised 1992) (WHO Technical Report Series, No. 840, 1994) and Note (WHO Technical Report Series, No. 848, 1994); Poliomyelitis Vaccine (Oral) (Revised 1989) (WHO Technical Report Series, No. 800, 1990); Poliomyelitis Vaccine (Inactivated) (Revised 1981) (WHO Technical Report Series, No. 673, 1982) and Addendum 1985 (WHO Technical Report Series, No. 745, 1987); Hepatitis B Vaccine Prepared from Plasma (Revised 1994) (WHO Technical Report Series, No. 858, 1995); Influenza Vaccine (Inactivated) (Revised 1990) (WHO Technical Report Series, No. 814, 1991); Meningococcal Polysaccharide Vaccine (WHO Technical Report Series, No. 594, 1976) and Addendum 1980, incorporating Addendum 1976 and Addendum 1977 (WHO Technical Report Series, No. 658, 1981); Rabies Vaccine for Human Use (Revised 1980) (WHO Technical Report Series, No. 658, 1981) and Amendment 1992 (WHO Technical Report Series, No. 840, 1994); Rabies Vaccine (Inactivated) for Human Use Produced in Continuous Cell Lines (Revised 1986) (WHO Technical Report Series, No. 760, 1987) and Amendment 1992 (WHO Technical Report Series, No. 840, 1994); Typhoid Vaccine (Live, Attenuated, Ty 21a, Oral) (WHO Technical Report Series, No. 700, 1984); Vi Polysaccharide Typhoid Vaccine (WHO Technical Report Series, No. 840, 1994); Yellow Fever Vaccine (Revised 1995) (WHO Technical Report Series, in press).

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
19. Immunologicals *(continued)*	
19.3 *Vaccines*[b] (continued)	
19.3.1 For universal immunization (continued)	
diphtheria–pertussis–tetanus vaccine	injection
diphtheria–tetanus vaccine	injection
hepatitis B vaccine	injection
measles–mumps–rubella vaccine	injection
measles vaccine	injection
poliomyelitis vaccine (inactivated)	injection
poliomyelitis vaccine (live attenuated)	oral solution
tetanus vaccine	injection
tetanus–diphtheria (Td) vaccine	injection
19.3.2 For specific groups of individuals	
influenza vaccine	injection
meningococcal vaccine	injection
rabies vaccine (inactivated) (prepared in cell culture)	injection
rubella vaccine	injection
typhoid vaccine	injection
yellow fever vaccine	injection
20. Muscle relaxants (peripherally acting) and cholinesterase inhibitors	
□alcuronium chloride (2)	injection, 5mg/ml in 2-ml ampoule
□neostigmine bromide	tablet, 15mg
	injection, 500µg, 2.5mg (metilsulfate) in 1-ml ampoule

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

[b] See footnote c on page 46.

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
20. Muscle relaxants (peripherally acting) and cholinesterase inhibitors *(continued)*	
pyridostigmine bromide (2, 8)	tablet, 60mg
	injection, 1mg in 1-ml ampoule
suxamethonium chloride (2)	injection, 50mg/ml in 2-ml ampoule
	powder for injection
Complementary drug	
vecuronium bromide (C)	powder for injection, 10mg in vial
21. Ophthalmological preparations	
21.1 *Anti-infective agents*	
□gentamicin	solution (eye drops), 0.3%
□idoxuridine	solution (eye drops), 0.1%
	eye ointment, 0.2%
silver nitrate	solution (eye drops), 1%
□tetracycline	eye ointment, 1% (hydrochloride)
21.2 *Anti-inflammatory agents*	
□prednisolone	solution (eye drops), 0.5%
21.3 *Local anaesthetics*	
□tetracaine	solution (eye drops), 0.5% (hydrochloride)
21.4 *Miotics and antiglaucoma drugs*	
acetazolamide	tablet, 250mg
□pilocarpine	solution (eye drops), 2%, 4% (hydrochloride or nitrate)
□timolol	solution (eye drops), 0.25%, 0.5% (maleate)
21.5 *Mydriatics*	
atropine	solution (eye drops), 0.1%, 0.5%, 1% (sulfate)

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
21. Ophthalmological preparations *(continued)*	
21.5 *Mydriatics* (continued)	
Complementary drug	
epinephrine (A)	solution (eye drops), 2% (as hydrochloride)
22. Oxytocics and antioxytocics	
22.1 *Oxytocics*	
□ergometrine (1c)	tablet, 200µg (hydrogen maleate)
	injection, 200µg (hydrogen maleate) in 1-ml ampoule
oxytocin	injection, 10IU in 1-ml ampoule
22.2 *Antioxytocics*	
□salbutamol (2)	tablet, 4mg (as sulfate)
	injection, 50µg (as sulfate)/ml in 5-ml ampoule
23. Peritoneal dialysis solution	
intraperitoneal dialysis solution (of appropriate composition)	parenteral solution
24. Psychotherapeutic drugs	
24.1 *Drugs used in psychotic disorders*	
□chlorpromazine	tablet, 100mg (hydrochloride)
	syrup, 25mg (hydrochloride)/5ml
	injection, 25mg (hydrochloride)/ml in 2-ml ampoule
□fluphenazine (5)	injection, 25mg (decanoate or enantate) in 1-ml ampoule
□haloperidol	tablet, 2mg, 5mg
	injection, 5mg in 1-ml ampoule

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
24. Psychotherapeutic drugs *(continued)*	
24.2 *Drugs used in mood disorders*	
□amitriptyline	tablet, 25mg (hydrochloride)
lithium carbonate (2, 4)	capsule or tablet, 300mg
24.3 *Drugs used for sedation and in generalized anxiety disorders*	
□diazepam (1b)	scored tablet, 2mg, 5mg
24.4 *Drugs used for obsessive–compulsive disorders and panic attacks*	
clomipramine	capsules, 10mg, 25mg (hydrochloride)
25. Drugs acting on the respiratory tract	
25.1 *Antiasthmatic drugs*	
□aminophylline (2)	injection, 25mg/ml in 10-ml ampoule
□beclometasone	inhalation (aerosol), 50µg (dipropionate) per dose
□epinephrine	injection, 1mg (as hydrochloride or hydrogen tartrate) in 1-ml ampoule
□salbutamol	tablet, 2mg, 4mg (as sulfate)
	inhalation (aerosol), 100µg (as sulfate) per dose
	syrup, 2mg (as sulfate)/5ml
	injection, 50µg (as sulfate)/ml in 5-ml ampoule
	respirator solution for use in nebulizers, 5mg (as sulfate)/ml
theophylline (10)	tablet, 100mg, 200mg
Complementary drug	
□cromoglicic acid (B)	inhalation (aerosol), 20mg (sodium salt) per dose
25.2 *Antitussives*	
□codeine (1a)	tablet, 10mg (phosphate)

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
26. Solutions correcting water, electrolyte and acid–base disturbances	
26.1 *Oral*	
oral rehydration salts (for glucose–electrolyte solution)	for composition see 17.7.1 (p 431)
potassium chloride	powder for solution
26.2 *Parenteral*	
glucose	injectable solution, 5% isotonic, 50% hypertonic
glucose with sodium chloride	injectable solution, 4% glucose, 0.18% sodium chloride (equivalent to Na^+ 30 mmol/l, Cl^- 30 mmol/l)
potassium chloride (2)	11.2% solution in 20-ml ampoule (equivalent to K^+ 1.5 mmol/ml, Cl^- 1.5 mmol/ml)
sodium chloride	injectable solution, 0.9% isotonic (equivalent to Na^+ 154 mmol/l, Cl^- 154 mmol/l)
sodium hydrogen carbonate	injectable solution, 1.4% isotonic (equivalent to Na^+ 167 mmol/l, HCO_3^- 167 mmol/l)
	8.4% solution in 10-ml ampoule (equivalent to Na^+ 1 mol/l, HCO_3^- 1 mol/l)
□ compound solution of sodium lactate	injectable solution
26.3 *Miscellaneous*	
water for injection	2-ml, 5-ml, 10-ml ampoules
27. Vitamins and minerals	
ascorbic acid	tablet, 50 mg
□ ergocalciferol	capsule or tablet, 1.25 mg (50000 IU)
	oral solution, 250 µg/ml (10000 IU/ml)

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

Drug	*Route of administration, dosage forms and strengths*[a]
27. Vitamins and minerals *(continued)*	
iodine	iodized oil, 1ml (480mg iodine), 0.5ml (240mg iodine) in ampoule (oral or injectable), 0.57ml (308mg iodine) in dispenser bottle
	capsule, 200mg
□nicotinamide	tablet, 50mg
pyridoxine	tablet, 25mg (hydrochloride)
□retinol	sugar-coated tablet, 10000 IU (as palmitate) (5.5mg)
	capsule, 200000IU (as palmitate) (110mg)
	oral oily solution, 100000IU/ml in multidose dispenser (as palmitate)
	water-miscible injection, 100000IU (as palmitate) (55mg) in 2-ml ampoule
riboflavin	tablet, 5mg
□sodium fluoride	in any appropriate formulation
thiamine	tablet, 50mg (hydrochloride)
Complementary drug	
calcium gluconate (C) (2, 8)	injection, 100mg/ml in 10-ml ampoule

[a] When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

□ Example of a therapeutic group.

17. Considerations and changes made in revising the model list

Amendments to the individual entries in the list are detailed below. In order to remind readers of recent changes made to the model list, the Committee decided to include those changes made at the previous meeting in 1993.

Section 1. Anaesthetics

1.1 *General anaesthetics and oxygen*

Diazepam injection was deleted from this section at the previous meeting since it is not recommended for anaesthetic procedures of long duration.

1.3 *Preoperative medication and sedation for short-term procedures*

Diazepam, 5-mg tablets, are added for preoperative procedures.

Section 2. Analgesics, antipyretics, nonsteroidal anti-inflammatory drugs and drugs used to treat gout

2.1 *Non-opioids*

Indometacin is deleted from this section since there are many nonsteroidal anti-inflammatory drugs with a similar action. The Committee considered that the square symbol preceding ibuprofen could cover all these agents provided that both the 200-mg and 400-mg tablet forms are included. The Committee recognized that although ibuprofen caused fewer adverse effects than other nonsteroidal anti-inflammatory drugs, it could not be used for the treatment of all rheumatological diseases. The choice of nonsteroidal anti-inflammatory drugs would be a national decision.

2.2 *Opioid analgesics*

A toxic metabolite of pethidine, norpethidine, accumulates during therapy and can cause central nervous system excitation, including myoclonus and seizures. Morphine or alternatives including hydromorphone and levorphanol are preferred when they are available.

The emergency health kit referred to in section 8 (*36*) contains pentazocine as the strong analgesic even though it is considered inferior to morphine by the Committee. The reason given for its inclusion in the kit is the administrative and regulatory difficulties of including an opioid for immediate distribution to sites of emergencies. At its previous meeting, the Committee had rejected a request to add

pentazocine to the model list for this reason, since it would have been endorsing the use of an inferior analgesic for victims of large-scale emergencies or disasters because of regulatory requirements. Rather, the Committee strongly urged that administrative and regulatory requirements be modified to permit the use of the essential drug morphine in emergency health care.

Section 3. Antiallergics and drugs used in anaphylaxis

Chlorphenamine is listed as the prototype for the antihistamine H_1 antagonist class. This class includes drugs with less sedative action than the traditional antihistamines or with different therapeutic potencies. The selection of drugs in this class should be based on the intended therapeutic uses, the adverse reaction profile and the cost.

Section 4. Antidotes and other substances used in poisonings

4.1 *Non-specific*

The name of this subsection is changed.

Section 5. Anticonvulsants

The name of this section is changed to accommodate magnesium sulfate, which is added for the treatment of eclampsia.

The number (10) was added to carbamazepine at the previous meeting since sustained-release preparations hold significant clinical advantage.

A 50-mg tablet of phenytoin was added at the previous meeting to improve dose titration.

Clonazepam is added to the complementary list as an alternative drug for the treatment of myoclonic epilepsy. The square symbol is to accommodate clobazam, for the treatment of refractory epilepsy.

Section 6. Anti-infective drugs

6.1.1 *Intestinal anthelminthics*

Piperazine is deleted from this section since it has a narrow spectrum of activity and the Committee recognizes that there are more effective broad-spectrum anthelminthics available.

For albendazole, the 200-mg tablet is replaced by a 400-mg tablet.

For mebendazole, a 500-mg tablet is added to accommodate single-dose therapy.

Albendazole was transferred to the main list at the previous meeting, since its use as a broad-spectrum anthelminthic is now well estab-

lished. Tiabendazole was deleted from this section on account of its general toxicity.

6.1.2 *Antifilarials*

Suramin sodium was moved to the complementary list with the letter (B) at the previous meeting, since its use in onchocerciasis is limited to curative treatment of individual patients.

6.1.3 *Antischistosomals*

The Committee considered a request to add triclabendazole to the model list, since this drug has been shown to be well tolerated and effective for the treatment of fascioliasis and paragonimiasis. However, the Committee considered it premature to include this drug in the list at this time, since it is not yet registered in any country.

6.2.1 *Penicillins*

The prevalence of penicillin-resistant pneumococci has risen in many areas. However, amoxicillin, ampicillin and benzylpenicillin and its repository formulations are still considered essential for the treatment of respiratory tract infections. Oral amoxicillin is preferred to oral ampicillin except in the treatment of shigellosis, for which the latter drug is still recommended.

Piperacillin is deleted from this section because it is degraded by β-lactamases and other antipseudomonal agents are now included in the list.

The number (5) after benzathine benzylpenicillin was deleted at the previous meeting since the Committee considered that it is open to misinterpretation.

6.2.2 *Other antibacterials*

Ciprofloxacin is transferred to the main list since it is now recognized to be a first-line antimicrobial agent in many infections.

The numbers (2) and (7) after gentamicin are retained in order to discourage its indiscriminate use. Dosage must always be calculated according to the weight and renal clearance of the patient.

Tetracycline is deleted from this section since doxycycline has a more favourable pharmacokinetic profile.

Nalidixic acid, nitrofurantoin and trimethoprim are all transferred to the main list with the number (8) to indicate that they are used in the treatment of acute uncomplicated urinary tract infections. Nalidixic acid is also used in the treatment of resistant shigellosis.

Chloramphenicol oily suspension was added to the complementary list with the letter (C) at the previous meeting. It has been found to be helpful in situations of catastrophic epidemics of meningococcal meningitis when the medical services are overwhelmed by the epidemic. For this reason, this product should be reserved for use in epidemics of meningococcal meningitis when the scale of the epidemic precludes any other form of antibiotic therapy.

The Committee considered information on the difficulties of obtaining accurate information on the susceptibility of *Streptococcus pneumoniae* to sulfamethoxazole + trimethoprim. It was agreed that this remains an essential antibiotic for the treatment of respiratory infections.

β-Lactams

β-Lactam antibiotics are generally used as first-line treatment. However, most of the penicillins included in the model list are labile to many different β-lactamases. These β-lactamases are prevalent in many bacterial species, including staphylococci, enterobacteria, *Haemophilus* spp. and *Neisseria gonorrhoeae*. For this reason, β-lactamase inhibitors are often used in combination with β-lactam antibiotics. However, because of concerns about possible misuse and the cost of these inhibitors, the Committee considered that they should not be included in the model list at this time.

Restricted indications

This new category is now added to the list. It contains ceftriaxone, ceftazidime and vancomycin. The Committee considered that these drugs should be used only if no alternatives are effective.

6.2.4 *Antituberculosis drugs*

The combination products rifampicin + isoniazid + pyrazinamide and isoniazid + ethambutol are added to the list since they improve patient compliance and there are fewer problems with prescription errors compared with when these drugs are given separately. They also facilitate case management by health staff.

For rifampicin + isoniazid, the 150-mg + 100-mg tablet is replaced by a 150-mg + 75-mg tablet. A 150-mg + 150-mg tablet is added for intermittent use three times weekly.

It is essential that all combination tablets containing rifampicin are shown to have adequate bioavailability.

For pyrazinamide, the 500-mg tablet is replaced by a 400-mg tablet.

The frequency of severe adverse reactions to thioacetazone appears to be much higher in tuberculosis patients who are infected with HIV than in those who are HIV-negative. Because of the high frequency of these adverse reactions, the combination tablets containing thioacetazone remain in the complementary list with the letter (A) and the number (7), to be used when the drugs in the main list are unavailable.

6.3 *Antifungal drugs*

The number (7) was added to griseofulvin at the previous meeting in view of its adverse reaction profile.

Potassium iodide is added to the complementary list since it is a low-cost, highly effective agent for the treatment of sporotrichosis.

6.4.1 *Antiamoebic and antigiardiasis drugs*

Chloroquine is deleted from the complementary list since the Committee considers that treatment with metronidazole is adequate.

6.4.2 *Antileishmaniasis drugs*

Amphotericin B is added to the complementary list with the letter (B) for the treatment of leishmaniasis resistant to the pentavalent antimonials, which is becoming a major problem in some countries.

6.4.3 *Antimalarial drugs*

(a) For curative treatment

The square symbol preceding chloroquine is retained solely to accommodate hydroxychloroquine. A 100-mg tablet was added at the previous meeting. Chloroquine injection, 40-mg base (as hydrochloride, phosphate or sulfate)/ml in 5-ml ampoules, was also added since parenteral chloroquine is recommended for the treatment of severe and complicated falciparum malaria where the organism remains fully sensitive to chloroquine.

Tetracycline in the complementary list is replaced by doxycycline since the Committee considers that this drug has a more favourable pharmacokinetic profile. The footnote stating that it should be used only in combination with quinine is retained.

Restricted indications

This new category contains injectable artemether which should be used only in areas with quinine resistance.

(b) For prophylaxis

Mefloquine was transferred to the main list at the previous meeting since it is increasingly being used in prophylaxis.

Proguanil should be used only in combination with chloroquine.

It should be noted that no antimalarial drug can guarantee 100% protection. Prophylaxis should be restricted to pregnant women, non-immune visitors to endemic areas, and special groups such as labour teams and military personnel living in closed communities.

Section 7. Antimigraine drugs

7.1 *For treatment of acute attack*

For ergotamine, the 2-mg tablet was replaced by a 1-mg tablet at the previous meeting.

7.2 *For prophylaxis*

For propranolol, a 40-mg tablet was added and the 10-mg tablet deleted at the previous meeting.

Section 8. Antineoplastic and immunosuppressant drugs and drugs used in palliative care

8.2 *Cytotoxic drugs*

Chlormethine (mustine or mechlorethamine hydrochloride), levamisole and asparaginase were added for the treatment of various cancers at the previous meeting (see "Essential drugs for cancer chemotherapy", *53*).

Calcium folinate was moved from the complementary list and the footnote was deleted since this drug is used as adjunctive therapy in cancer of the colon.

8.3 *Hormones and antihormones*

Dexamethasone was deleted from this section at the previous meeting since the Committee considered that the square symbol preceding prednisolone is sufficient. Ethinylestradiol was deleted from this section since it is not recommended as first-line treatment in prostate cancer.

Section 10. Drugs affecting the blood

10.2 *Drugs affecting coagulation*

A nasal formulation of desmopressin was added to the list at the previous meeting since it is available in some countries.

Section 11. Blood products and plasma substitutes

11.2 *Plasma fractions for specific uses*

A square symbol was added to albumin at the previous meeting to accommodate plasma and cryoprecipitate-poor plasma.

Section 12. Cardiovascular drugs

12.1 *Antianginal drugs*

Atenolol is transferred to the main list since it acts specifically on the heart and is longer acting and better tolerated than propranolol, which is deleted.

Nifedipine capsules or tablets, 10mg, were replaced by verapamil tablets, 40mg and 80mg, at the previous meeting since the Committee considered this drug to be the calcium-channel blocker of choice. The number (10) was added because sustained-release preparations hold significant clinical advantage.

12.2 *Antidysrhythmic drugs*

Atenolol is transferred to the main list since it acts specifically on the heart and is longer acting and better tolerated than propranolol, which is deleted.

Isoprenaline injection, 1mg/ml, was added at the previous meeting as a complementary drug with the letter (C) for the emergency treatment of severe bradycardia.

The number (7) was added to quinidine in view of its adverse reaction profile.

The number (10) was added to verapamil because sustained-release preparations hold significant clinical advantage.

12.3 *Antihypertensive drugs*

Captopril is transferred to the main list since acetyl cholinesterase inhibitors are now recommended as part of the first-line treatment of hypertension.

Atenolol is transferred to the main list since it acts specifically on the heart and is longer acting and better tolerated than propranolol, which is deleted.

Methyldopa in the complementary list refers to the L-isomer only.

The number (10) was added to nifedipine at the previous meeting because sustained-release preparations hold significant clinical advantage.

Doxazosin is added to the complementary list with the letter (B) for the treatment of hypertension.

12.6 *Antithrombotic drugs*

For streptokinase, a strength of 750000 IU was added at the previous meeting since the standard dose in myocardial infarction is 1.5 million IU.

Lipid-lowering agents

The Committee recognizes the value of lipid-lowering drugs in the treatment of hyperlipidaemia. However, there are many other risk factors for atherosclerosis and its complications, including tobacco smoking and inadequately controlled hypertension. Since most hyperlipidaemias can be controlled by diet, the Committee judged that the current cost/benefit considerations of lipid-lowering drugs do not justify their inclusion in the model list at this time.

Section 13. Dermatological drugs (topical)

13.1 *Antifungal drugs*

Nystatin was deleted as a topical agent at the previous meeting because the other drugs listed are more effective.

13.2 *Anti-infective drugs*

Mupirocin was deleted at the previous meeting because it is expensive and because the other drugs listed are adequate.

Potassium permanganate is added to the main list as it is a very inexpensive anti-infective agent.[1]

Neomycin + bacitracin is retained in the main list. Neomycin is added to the main list. The number (7) is added to both drugs to indicate the high risk of adverse effects.

13.5 *Keratoplastic and keratolytic agents*

Urea is added to the main list as it is a very inexpensive keratolytic agent.[1]

13.6 *Scabicides and pediculicides*

For permethrin, a 5% cream was added at the previous meeting, since this is widely used in the treatment of scabies.

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[1] An older pharmaceutical agent without formal scientific evaluation but considered essential

13.7 *Ultraviolet-blocking agents*

p-Aminobenzoic acid is deleted from this section since other ultraviolet-blocking agents are more effective. The square symbol preceding zinc oxide is retained to accommodate titanium oxide.

Section 15. Disinfectants and antiseptics

15.1 *Antiseptics*

Polyvidone iodine, 10% solution, replaced iodine as the topical antiseptic agent of choice at the previous meeting.

15.2 *Disinfectants*

A phenolic disinfectant with a square symbol is added to this section as an example since this chemical group is the preferred disinfectant for general use.

Section 16. Diuretics

The square symbol preceding mannitol is retained to indicate that sorbitol could serve as an alternative.

Section 17. Gastrointestinal drugs

17.1 *Antacids and other antiulcer drugs*

The Committee recognizes the need to treat *Helicobacter pylori* infection. The drugs already on the list are considered to be adequate.

17.4 *Anti-inflammatory drugs*

A square symbol was added to sulfasalazine at the previous meeting to accommodate mesalazine, for the treatment of patients who are allergic to sulfonamides.

Section 18. Hormones, other endocrine drugs and contraceptives

18.3.1 *Hormonal contraceptives*

Medroxyprogesterone acetate depot injection, 50mg/ml in 3-ml vial, is deleted from the complementary list since a 3-ml injection is not well tolerated.

Levonorgestrel, 30-μg tablets, replaces norethisterone as the progestogen of choice since it is considered safer in mothers who are breast-feeding.

Ethinylestradiol + levonorgestrel, 50μg + 250μg (pack of four), is added to the complementary list with the letter (C) for emergency contraception.

18.4 ***Estrogens***

For ethinylestradiol, a 10-μg tablet is added to improve dose titration.

18.6 ***Ovulation inducers***

Clomifene was transferred to the main list at the previous meeting since it is considered essential if a programme for the treatment of infertility is planned. It is not needed for any other purpose.

18.7 ***Progestogens***

Medroxyprogesterone acetate was added to the complementary list at the previous meeting as an alternative drug for hormone replacement therapy and for the treatment of dysfunctional uterine bleeding.

Section 19. Immunologicals

19.2 ***Sera and immunoglobulins***

Intramuscular and intravenous preparations of immunoglobulin are listed separately since the indications for these two immunoglobulins are different. The numbers (2) and (8) were added to the intravenous preparation and the number (2) to the intramuscular preparation at the previous meeting.

19.3.1 ***For universal immunization***

Hepatitis B vaccine was transferred to the main list at the previous meeting since it is now recommended by WHO as the seventh vaccine for childhood immunization.

Tetanus–diphtheria (Td) vaccine, which contains less diphtheria toxoid than diptheria–tetanus vaccine, is added for use in older children and adults.

19.3.2 ***For specific groups of individuals***

The Committee noted that meningococcal vaccines containing antigens A and C were appropriate for most countries.

Rabies vaccine (inactivated) is now described as "prepared in cell culture".

Section 20. Muscle relaxants (peripherally acting) and cholinesterase inhibitors

Alcuronium chloride with a square symbol replaced gallamine as the prototype muscle relaxant at the previous meeting.

Pyridostigmine bromide was transferred to the main list because of its importance in the treatment of myasthenia gravis.

Section 24. Psychotherapeutic drugs

24.1 *Drugs used in psychotic disorders*

The square symbol preceding chlorpromazine is retained to accommodate any non-depot phenothiazine preparation and that preceding fluphenazine is retained to accommodate any neuroleptic depot preparation.

The square symbol preceding haloperidol is retained to indicate that any non-phenothiazine, non-depot preparation can be used in its place.

24.2 *Drugs used in mood disorders*

The square symbol preceding amitriptyline is retained to accommodate any tricyclic antidepressant.

24.3 *Drugs used for sedation and in generalized anxiety disorders*

The square symbol preceding diazepam is retained to indicate that any long-acting (half-life >12 hours) benzodiazepine can be used in its place.

24.4 *Drugs used in obsessive–compulsive disorders and panic attacks*

Clomipramine was added to this section at the previous meeting in view of its usefulness in the treatment of panic attacks and obsessive–compulsive disorders.

Section 25. Drugs acting on the respiratory tract

Aminophylline tablets, 100mg and 200mg, are replaced by theophylline tablets, 100mg and 200mg, since this drug is the more commonly used oral dosage form. The number (10) is added to theophylline because sustained-release preparations hold significant clinical advantage.

The square symbol preceding beclometasone was added at the previous meeting to accommodate other inhaled corticosteroids and that preceding epinephrine was added to accommodate the use of isoprenaline.

Ephedrine was deleted from the complementary list since it is no longer considered appropriate in the treatment of asthma.

Section 26. Solutions correcting water, electrolyte and acid–base disturbances

26.1 *Oral rehydration*

For potassium chloride, the powder should be dissolved in water to make a 1mmol/ml (74.5mg/ml) solution for dispensing.

Section 27. Vitamins and minerals

Ascorbic acid was transferred to the main list at the previous meeting.

An additional dosage form of iodized oil, 0.57 ml (308 mg iodine) in a dispenser bottle, was added because of its importance in the treatment of children.

Sodium fluoride in any appropriate formulation replaced the specific dosage forms. The number (8) was deleted since these preparations are widely used in dental health care programmes and a square symbol was added to indicate that other formulations for dental prophylaxis are available.

18. Glossary of terms used in the report

In the course of its work, the Expert Committee used certain terms with the meanings given below:

Benefit/risk ratio	The ratio of benefit to risk in the use of a drug; a means of expressing a judgement concerning the role of the drug in the practice of medicine, based on efficacy and safety data along with consideration of misuse potential, severity and prognosis of the disease, etc. The concept may be applied to a single drug or in comparisons between two or more drugs used for the same condition.
Bioavailability	The rate and extent of absorption of a drug from a dosage form as determined by its concentration/time curve in the systemic circulation or by its excretion in urine.
Compliance	Faithful adherence by the patient to the prescriber's instructions.
Dosage form	The form of the completed pharmaceutical product, e.g. tablet, capsule, elixir, suppository.
Drug	Any substance in a pharmaceutical product that is used to modify or explore physiological systems or pathological states for the benefit of the recipient.

Drug formulation	The composition of a dosage form, including the characteristics of its raw materials and the operations required to process it.
Drug utilization	The marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences.
Efficacy	The ability of a drug to produce the purported effect as determined by scientific methods.
Excipient	Any component of a finished dosage form other than the claimed therapeutic ingredient or ingredients.
Pharmaceutical product	Synonymous with dosage form.
Pharmacokinetics	The study of the rate of drug action, particularly with respect to: – the variation of drug concentrations in tissues with time, and – the absorption, distribution, metabolism and excretion of drugs and metabolites.

19. Alphabetical list of essential drugs

Acknowledgement

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Annex 1
Application form for inclusion in the Model List of Essential Drugs[1]

Submitted by:

Name of responsible officer:

Address:

Contact person (if submitted by an organization):

Telephone No.: Fax No.:

We hereby request the World Health Organization to consider the following pharmaceutical product for inclusion in the WHO Model List of Essential Drugs

Signature _____ *Date* _____

Name of drug (INN and trade name):

Dosage form and strength:

Why is this drug being proposed for inclusion in the list?

Please state how it conforms to the criteria for inclusion as an essential drug:

Please provide evidence of efficacy (with references):

If a therapeutic class for this drug already exists in the list, please summarize the advantages of this product:

Describe the drug's pharmacokinetics:

List any contraindications, precautions and toxic effects:

Is this drug available as a generic product?

Please state any restrictions on the use of this drug. Should a note be included in the list regarding its use?

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[1] A summary (maximum 3 pages) of relevant background information should be attached, together with relevant literature to support the therapeutic use.