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The use of essential drugs

Third report of the WHO
Expert Committee

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Geneva, 30 November–4 December 1987

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THE USE OF ESSENTIAL DRUGS

Third report of the WHO Expert Committee

The WHO Expert Committee on the Use of Essential Drugs met in Geneva from 30 November to 4 December 1987. The meeting was opened on behalf of the Director-General by Dr J. Cohen, Adviser on Health Policy, who emphasized that the concept of essential drugs is 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 is, indeed, essential in maintaining the momentum of the revised drug strategy and also as a basic element of the validated information required by the majority of WHO's Member States for optimal rationalization of drug procurement and supply.

The Expert Committee decided to prepare its report as a self-contained document and to incorporate into it parts of the previous report[3] that require no modification or merely bringing up to date. The increasing acceptance of the essential-drugs concept and the action that has been taken at the national and international levels to apply it in practice are reflected in the present report, together with the modifications that have been made to the Model List of Essential Drugs. This fifth list will be found in section 12 of the report, and the explanation of the changes in section 13.

1. INTRODUCTION

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

[1] WHO document WHA39/1986/REC/1, Annex 5, pp. 93–101.

[2] *Handbook of resolutions and decisions of the World Health Assembly and Executive Board, Volume III, 1985–1986.* 1st ed., Geneva, World Health Organization, 1987, p. 22.

[3] WHO Technical Report Series, No. 722, 1985.

[4] WHO Official Records, No. 226, 1975, Annex 13, pp. 96–110.

implemented. Such schemes were intended to extend the accessibility of the most necessary drugs to those 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 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,[1] 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.[2] This was subsequently revised and updated in three further reports.[3, 4, 5]

In undertaking a further review of the list, the present Expert Committee has been 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 and acceptability 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 draws attention to the following guidelines set out in the initial report:

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[1] *Handbook of resolutions and decisions of the World Health Assembly and Executive Board, Volume II, 1973–1984.* Geneva, World Health Organization, 1985, p. 129.

[2] WHO Technical Report Series, No. 615, 1977.

[3] WHO Technical Report Series, No. 641, 1979.

[4] WHO Technical Report Series, No. 685, 1983.

[5] WHO Technical Report Series, No. 722, 1985.

(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 those Member States whose health needs far exceed their resources and which 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 in education, training and information of health personnel in the proper use of the drugs.

(6) Finally, the WHO Action Programme on Essential Drugs should furnish a focus 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.

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 become 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, in an advanced stage of implementation.

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

(1) The establishment of a list of essential drugs, based on the recommendations of a local committee, is the starting-point of the programme. The committees 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.

(2) The international nonproprietary (generic) names for drugs or pharmaceutical substances[1] 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.

(4) Quality, including stability and bioavailability, should be assured through testing or regulation, as discussed in section 7. 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) Local health authorities should decide 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

[1] See *International nonproprietary names (INN) for pharmaceutical substances: cumulative list no. 7,* Geneva, World Health Organization, 1988. Further lists of proposed and recommended INN are issued periodically in *WHO drug information.*

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.

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.

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 approximately 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. 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.

In the great majority of cases 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 provides a proven advantage over single compounds administered separately in the 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 the cost factor 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, exemplified by acetylsalicylic acid and paracetamol, a range of dosage strengths is provided from which suitable 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 most instances, dosage is specified in terms of a selected salt or ester but, in other instances—for example, that of chloroquine—it is calculated, in accordance with common practice, in terms of the active moiety.

5. 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 what is regarded as essential remains a national responsibility.

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.

Such lists have proved to be of particular value in emergency situations. An emergency health kit[1] designed to cover the basic needs of a population of 10 000 for a period of about 3 months, has been jointly developed and evaluated by WHO, the Office of the United Nations High Commissioner for Refugees, and several nongovernmental organizations and is now used by many relief agencies. An updated version will be field-tested in 1988.

6. ESSENTIAL DRUGS AND PRIMARY HEALTH CARE

6.1 Criteria for the selection of drugs for primary health care

It cannot be emphasized too strongly that, in practice, 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 appropriate to other diagnostic skills with acceptable safety, and decisions regarding the availability of specific drugs to community health workers can be made only when all relevant locally operative factors have been taken into account. The following considerations will inevitably influence the compilation of such drug lists.

(1) *Existing systems of medicine.* The establishment of primary health care services in developing countries should not result in

[1] *WHO emergency health kit. Standard drugs and clinic equipment for 10 000 persons for 3 months.* Geneva, World Health Organization, 1984.

abrupt disruption of prevailing cultural patterns in rural communities. The work of traditional healers, for example, should be adapted and supplemented in such a way as to ensure that innovation is successfully integrated into existing systems of care.

(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 manned health post to be one or more days' travelling time from isolated villages in its catchment area.

(3) *Training and supplies*. The numbers of trained personnel, the facilities placed at their disposal, and the supplies entrusted to them determine both the scope and the limitations of the primary health care system. Workers with one or more years' vocational training can obviously accomplish more than personnel reliant upon an intensive course of practical instruction lasting only a few weeks. But, whatever the circumstances, little can be accomplished unless continuity of essential supplies and information is assured.

(4) *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.

7. QUALITY ASSURANCE

Quality assurance of drugs, as embodied in good manufacturing practice and subsequent monitoring of quality through to utilization, is a critical element in any essential drugs programme. All aspects of these procedures have been dealt with *in extenso* in the twenty-sixth to thirtieth reports of the WHO Expert Committee on Specifications for Pharmaceutical Preparations[1, 2, 3, 4, 5] (see also section 10.2.2(8)).

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[1] WHO Technical Report Series, No. 614, 1977.
[2] WHO Technical Report Series, No. 645, 1980.
[3] WHO Technical Report Series, No. 681, 1982.
[4] WHO Technical Report Series, No. 704, 1984.
[5] WHO Technical Report Series, No. 748, 1987.

In accordance with resolution WHA28.65,[1] WHO has set up a Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce, which provides valuable safeguards in relation to imported products, particularly for countries lacking adequate laboratory facilities for drug analyses (see section 10.2.2(7)).

Bioavailability is a specific problem that is of particular importance for products of low solubility or a narrow therapeutic index. In addition, unsatisfactory formulation can result in therapeutic failure due to lack of absorption. This has been discussed in the report of a WHO Scientific Group on the Bioavailability of Drugs[2] and a list should be prepared for the next revision of the Model List of Essential Drugs that identifies the drugs known to have given rise to problems of bioavailability that have clinical relevance.

8. DRUG UTILIZATION SURVEYS

It has become evident that drugs are frequently not used to their full potential or according to generally accepted criteria. Little is known about the clinical consequences of the major differences that exist in prescribing patterns between countries or between regions within individual countries. Drug utilization data are rarely obtained systematically and comprehensively after a drug has been marketed. This information is needed, however, if drug selection committees are to function optimally.

Depending on their purpose and on the facilities available, drug utilization studies can be carried out at various levels. The value of such studies is enhanced by employing 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 both to cost and quantities prescribed, and taking differences in therapeutic practice into consideration. Studies can be designed either to quantify the drug inventory only or to evaluate drug utilization.

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[1] WHO Official Records, No. 226, p. 35 and Annex 12, p. 88. Republished as a supplement to the *WHO Chronicle*, Vol. 31, No. 12, 1977.

[2] WHO Technical Report Series, No. 536, 1974.

The basic objective of drug utilization surveys is to quantify present usage and possible future demands. Data can also be used: (1) to measure the effects of informational and regulatory measures, price policy, etc; (2) to define areas for further investigation on the absolute and relative efficacy and safety of drug therapy; (3) to aid in the determination of benefit/risk and cost-effectiveness; and (4) when properly interpreted, to indicate the overuse, underuse, or misuse of individual drugs or therapeutic classes of drugs.

9. 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.

Pharmaceutical aspects

(1) Development of local or regional quality control facilities in order to ensure the quality of drugs on a continuing basis.

(2) Development of procurement procedures to take advantage of the benefits of purchasing large quantities of drugs.

(3) Development of research facilities to study dosage forms, particularly for vaccines and other heat-sensitive drugs.

(4) Development of facilities for processing simple dosage forms, in preparation for later decisions concerning the possibility of local manufacture of raw materials.

(5) Development of an efficient country-wide distribution system with suitably trained personnel.

(6) Development of packaging of essential drugs to improve product stability and patient compliance.

Clinical aspects

Development of facilities and expertise to carry out therapeutic trials in order to assess:

(*a*) the relative efficacy and safety of new candidate compounds for inclusion in an essential drugs list;

(*b*) the benefits and safety of traditional medicines, including medicinal plants;

(*c*) the effects of genetic and environmental differences among populations on pharmacokinetic, pharmacodynamic, and therapeutic parameters.

Educational aspects

(1) Development of simple, concise labels for each dosage form.

(2) 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.

(3) Development of training programmes in policy formulation, quality control, development of pharmaceutical information systems, procurement, production, storage, and distribution procedures.

10. DRUG INFORMATION AND EDUCATION ACTIVITIES

10.1 National responsibilities

The provision of relevant information about drug therapy and specific pharmaceutical products is vital in every health care setting to ensure satisfactory therapeutic standards and to promote rational prescribing. In every instance the information should be adapted to the needs of the recipient, which may be a national regulatory authority required to assess the product, a pharmacist responsible for its distribution or sale, a doctor or other person involved in health care delivery, or a consumer. In some instances, in addition to clinically relevant information on the properties of the product, data on pharmaceutical aspects and cost will also be required.

Highly evolved drug regulatory authorities, which in their product licensing activities have a responsibility to approve prescribing information, need to be provided with complete and comprehensive technical data about each specific product as a prerequisite to registration. In developing countries, however, adequate manpower and expertise to evaluate such information are often lacking; the decision on whether a product should be made available has then to be taken, in part, in the light of regulatory

decisions and collateral information derived from other countries. The committee or other appointed body responsible for selecting essential drugs should be involved in gathering, analysing, collating, and distributing information on each product. In addition to these product-specific data, more broadly based information needs to be offered within the context of training seminars, articles in medical journals, and newsletters.

The use of any drug without adequate knowledge can be dangerous. As a general rule, no product should be made available for routine use unless it is accompanied by sufficient concisely presented information to enable any potential prescriber to obtain the optimal therapeutic effect and to minimize adverse effects. Both prescriber and consumer must be persuaded that, when therapeutically equivalent, cheaper generic products are as effective as more expensive proprietary name products.

Consumer education is particularly important in relation to products intended for self-medication. Whenever a product is likely to be used unsupervised, it is imperative that adequate information be provided in a form that can be understood by consumers and that, whenever appropriate, clear diagnostic criteria be provided for each indication. Information can be channelled through pamphlets, the mass media and posters. Government support for these educational programmes will be necessary in many instances, not only to ensure their availability but also to minimize bias in their content.

Health care professionals should receive education about the use of drugs not only during their preliminary training, but throughout their entire professional careers. The more-highly trained individuals should assume a responsibility to educate those with less training. In particular, pharmacists should accept every opportunity to inform consumers about the rational use of products at the time they are dispensed.

Drug information sheets

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

(1) International Nonproprietary Name (INN) of each active substance.

(2) Pharmacological data: a brief description of pharmacological effects 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 increased or 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 nonprescription).
  (*h*) Name and address of manufacturer(s) and importer(s).

10.2 The role of WHO

The promulgation of the Model List of Essential Drugs is only one aspect of the support that WHO offers to the implementation of effective national drug policies. National health regulators should be aware of—and, where appropriate, contribute to—the various complementary services that WHO provides to facilitate the work of their authorities.

10.2.1 *The WHO Action Programme on Essential Drugs*

The Action Programme was established in 1981 with the aim of providing practical assistance to countries wishing to establish essential drugs programmes.

One hundred and nine countries have now developed lists of essential drugs and more than 40 countries are making great efforts to implement programmes based on the essential-drugs concept. The priorities and approaches differ from country to country in accordance with each country's socioeconomic situation, but the conceptual basis is the same. The WHO Action Programme on Essential Drugs provides a platform for a harmonized and collective search for suitable and feasible solutions to the problem of the unavailability of the most essential drugs to the majority of the world's population.

The objective of the Programme is thus to ensure for all people the regular supply and rational use of safe and effective drugs of acceptable quality at the lowest possible cost in order to reach the overall objective of Health for All by the Year 2000 through health systems based on primary health care. This objective is accomplished through programmes designed to meet the needs of countries on an individual basis and that emphasize the development and strengthening of national capabilities in the pharmaceutical sector.

The Programme promotes the actions required in and by the Member States of WHO, helps to ensure the availability of the necessary expertise, and cooperates with the countries concerned in applying this expertise. It assists countries in the development of a national drug policy within the context of broader health policies. Consequently, the Programme is collaborating with countries and international organizations in the following components of a national drug policy:

(1) *identifying therapeutic needs* in the community;

(2) *selecting essential drugs* for the different levels of the health care system;

(3) *estimating quantities needed* for the various drugs;

(4) *improving drug supply and management,* including procurement, storage, distribution, and the related training of personnel;

(5) *ensuring the proper use of essential drugs* through the provision of appropriate information and training for prescribers at various levels of expertise;

(6) *providing information and education* for health workers and the general public concerning the proper use of drugs;

(7) *developing financing mechanisms* to ensure the availability and certainty of drug supplies while promoting equity and efficiency in the health care system;

(8) setting up and strengthening *local production* of certain essential drugs whenever this proves to be technically and economically feasible and desirable;

(9) *ensuring quality control* by the means that are the most appropriate for the country concerned;

(10) *introducing appropriate legislation* covering such matters as drug registration; proprietary and generic names; quality assurance; legal authorization of different categories of health workers to prescribe and/or administer various kinds of drugs, including injectables; and price regulation;

(11) *ensuring that manpower requirements are met,* through the development of adequate manpower of all levels and categories to implement national drug policies according to the concept of essential drugs;

(12) *ensuring coordinated multisectoral action* by all other sectors involved, such as education, planning, finance, industry, trade, and communications;

(13) *introducing an evaluation process* to assess the progress of implementation and ultimate effectiveness of the national drug policy.

The Programme, in addition: (*a*) sponsors operational research on issues that will improve programme impact and its efficiency at country level; (*b*) develops and evaluates new methodologies for tackling critical issues related to rational drug availability and use (estimating drug requirements, computer application in procurement and stock control, etc); (*c*) provides up-to-date information on international prices and sources of pharmaceutical supplies; (*d*) facilitates an exchange of experiences between countries on issues connected with the implementation of essential drugs programmes; and (*e*) publishes quarterly in three languages the *Essential drugs monitor,* which contains relevant information from regions and countries on essential drugs issues.

10.2.2 *Other supporting activities*

The constitutional status of WHO as the directing and coordinating authority in international health work confers upon it a unique responsibility to set basic standards for the quality of pharmaceutical products moving in international commerce, to provide model information on their rational and effective use, and to disseminate information on their safety and efficacy.

(1) *Prescribing information on essential drugs.* The Expert Committee takes note of, and commends, the model prescribing information on essential drugs that is being prepared within the WHO Secretariat and urges that the material be maintained in a complete and regularly updated form. It recognizes the need for broad consultation with WHO's expert advisory panels and interested nongovernmental organizations in accomplishing this task, and it is encouraged to know of the broad support that the work is receiving. It acknowledges that, because of the widely differing circumstances under which drugs are used, this information must be adapted to national needs, wherever it is used. It therefore endorses the Secretariat's current policy of supplying this information to national health authorities on the clear understanding that it constitutes source material for countries wishing to produce drug formularies or compendia.

(2) *Exchange of information on regulatory decisions.* Over a period of many years the World Health Assembly has adopted a series of resolutions to promote the development of efficient channels of communication between national authorities concerning the safety and efficacy of drugs moving in international commerce. The basic fields of activity were identified in resolution WHA15.41 adopted in 1962, which, *inter alia,* requested the Director-General to study means of:

—securing regular exchange of information on the safety and efficacy of pharmaceutical preparations; and, in particular,
—securing prompt transmission to national health authorities of new information on serious side-effects of pharmaceutical preparations.

In order to stimulate more effective use of the established channels of communication, and to ensure that they respond adequately to the needs of all Member States, the Director-General invited all national health authorities in 1980 to designate a senior official responsible for technical aspects of drug control to whom

information could be directed. It was understood that this official would also arrange for WHO to be kept informed of any regulatory decisions taken nationally that were of wider relevance and concern.

The Expert Committee notes that, so far, 132 countries have responded to this request. The creation of a network of officials with assigned responsibilities has increased the flow of information to an extent that justifies its collation and distribution to national drug regulatory authorities on a monthly basis. This material also provides the input for updating the section on pharmaceuticals in the United Nations Consolidated List of Products whose Consumption and/or Sale have been Banned, Withdrawn, Severely Restricted or Not Approved by Governments.[1]

(3) *Postmarketing surveillance.* Many drugs are liable, on occasion, to produce serious adverse effects. 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.

Highly evolved national drug regulatory authorities are currently increasing their investment in postmarketing surveillance. This is a cost-intensive activity calling for sustained international collaboration. For many years the WHO Collaborating Centre on International Drug Monitoring has collated the reports generated in the spontaneous monitoring schemes of some 27 industrial countries and, more recently, WHO has collaborated with the Council for International Organizations of Medical Sciences to promote epidemiologically based methods of monitoring.[2,3]

The potential for most developing countries to engage in such activities is limited by cost. Nevertheless, when concern arises over the safety of a drug used exclusively for a tropical disease the need for postmarketing surveillance is as great as in any other situation. Such surveillance may require the establishment of special reporting facilities, and, exceptionally, small follow-up studies of persons exposed to specific drugs may be necessary.

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[1] *Consolidated list of products whose consumption and/or sale have been banned, withdrawn, severely restricted or not approved by governments. Second issue 1986.* New York, United Nations, 1987 (document ST/ESA/192).

[2] *Monitoring and assessment of adverse drug effects, CIOMS working group report,* Geneva, Council for International Organizations of Medical Sciences, 1986.

[3] *International reporting of adverse drug reactions, CIOMS working group report.* Geneva, Council for International Organizations of Medical Sciences, 1987.

(4) *WHO drug information.* Without supporting background information, regulatory decisions taken in one country are open to misinterpretation elsewhere. The Expert Committee commends the Secretariat's initiative in producing the quarterly *WHO drug information* as an official sales publication of the Organization in an attempt to respond to the need for such information, and to bring issues that are of primary concern to drug regulators and pharmaceutical manufacturers to the attention of a wider audience of health professionals and policy-makers concerned with the rational use of drugs.

(5) *The international conferences of drug regulatory authorities.* The first International Conference of Drug Regulatory Authorities, which was jointly sponsored by WHO and the United States Food and Drug Administration, was held in Annapolis, MD, USA in 1980. Subsequent conferences have been convened biennially. The second was held in Rome in 1982, the third in Stockholm in 1984, and the fourth in Tokyo in 1986. An indication of the success of these meetings is provided by the support they command: each has attracted representatives from some 50 countries, the majority being developing countries.

The Expert Committee regards these conferences as a valuable means of intercommunication between national drug regulatory authorities. It strongly recommends that they continue to be held under the auspices of WHO.

(6) *International Nonproprietary Names (INN).* 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 which, since 1950, has published the names of roughly 5000 new products.[1] Its role is to coordinate and harmonize the activities of existing national drug nomenclature commissions, which have come to accept a common set of conventions for devising generic names. Officially assigned generic names now rarely differ from the INNs, and some countries

[1] *International nonproprietary names (INN) for pharmaceutical substances: cumulative list no. 7.* Geneva, World Health Organization, 1988. Further lists of proposed and recommended INN are issued periodically in *WHO drug information.*

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 trademarks. In contrast, trademark applications are disallowed, in accordance with 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 trademark derived from an INN. 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.

The Expert Committee consequently perceives an urgent need:

—for international organizations to discourage the use of trademarks that are derived from INNs;
—for manufacturers to refrain from applying for such trademarks; and
—for drug regulatory authorities to disallow the use of such trademarks.

While INNs are widely used in reference books and publications, 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 preferential use to INNs in reference works, journals, and data banks and to allow the use of a code name for a new substance (pending the assignment of an INN) rather than an unofficial name.

(7) *Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce.* Drugs intended for export are not always subjected to the same control procedures as those produced for the home market. In this case, developing countries lacking adequate laboratory facilities for drug analysis are at a particular disadvantage. To redress this unsatisfactory situation, WHO has sought to extend and unify schemes already operated by the health authorities of some exporting countries under which certificates are issued on request to foreign importers in respect of drugs subjected to statutory control.

The Expert Committee wishes to emphasize, in this connection, the importance of WHO's Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce, which, since 1975, has been available as a vehicle for exchanging information between regulatory authorities in importing and exporting countries.[1] Its purpose is:

(*a*) to provide assurance that a given product has been authorized to be placed on the market in the exporting country, and, if not, to provide information on the reasons why authorization has been withheld;

(*b*) to provide assurance that the plant in which the product is manufactured (*i*) is subject to inspections at suitable intervals and (*ii*) conforms to the requirements for good practices in the manufacture and quality control of drugs, as recommended by WHO;[1]

(*c*) to provide for exchange of information on the implementation of inspections and controls exercised by the authorities in the exporting country. In the case of serious quality defects requests for inquiries may also be made.

The Committee notes that a formal proposal has been prepared to extend the scheme to provide for more comprehensive exchange of information between governments both on the quality of drug substances and on officially approved, product-specific prescribing information concerning the safety and efficacy of finished products.

It also encourages national authorities to issue certificates in precise conformity with the format proposed by WHO in order to ensure that explicit explanations are provided on where the product in question has been manufactured or assembled and on whether or not WHO's standards of good manufacturing practice have been applied. It also urges countries that have not already done so to extend the system of licensing to manufacturers of pharmaceutical products destined exclusively for export. The licensing system should ensure that these manufacturers are subject to inspection, that they comply with internationally recognized requirements for good manufacturing practices, and that every reasonable precaution is taken to ensure that the quality of their products meets the labelled pharmacopoeial specifications.

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[1] WHO Official Records, No. 226, p. 35 and Annex 12, p. 88. Republished as a supplement to the *WHO Chronicle,* Vol. 31, No. 12, 1977.

(8) *Quality control of drugs.* The development of the WHO Model List of Essential Drugs has provided a natural focus for *The international pharmacopoeia.*[1, 2] It has also enhanced its potential value to developing countries. Essential drugs have thus been accorded priority in the third edition of *The international pharmacopoeia;* all quality specifications are supported by classical methods of testing and analysis; and a plan for a small quality-control laboratory has been provided in which the majority of these tests can be performed.[3] Guidelines for its management and operation are also provided. Having regard to the importance of assuring the quality of essential drugs, the Expert Committee commends the institution of such a laboratory and the adoption of *The international pharmacopoeia* by countries currently lacking means to confirm independently the quality of the supplies they procure.

It also welcomes the WHO publication *Basic tests for pharmaceutical substances,*[4] which is meant for use when full laboratory facilities are not available and it is necessary to verify the identity of drug substances or to detect or exclude gross degradation.

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 of those substances that are specified in the Model List of Essential Drugs, together with additional information on their bioavailability, stability, and recommended packaging and storage conditions.

11. UPDATING OF LISTS OF ESSENTIAL DRUGS

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

[1] *The international pharmacopoeia,* third edition, Geneva, World Health Organization, Volume 1, 1979; Volume 2, 1981; Volume 3, 1988.

[2] WHO Technical Report Series, No. 681, 1982.

[3] WHO Technical Report Series, No. 704, 1984.

[4] *Basic tests for pharmaceutical substances,* Geneva, World Health Organization, 1986.

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.

The present Expert Committee introduced changes only where definite advantages were considered to accrue. However, several important modifications have been made, and these are listed in section 13 of this report. Detailed consideration was accorded to specialist opinion canvassed and documented in advance of the meeting, and the members of the Committee reiterated the request of previous committees that, as far as is possible, each section of the list should be reviewed on the basis of specialist advice.

12. MODEL LIST OF ESSENTIAL DRUGS

(Fifth 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 be 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 such as diphenoxylate or loperamide or, when indicated for cough relief, noscapine or 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, systematically active sulfonamide unlikely to cause crystalluria.

[1] The numbers preceding the drug sections and subsections in the model list (e.g. 11; 17.7.2) 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,[1] or (*b*) the Convention on Psychotropic Substances, 1971;[2]
(2) Specific expertise, diagnostic precision, 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 for purpose;
(7) Adverse effects diminish benefit/risk ratio;
(8) Limited indications or narrow spectrum of activity;
(9) For epidural anaesthesia.

Letters in parentheses following 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.
(D) For use only where appropriate facilities for drug surveillance are available.

[1] *Single convention on narcotic drugs, 1961.* New York, United Nations, 1977.
[2] *Convention on psychotropic substances, 1971.* New York, United Nations, 1977.

Main list	Complementary list	Route of administration, dosage forms, and strengths[a]
1. Anaesthetics		
1.1 *General anaesthetics and oxygen*		
ether, anaesthetic (2)		inhalation
diazepam (1b, 2)		injection, 5 mg/ml in 2-ml ampoule
halothane (2)		inhalation
ketamine (2)		injection, 50 mg/ml in 10-ml vial
nitrous oxide (2)		inhalation
oxygen		inhalation (medicinal gas)
□thiopental (2)		powder for injection, 0.5 g, 1.0 g (sodium salt) in ampoule
1.2 *Local anaesthetics*		
□bupivacaine (2, 9)		injection, 0.25%, 0.5% (hydrochloride) in vial
□lidocaine		injection, 1%, 2% (hydrochloride) in vial
		injection, 1%, 2% + epinephrine 1:200 000 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 1:80 000
1.3 *Preoperative medication*		
atropine		injection, 1 mg (sulfate) in 1-ml ampoule
chloral hydrate		syrup, 200 mg/5 ml
□diazepam (1b)		injection, 5 mg/ml in 2-ml ampoule
□morphine (1a)		injection, 10 mg (sulfate or hydrochloride) in 1-ml ampoule
□promethazine		elixir or syrup, 5 mg (hydrochloride)/5 ml
2. Analgesics, Antipyretics, Nonsteroidal Antiinflammatory Drugs, and Drugs Used to Treat Gout		
2.1 *Non-opioids*		
acetylsalicyclic acid		tablet, 100–500 mg
		suppository, 50–150 mg
allopurinol (4)		tablet, 100 mg
□ibuprofen		tablet, 200 mg
□indometacin		capsule or tablet, 25 mg

[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".

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
2. Analgesics, Antipyretics, Nonsteroidal Antiinflammatory Drugs, and Drugs Used to Treat Gout *(continued)*		
2.1 *Non-opioids* (continued)		
paracetamol		tablet, 100–500 mg
		suppository, 100 mg
		syrup, 125 mg/5 ml
	colchicine (C) (7)	tablet, 500 µg
	□probenecid (C)	tablet, 500 mg
2.2 *Opioid analgesics*		
□codeine (1a)		tablet, 30 mg (phosphate)
□morphine (1a)		injection, 10 mg (sulfate or hydrochloride) in 1-ml ampoule
		oral solution, 10 mg/5 ml
		tablet, 10 mg (sulfate)
	□pethidine (A) (1a, 4)	injection, 50 mg (hydrochloride) in 1-ml ampoule
		tablet, 50 mg, 100 mg (hydrochloride)
3. Antiallergics and Drugs Used in Anaphylaxis		
□chlorphenamine		tablet, 4 mg (hydrogen maleate)
		injection, 10 mg (hydrogen maleate) in 1-ml ampoule
□dexamethasone		tablet, 500 µg, 4 mg
		injection, 4 mg (as sodium phosphate) in 1-ml ampoule
epinephrine		injection, 1 mg (as hydrochloride) in 1-ml ampoule
hydrocortisone		powder for injection, 100 mg (as sodium succinate) in vial
□prednisolone		tablet, 5 mg
4. Antidotes and Other Substances Used in Poisonings		
4.1 *General*		
□charcoal, activated		powder
ipecacuanha		syrup, containing 0.14% ipecacuanha alkaloids calculated as emetine
4.2 *Specific*		
atropine		injection, 1 mg (sulfate) in 1-ml ampoule
deferoxamine		powder for injection, 500 mg (mesilate) 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".

Main list	Complementary list	Route of administration, dosage forms, and strengths[a]
4. Antidotes and Other Substances Used in Poisonings *(continued)*		
4.2 *Specific* (continued)		
dimercaprol (2)		injection in oil, 50 mg/ml in 2-ml ampoule
□methionine		tablet, 250 mg (DL)
methylthioninium chloride (methylene blue)		injection, 10 mg/ml in 10-ml ampoule
naloxone		injection 400 µg (hydrochloride) in 1-ml ampoule
penicillamine (2)		capsule or tablet, 250 mg
sodium calcium edetate (2)		injection, 200 mg/ml in 5-ml ampoule
sodium nitrite		injection, 30 mg/ml in 10-ml ampoule
sodium thiosulfate		injection, 250 mg/ml in 50-ml ampoule
5. Antiepileptics		
carbamazepine		scored tablet, 100 mg, 200 mg
□diazepam (1b)		injection, 5 mg/ml in 2-ml ampoule[b]
ethosuximide		capsule or tablet, 250 mg
		syrup, 250 mg/5 ml
phenobarbital (1b)		tablet, 15–100 mg
		elixir, 15 mg/5 ml
phenytoin		capsule or tablet, 25 mg, 100 mg (sodium salt)
		injection, 50 mg (sodium salt)/ml in 5-ml vial
valproic acid (7)		enteric coated tablet, 200 mg, 500 mg (sodium salt)
6. Antiinfective Drugs		
6.1 *Anthelminthic drugs*		
6.1.1 Intestinal anthelminthics		
□mebendazole		chewable tablet, 100 mg
niclosamide		chewable tablet, 500 mg
piperazine		tablet, 500 mg hydrate (as adipate or citrate)
		elixir or syrup (as citrate) equivalent to 500 mg hydrate/5 ml
praziquantel		tablet, 150 mg, 600 mg
pyrantel		chewable tablet, 250 mg (as embonate)
		oral suspension, 50 mg (as embonate)/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".

[b] This solution may be used rectally if sterile preparations are not available.

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
6. Antiinfective Drugs *(continued)*		
6.1 *Anthelminthic drugs* (continued)		
6.1.1 Intestinal anthelminthics (continued)		
tiabendazole		chewable tablet, 500 mg
		lotion, 500 mg/5 ml
	levamisole (B)	tablet, 50 mg, 150 mg
6.1.2 Antifilarials		
diethylcarbamazine		tablet, 50 mg (dihydrogen citrate)
suramin sodium		powder for injection, 1 g in vial
	ivermectin (D)	scored tablet, 6 mg
6.1.3 Antischistosomals		
metrifonate		tablet, 100 mg
oxamniquine		capsule, 250 mg
		syrup, 250 mg/5 ml
praziquantel		tablet, 600 mg
6.2 *Antibacterials*		
6.2.1 Penicillins		
□ampicillin (4)		capsule or tablet, 250 mg, 500 mg (anhydrous)
		powder for oral suspension, 125 mg (anhydrous)/5 ml
		powder for injection, 500 mg (as sodium salt) in vial
benzathine benzylpenicillin (5)		powder for injection, 1.44 g benzylpenicillin (= 2.4 million IU) in 5-ml vial
benzylpenicillin		powder for injection, 600 mg (= 1 million IU), 3 g (= 5 million IU) (as sodium or potassium salt) in vial
□cloxacillin		capsule, 500 mg (as sodium salt)
		powder for oral solution, 125 mg (as sodium salt)/5 ml
		powder for injection, 500 mg (as sodium salt) in vial
phenoxymethylpenicillin		tablet, 250 mg (as potassium salt)
		powder for oral suspension, 250 mg (as potassium salt)/5 ml
□piperacillin		powder for injection, 1 g, 2 g (as sodium salt) in vial
procaine benzylpenicillin		powder for injection, 1 g (= 1 million IU) 3 g (= 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".

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
6. Antiinfective Drugs *(continued)*		
6.2 *Antibacterials* (continued)		
6.2.2 Other antibacterial drugs		
□chloramphenicol (7)		capsule, 250 mg
		oral suspension, 150 mg/5 ml (as palmitate salt)
		powder for injection, 1 g (as sodium succinate) in vial
□erythromycin		tablet or capsule, 250 mg (as stearate or ethyl succinate)
		powder for oral suspension, 125 mg (as stearate or ethyl succinate)
		powder for injection, 500 mg (as lactobionate) in vial
□gentamicin (4)		injection, 10 mg, 40 mg (as sulfate)/ml, in 2-ml vial
□metronidazole		tablet, 200–500 mg
		injection, 500 mg in 100-ml vial
		suppository, 500 mg, 1 g
		oral suspension, 200 mg, (as benzoate)/5 ml
spectinomycin (8)		powder for injection, 2 g (as hydrochloride) in vial
□sulfadimidine (4)		tablet, 500 mg
		oral suspension, 500 mg/5 ml
		injection, 1 g (sodium salt) in 3-ml ampoule
□sulfamethoxazole + trimethoprim (4)		tablet, 100 mg + 20 mg, 400 mg + 80 mg
		oral suspension, 200 mg + 40 mg/5 ml
□tetracycline		capsule or tablet, 250 mg (hydrochloride)
	doxycycline (B) (5, 6)	capsule or tablet, 100 mg (as hyclate)
		injection, 100 mg (as hyclate)/5 ml in ampoule
	nitrofurantoin (B) (4, 7)	tablet, 100 mg
	trimethoprim (B)	tablet, 100 mg, 200 mg
6.2.3 Antileprosy drugs		
clofazimine		capsule, 50 mg, 100 mg
dapsone		tablet, 50 mg, 100 mg
rifampicin		capsule or tablet, 150 mg, 300 mg

[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".

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
6. Antiinfective Drugs *(continued)*		
6.2 *Antibacterials* (continued)		
6.2.4 Antituberculosis drugs		
ethambutol (4)		tablet, 100–500 mg (hydrochloride)[b]
isoniazid		tablet, 100–300 mg
pyrazinamide		tablet, 500 mg
rifampicin		capsule or tablet, 150 mg, 300 mg
streptomycin (4)		powder for injection, 1 g (as sulfate) in vial
thioacetazone + isoniazid		tablet, 50 mg + 100 mg, 150 mg + 300 mg
6.3 *Antifungal drugs*		
amphotericin B (4)		powder for injection, 50 mg in vial
griseofulvin		capsule or tablet, 125 mg, 250 mg
ketoconazole (2, 7)		tablet, 200 mg
		oral suspension, 100 mg/5 ml
nystatin		tablet, 500 000 IU
		pessary, 100 000 IU
	flucytosine (B) (4, 8)	capsule, 250 mg
		infusion, 2.5 g in 250 ml
6.4 *Antiprotozoal drugs*		
6.4.1 Antiamoebic drugs		
□diloxanide		tablet, 500 mg (furoate)
□metronidazole		tablet, 200–500 mg
		injection, 500 mg in 100-ml vial
		oral suspension, 200 mg (as benzoate)/5 ml
	chloroquine (B)	tablet, 150 mg (as phosphate or sulfate)
	dehydroemetine (B) (7)	injection, 60 mg (hydrochloride) in 1-ml ampoule
6.4.2 Antileishmaniasis drugs		
meglumine antimoniate		injection, 30%, equivalent to approx. 8.5% antimony in 5-ml ampoule
pentamidine (5)		powder for injection, 200 mg (as isetionate) in vial
□sodium stibogluconate		injection, 33%, equivalent to 10% antimony, in 30-ml 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".

[b] Two strengths are required for individual dosage adjustment.

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
6. Antiinfective Drugs *(continued)*		
6.4 ***Antiprotozoal drugs*** (continued)		
6.4.3 Antimalarial drugs		
6.4.3(a) For curative treatment		
□chloroquine		tablet, 150 mg (as phosphate or sulfate)
		syrup, 50 mg (as phosphate or sulfate)/5 ml
primaquine		tablet, 7.5 mg, 15 mg (as diphosphate)
□quinine		tablet, 300 mg (as bisulfate or sulfate)
		injection, 300 mg (as dihydrochloride)/ml in 2-ml ampoule
	mefloquine (B)	tablet 250 mg (as hydrochloride)
	□sulfadoxine + pyrimethamine (B)	tablet, 500 mg + 25 mg
	□tetracycline (B)	capsule or tablet, 250 mg (hydrochloride)
6.4.3(b) For prophylaxis		
chloroquine		tablet, 150 mg (as phosphate or sulfate)
		syrup, 50 mg (as phosphate or sulfate)/5 ml
proguanil		tablet, 100 mg (hydrochloride)
6.4.4 Antitrypanosomal drugs		
6.4.4(a) African trypanosomiasis		
melarsoprol (5)		injection, 3.6% solution
pentamidine (5)		powder for injection, 200 mg (as isetionate) in vial)
suramin sodium		powder for injection, 1 g in vial
6.4.4(b) American trypanosomiasis		
benznidazole (7)		tablet 100 mg
nifurtimox (2, 8)		tablet, 30 mg, 120 mg, 250 mg
7. Antimigraine Drugs		
acetylsalicyclic acid		tablet, 300–500 mg
ergotamine (7)		tablet, 2 mg (tartrate)
paracetamol		tablet, 300–500 mg
8. Antineoplastic and Immunosuppressive Drugs		
8.1 ***Immunosuppressive drugs***		
□azathioprine (2)		tablet, 50 mg
		powder for injection, 100 mg (as sodium salt) 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".

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
8. Antineoplastic and Immunosuppressive Drugs *(continued)*		
8.2 ***Cytotoxic drugs***		
bleomycin (2)		powder for injection, 15 mg (as sulfate) in vial
cisplatin (2)		powder for injection, 10 mg, 50 mg in vial
cyclophosphamide (2)		tablet, 25 mg
		powder for injection, 500 mg in vial
cytarabine (2)		powder for injection, 100 mg in vial
dactinomycin (2)		powder for injection, 500 µg in vial
□doxorubicin (2)		powder for injection, 10 mg, 50 mg (hydrochloride) in vial
etoposide (2)		capsule, 100 mg
		injection, 20 mg/ml in 5-ml ampoule
fluorouracil (2)		injection, 50 mg/ml in 5-ml ampoule
mercaptopurine (2)		tablet, 50 mg
methotrexate (2)		tablet, 2.5 mg (as sodium salt)
		injection, 50 mg (as sodium salt) in vial
procarbazine		capsule, 50 mg (as hydrochloride)
vinblastine (2)		powder for injection, 10 mg (sulfate) in vial
vincristine (2)		powder for injection, 1 mg, 5 mg (sulfate) in vial
	calcium folinate (c) (2)[b]	tablet, 15 mg
		injection, 3 mg/ml in 10-ml ampoule
8.3 ***Hormones and antihormones***		
□dexamethasone		tablet, 500 µg, 4 mg
		injection, 4 mg (as sodium phosphate) in 1-ml ampoule
□ethinylestradiol		tablets, 50 µg
□prednisolone		tablet, 5 mg
		injection, 20 mg, 25 mg (as sodium phosphate or sodium succinate) in vial
tamoxifen		tablet, 10 mg, 20 mg (as citrate)
9. Antiparkinsonism Drugs		
□biperiden		tablet, 2 mg (hydrochloride)
		injection, 5 mg (lactate) in 1-ml ampoule
levodopa + □carbidopa (5, 6)		tablet, 100 mg + 10 mg, 250 mg + 25 mg

[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] Drug for "rescue therapy" with methotrexate.

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
10. Blood, Drugs affecting the		
10.1 ***Antianaemia drugs***		
ferrous salt		tablet, equivalent to 60 mg iron
		oral solution, equivalent to 25 mg iron (as sulfate) in 1-ml
ferrous salt + folic acid[b]		tablet, 60 mg + 250 µg
folic acid (2)		tablet, 1 mg
		injection, 1 mg (as sodium salt) in 1-ml ampoule
□hydroxocobalamin (2)		injection, 1 mg in 1-ml ampoule
	□iron dextran (B) (5)	injection, equivalent to 50 mg iron/ml in 2-ml ampoule
10.2 ***Anticoagulants and antagonists***		
heparin		injection, 1000 IU/ml, 5000 IU/ml 20 000 IU/ml in 1-ml ampoule
phytomenadione		injection, 10 mg/ml in 5-ml ampoule
protamine sulfate		injection, 10 mg/ml in 5-ml ampoule
□warfarin (2, 6)		tablet, 1, 2 and 5 mg (sodium salt)
11. Blood Products and Blood Substitutes		
11.1 ***Plasma substitute***		
□dextran 70		injectable solution, 6%
11.2 ***Plasma fractions for specific uses***		
albumin, human (2, 8)		injectable solution, 25% (dried) — All plasma fractions should comply with the WHO Requirements for the Collection, Processing and Quality Control of Human Blood and Blood Products[c]
	factor VIII concentrate (C) (2, 8)	
	factor IX complex (coagulation factors II, VII, IX, X) concentrate (C) (2, 8)	(dried)
12. Cardiovascular Drugs		
12.1 ***Antianginal drugs***		
glyceryl trinitrate		tablet (sublingual), 500 µg
□isosorbide dinitrate		tablet (sublingual), 5 mg
□propranolol		tablet, 10 mg, 40 mg (hydrochloride)
		injection, 1 mg (hydrochloride) in 1-ml ampoule
□nifedipine		capsule or tablet, 10 mg

[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.

[c] Twenty-seventh report of the WHO Expert Committee on Biological Standardization (WHO Technical Report Series, No. 626, 1978, Annex 1).

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
12. Cardiovascular Drugs *(continued)*		
12.2 *Antidysrhythmic drugs*		
lidocaine		injection, 20 mg (hydrochloride)/ml in 5-ml ampoule
□propranolol		tablet, 10 mg, 40 mg (hydrochloride)
		injection, 1 mg (hydrochloride) in 1-ml ampoule
verapamil (8)		tablet, 40 mg, 80 mg (hydrochloride)
		injection, 2.5 mg (hydrochloride)/ml in 2-ml ampoule
	□procainamide (B)	tablet, 250 mg, 500 mg (hydrochloride)
		injection, 100 mg (hydrochloride)/ml in 10-ml ampoule
	□quinidine (A)	tablet, 200 mg (sulfate)
12.3 *Antihypertensive drugs*		
□hydralazine		tablet, 25 mg, 50 mg (hydrochloride)
		powder for injection, 20 mg (hydrochloride) in ampoule
□hydrochlorothiazide		tablet, 25 mg, 50 mg
□nifedipine		capsule or tablet, 10 mg
□propranolol		tablet, 40 mg, 80 mg (hydrochloride)
	methyldopa (B) (7)	tablet, 250 mg
	□reserpine (A)	tablet, 100 µg, 250 µg
		injection, 1 mg in 1-ml ampoule
	□sodium nitroprusside (C) (2, 8)	powder for preparing infusion, 50 mg in ampoule
12.4 *Cardiac glycosides*		
digoxin (4)		tablet, 62.5 µg, 250 µg
		oral solution, 50 µg/ml
		injection, 250 µg/ml in 2-ml ampoule
	digitoxin (B) (6)	tablet, 50 µg, 100 µg
		oral solution, 1 mg/ml
		injection, 200 µg in 1-ml ampoule
12.5 *Drugs used in vascular shock*		
dopamine		injection, 40 mg (hydrochloride)/ml in 5-ml vial
13. Dermatological Drugs		
13.1 *Antifungal drugs*		
benzoic acid + salicylic acid		ointment or cream, 6% + 3%
□miconazole		ointment or cream, 2% (nitrate)
nystatin		ointment or cream, 100 000 IU/g

[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".

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
13. Dermatological Drugs *(continued)*		
13.2 *Antiinfective drugs*		
methylrosanilinium chloride (gentian violet)		aqueous solution, 1% tincture, 1%
□neomycin + □bacitracin		ointment, 5 mg neomycin sulfate + 500 IU bacitracin zinc/g
silver sulfadiazine		cream 1%, in 500-g container
13.3 *Antiinflammatory 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*		
coal tar		solution, topical 20%
dithranol		ointment, 0.1–2%
□podophyllum resin (7)		solution, 10–25%
salicylic acid		solution, topical 5%
13.6 *Scabicides and pediculicides*		
benzyl benzoate		lotion, 25%
lindane (7)		cream, lotion or powder, 1%
14. Diagnostic Agents		
14.1 *Ophthalmic drugs*		
fluorescein		eye drops, 1% (sodium salt)
□tropicamide		eye drops, 0.5%
14.2 *Radiocontrast media*		
□amidotrizoate		injection, 140–420 mg iodine (as sodium or meglumine salts)/ml in 20-ml ampoule
barium sulfate		powder suspended in water
□iopanoic acid		tablet, 500 mg
□propyliodone		water suspension, 500–600 mg/ml in 20-ml ampoule[b]
	□iohexol (c)	injection, 140–350 mg iodine/ml in 5, 10 or 20-ml ampoule
	□iotroxate (c)	solution, 5–8 g iodine (as meglumine) in 100 to 250 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".

[b] This suspension is for administration only into the bronchial tree.

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
15. Disinfectants		
□chlorhexidine		solution, 5% (digluconate) for dilution
□iodine		solution, 2.5%
16. Diuretics		
□amiloride (4, 7, 8)		tablet, 5 mg (hydrochloride)
□furosemide		tablet, 40 mg
		injection, 10 mg/ml in 2-ml ampoule
□hydrochlorothiazide		tablet, 25, 50 mg
	mannitol (c)	injectable solution, 10%, 20%
	spironolactone (c)	tablet, 25 mg
17. Gastrointestinal Drugs		
17.1 *Antacids and other antiulcer drugs*		
aluminium hydroxide		tablet, 500 mg
		oral suspension, 320 mg/5 ml
□cimetidine		tablet, 200 mg
		injection, 200 mg in 2-ml ampoule
magnesium hydroxide		oral suspension, equivalent to 550 mg magnesium oxide/10 ml
sodium citrate		oral solution, 8.82% (0.3 mol/l)
17.2 *Antiemetic drugs*		
metoclopramide		tablet, 10 mg (as hydrochloride)
		injection, 5 mg/ml in 2-ml ampoule
□promethazine		tablet, 10 mg, 25 mg (hydrochloride)
		elixir or syrup, 5 mg (hydrochloride)/5 ml
		injection, 25 mg (hydrochloride)/ml in 2-ml ampoule
17.3 *Antihaemorrhoidal drugs*		
□local anaesthetic, astringent and antiinflammatory drug		ointment or suppository
17.4 *Antiinflammatory drugs*		
hydrocortisone		suppositories, 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)

[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".

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]

17. Gastrointestinal Drugs *(continued)*

17.7 *Diarrhoea, Drugs used in*

17.7.1 For oral rehydration

oral rehydration salts (for glucose-electrolyte solution)		powder, 27.9 g/l
	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)		tabet, 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
hydrocortisone		powder for injection, 100 mg (as sodium succinate) in vial
□prednisolone		tablet, 1 mg, 5 mg
	fludrocortisone (C)	tablet, 100 µg (acetate)

18.2 *Androgens*

	testosterone (C) (2)	injection, 200 mg (enantate) in 1-ml ampoule

18.3 *Contraceptives*

18.3.1 Hormonal contraceptives

□ethinylestradiol + □levonorgestrel		tablet, 30 µg + 150 µg 50 µg + 250 µg
□ethinylestradiol + □norethisterone		tablet, 50 µg + 1.0 mg
	depot medroxy-progesterone acetate (B) (7, 8)	injection, 150 mg/ml in 1-ml, 3-ml vials
	□norethisterone (B)	tablet, 350 µg
	norethisterone enantate (B) (7, 8)	injection, 200 mg in vial

18.3.2 Intrauterine devices

copper-containing device

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[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 bicarbonate (sodium hydrogen carbonate) 2.5 g/l. However, as the stability of the latter formulation is very poor under tropical conditions, it is only recommended when manufactured for immediate use.

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
18. Hormones, Other Endocrine Drugs, and Contraceptives *(continued)*		
18.3 *Contraceptives* (continued)		
18.3.3 Barrier methods		
condoms with or without spermicide (nonoxinol)		
diaphragms with spermicide (nonoxinol)		
18.4 *Estrogens*		
□ethinylestradiol		tablet, 50 µg
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 (c) (2, 8)	tablet, 50 mg (citrate)
18.7 *Progestogens*		
norethisterone		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

[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".

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]	
19. Immunologicals			
19.1 ***Diagnostic agents***			
tuberculin, purified protein derivative (PPD)		injection	
19.2 ***Sera and immunoglobulins***			
anti-D immunoglobulin (human)		injection, 250 µg/ml	All plasma fractions should comply with the WHO Requirements for the Collection, Processing, and Quality Control of Human Blood and Blood Products[b]
antirabies hyperimmune serum		injection, 1000 IU in 5-ml ampoule	
antivenom sera		injection	
antiscorpion sera		injection	
diphtheria antitoxin		injection, 10 000 IU, 20 000 IU, in vial	
immunoglobulin, human normal (2)		injection	
tetanus antitoxin		injection, 50 000 IU, in vial	
tetanus antitoxin (human)		injection, 500 IU 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".

[b] WHO Technical Report Series, No. 626, 1978, Annex 1.

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]	
19. Immunologicals *(continued)*			
19.3 *Vaccines*			
19.3.1 For universal immunization			
BCG vaccine (dried)		injection	All vaccines should comply with the WHO Requirements for Biological Substances[b]
diphtheria-pertussis-tetanus vaccine		injection	
diphtheria-tetanus vaccine		injection	
measles vaccine		injection	
poliomyelitis vaccine (inactivated)		injection	
poliomyelitis vaccine (live attenuated)		oral solution	
tetanus vaccine		injection	
19.3.2 For specific groups of individuals			
hepatitis B vaccine		injection	
influenza vaccine		injection	
meningococcal vaccine		injection	
rabies vaccine		injection	
rubella vaccine		injection	
typhoid vaccine		injection	
yellow fever vaccine		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] Dried BCG Vaccine (Revised 1985) (WHO Technical Report Series, No. 745, 1987); Diphtheria Toxoid, Pertussis Vaccine, Tetanus Toxoid, and Combined Vaccines (Revised 1978) (WHO Technical Report Series, No. 638, 1979), Addendum 1983 (WHO Technical Report Series, No. 700, 1984). Addendum 1984 (WHO Technical Report Series, No. 725, 1985) and Addendum 1986 (WHO Technical Report Series No. 760, 1987); Measles Vaccine (Live) and Measles Vaccine (Inactivated) (WHO Technical Report Series, No. 329, 1966); Poliomyelitis Vaccine (Oral) (Revised 1982) (WHO Technical Report Series, No. 687, 1983) and Addendum 1986 (WHO Technical Report Series No. 760, 1987); 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 Human Plasma (Revised 1984) (WHO Technical Report Series No. 725, 1985); Influenza Vaccine (Inactivated) (Revised 1978) (WHO Technical Report Series, No. 638, 1979); Meningococcal Polysaccharide Vaccine (WHO Technical Report Series, No. 594, 1976), and Addendum 1980, incorporating Addendum 1976 (WHO Technical Report Series, No. 658, 1981); Rabies Vaccine for Human Use (Revised 1980) (WHO Technical Report Series, No. 658, 1981); Rubella Vaccine (Live) (WHO Technical Report Series, No. 610, 1977) and Addendum 1980 (WHO Technical Report Series, No. 658, 1981); Typhoid Vaccine (Live Attenuated, Ty 21a Oral) (WHO Technical Report Series, No. 700, 1984); Yellow Fever Vaccine (Revised 1975) (Who Technical Report Series, No. 594, 1976). [EDITORIAL NOTE: New or revised WHO Requirements or addenda to existing Requirements were adopted shortly after this meeting of the WHO Expert Committee on the Use of Essential Drugs, concerning the following vaccines on the above list: dried BCG vaccine, hepatitis B vaccine prepared from human plasma, measles vaccine (live), poliomyelitis vaccine (oral), and yellow fever vaccine. These will be published in the twenty-eighth report of the WHO Expert Committee on Biological Standardization (WHO Technical Report Series, 1988, in press)].

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
20. Muscle Relaxants (Peripherally Acting) and Cholinesterase Inhibitors		
□gallamine (2)		injection, 40 mg (triethiodide)/ml in 2-ml ampoule
□neostigmine		tablet, 15 mg (bromide)
		injection, 500 µg (metilsulfate) in 1-ml ampoule
suxamethonium (2)		injection, 50 mg (chloride)/ml in 2-ml ampoule
		powder for injection (chloride)
	pyridostigmine (B) (2, 8)	tablet, 60 mg (bromide)
		injection, 1 mg (bromide) in 1-ml ampoule
21. Ophthalmological Preparations		
21.1 ***Antiinfective agents***		
□idoxuridine		solution (eye drops), 0.1%
		eye ointment, 0.2%
silver nitrate		solution (eye drops), 1%
sulfacetamide		eye ointment, 10% (sodium salt)
		solution (eye drops), 10% (sodium salt)
□tetracycline		eye ointment, 1% (hydrochloride)
21.2 ***Antiinflammatory agents***		
□hydrocortisone (2, 7)		eye ointment, 1% (acetate)
21.3 ***Local anaesthetics***		
□tetracaine		solution (eye drops), 0.5% (hydrochloride)
21.4 ***Miotics and antiglaucoma drugs***		
acetazolamide		tablet, 250 mg
□pilocarpine		solution (eye drops), 2%, 4% (hydrochloride or nitrate)
□timolol		solution (eye drops), 0.25%, 0.5% (maleate)
21.5 ***Mydriatics***		
□homatropine		solution (eye drops), 2% (hydrobromide)
	epinephrine (A)	solution (eye drops), 2% (as hydrochloride)

[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".

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
22. Oxytocics and Antioxytocics		
22.1 *Oxytocics*		
□ergometrine		tablet, 200 µg (maleate)
		injection, 200 µg (maleate) in 1-ml ampoule
oxytocin		injection, 10 IU in 1-ml ampoule
22.2 *Antioxytocics*		
□salbutamol		tablet, 4 mg (as sulfate)
		injection, 50 µg (as sulfate)/ml in 5-ml ampoule
23. Peritoneal Dialysis Solution		
intraperitoneal dialysis solution (of appropriate composition)		parenteral solution
24. Psychotherapeutic Drugs		
□amitriptyline		tablet, 25 mg (hydrochloride)
□chlorpromazine		tablet, 100 mg (hydrochloride)
		syrup, 25 mg (hydrochloride)/5 ml
		injection, 25 mg (hydrochloride)/ml in 2-ml ampoule
□diazepam (1b)		scored tablet, 2 mg, 5 mg
□fluphenazine (5)		injection, 25 mg (decanoate or enantate) in 1-ml ampoule
□haloperidol		tablet, 2 mg, 5 mg
		injection, 5 mg in 1-ml ampoule
lithium carbonate (2, 4)		capsule or tablet, 300 mg
25. Respiratory Tract, Drugs acting on the		
25.1 *Antiasthmatic drugs*		
□aminophylline (2)		tablet, 100 mg, 200 mg
		injection, 25 mg/ml in 10-ml ampoule
epinephrine		injection, 1 mg (as hydrochloride) in 1-ml ampoule
□salbutamol		tablet, 2 mg, 4 mg (as sulfate)
		inhalation (aerosol), 100 µg (sulfate) per dose
		syrup, 2 mg (as sulfate)/5 ml
		injection, 50 µg (as sulfate)/ml in 5-ml ampoule
	beclometasone (B)	inhalation (aerosol), 50 µg (dipropionate) per dose

[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".

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
25. Respiratory Tract, Drugs acting on the *(continued)*		
25.1 ***Antiasthmatic drugs*** (continued)		
	□cromoglicic acid (B)	inhalation (cartridge), 20 mg (sodium salt) per dose
	ephedrine (A)	tablet, 30 mg (hydrochloride)
		elixir, 15 mg (hydrochloride)/5 ml
		injection, 50 mg (sulfate) in 1-ml ampoule
25.2 ***Antitussives***		
□codeine (1a)		tablet, 10 mg (phosphate)
26. Solutions Correcting Water, Electrolyte, and Acid-Base Disturbances		
26.1 ***For oral rehydration***		
oral rehydration salts (for glucose-electrolyte solution)		for composition see 17.7.1 (p. 42)
potassium chloride		oral solution
26.2 ***Parenteral***		
□compound solution of sodium lactate		injectable solution
glucose		injectable solution, 5% isotonic, 50% hypertonic
glucose with sodium chloride		injectable solution, 4% glucose, 0.18% sodium chloride (Na^+ 30 mmol, Cl^- 30 mmol/l)
potassium chloride		injectable solution
sodium bicarbonate		injectable solution, 1.4% isotonic (Na^+ 167 mmol/l, HCO_3^- 167 mmol/l)
		8.4% solution in 10-ml ampoule
sodium chloride		injectable solution, 0.9% isotonic (Na^+ 154 mmol/l, Cl^- 154 mmol/l)
26.3 ***Miscellaneous***		
water for injection		in 2-ml, 5-ml, 10-ml ampoules
27. Vitamins and Minerals		
□ergocalciferol		capsule or tablet, 1.25 mg (50 000 IU)
		oral solution, 250 µg/ml (10 000 IU/ml)
□nicotinamide		tablet, 50 mg
pyridoxine		tablet, 25 mg (hydrochloride)

[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".

Main list	*Complementary list*	*Route of administration, dosage forms, and strengths*[a]
27. Vitamins and Minerals *(continued)*		
□retinol		sugar-coated tablet, 10 000 IU (as palmitate) (5.5 mg)
		capsule, 200 000 IU (as palmitate) (110 mg)
		oral oily solution, 100 000 IU/ml in multidose dispenser (as palmitate)
		water-miscible injection, 100 000 IU (as palmitate) (55 mg) in 2-ml ampoule
riboflavin		tablet, 5 mg
sodium fluoride (8)		tablet, 500 µg
thiamine		tablet, 50 mg (hydrochloride)
	ascorbic acid (c)	tablet, 50 mg
	calcium gluconate (c), (2, 8)	injection, 100 mg/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".

13. CHANGES MADE IN REVISING THE MODEL LIST

Amendments to the individual entries in the list are detailed below. Where no other explanation is offered the transfer of a drug from the complementary list to the main list signifies accrued evidence of widespread use and acceptance. For drugs in the complementary list, only a single letter (A, B, C, or D) is now used to indicate the reason for their inclusion.

Section 1. Anaesthetics

1.1 General anaesthetics and oxygen: A square symbol is added to thiopental (2) to accommodate other compounds, notably methohexital.

1.2 Local anaesthetics: For □lidocaine a preparation for spinal anaesthesia and a preparation for local dental anaesthesia are added.

1.3 Preoperative medication: This new subsection is added. It includes atropine, which is also listed in sections 4.2 and 17.5; chloral hydrate, which is added as a premedication for paediatric use; □diazepam (1b), which is also listed in sections 1.1, 5, and 24; □morphine (1a), which is also listed in section 2.2; and □promethazine, which is also listed in section 17.2.

Section 2. Analgesics, Antipyretics, Nonsteroidal Antiinflammatory Drugs and Drugs Used to Treat Gout

2.1 Non-opioids: A square symbol is added to indometacin to accommodate other potent nonsteroidal antiinflammatory drugs. A syrup formulation of paracetamol is added for paediatric use.

2.2 Opioid analgesics: A square symbol is added to codeine (1a) to accommodate alternative drugs. Tablet formulations of pethidine (A) (1a, 4) have been added.

Section 3. Antiallergics and Drugs used in Anaphylaxis

The title of this section is altered to provide for a more rational classification. Hydrocortisone is added as a drug used as an *adjunct* to epinephrine in anaphylactic shock.

Section 4. Antidotes and Other Substances Used in Poisonings

4.1 General: A square symbol is added to activated charcoal to accommodate other adsorbants such as fuller's earth. Magnesium sulfate is deleted on grounds of questionable efficacy in poisonings.

4.2 Specific: □Methionine is added to the main list as a specific antidote to paracetamol.

Section 5. Antiepileptics

Carbamazepine is moved to the main list and a 100-mg scored tablet is added. A footnote is added to □diazepam (1b) regarding rectal use. A syrup formulation of ethosuximide is added for paediatric use. A range of tablet strengths of phenobarbital (1b) is included to provide for appropriate flexibility of dosage in all age groups. Valproic acid (7) is transferred to the main list and enteric coated tablet formulations are specified.

Section 6. Antiinfective Drugs

6.1 Anthelminthics: These are now distributed among 3 subsections to provide for a more rational classification.

6.1.1 Intestinal anthelminthics: A 150-mg tablet of praziquantel is added to provide for appropriate dosage in taeniasis. A lotion of tiabendazole is added for treatment of cutaneous larva migrans. Levamisole is added to the complementary list and qualified by (B) for single-dose treatment of ascariasis.

6.1.2 Antifilarials: Ivermectin is added to the complementary list and qualified by (D) since experience with this product is limited and it has been included exceptionally because of its unique therapeutic potential in onchocerciasis.

6.2.1 Penicillins: For □cloxacillin a powder for oral solution is added. □Piperacillin is added to the main list for the treatment of pseudomonal infections.

6.2.2 Other antibacterial drugs: A square symbol is added to erythromycin to accomodate other macrolide antibiotics. A suspension of □metronidazole is added for paediatric use. A suspension of □sulfamethoxazole + trimethoprim (4) is added

for paediatric use. Sulfasalazine (2)[1] is moved to section 17.4 (*Antiinflammatory Drugs*). Trimethoprim is added to the complementary list and qualified by (*B*) for use in urinary tract infections.

6.2.3 Antileprosy drugs: Ethionamide and protionamide have been deleted from the complementary list on the grounds that they are rarely required as replacements for clofazimine, which is a less toxic drug.

6.3 Antifungal drugs: Ketoconazole (2, 7) is added to the main list for the treatment of some systemic fungal infections.

6.4 Antiprotozoal drugs: The heading of this subsection is altered to provide for a more rational classification.

6.4.1 Antiamoebic drugs: Chloroquine is moved to the complementary list and qualified by (B). □Metronidazole injection is added for treatment of severe amoebiasis and a suspension is added for paediatric use.

6.4.2 Antileishmaniasis drugs: Meglumine antimoniate is added as an alternative first-line treatment for leishmaniasis. Pentamidine mesilate is deleted since this salt is no longer readily available.

6.4.3 Antimalarial drugs: This subsection is now further subdivided into: 6.4.3 (*a*) for curative treatment, and 6.4.3 (*b*) for prophylaxis.

6.4.3(a) For curative treatment: A square symbol is added to quinine to accommodate the use of quinidine when quinine is not available. Mefloquine is added to the complementary list and qualified by (B) for treatment of multiple-drug-resistant falciparum malaria. A square symbol is added to sulfadoxine + pyrimethamine (B) to accommodate combinations containing another sulfonamide, notably sulfalene. □Tetracycline is added to the complementary list and qualified by (B) for adjunctive treatment of severe falciparum malaria. Amodiaquine is deleted from this section since the square symbol before chloroquine adequately covers the use of this drug.

6.4.3(b) For prophylaxis: Chloroquine and proguanil are added for the prophylaxis of malaria.

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[1] Salazosulfapyridine in previous lists; sulfasalazine is now the International Nonproprietary Name.

6.4.4 Antitrypanosomal drugs: This subsection is divided into two further subsections.

6.4.4(a) African trypanosomiasis: Pentamidine mesilate is deleted because this salt is no longer readily available.

6.4.4(b) American trypanosomiasis: Benznidazole (7) is added and nifurtimox (2, 8) is moved to the main list since these are the only drugs useful in the treatment of American trypanosomiasis.

Section 7. Antimigraine Drugs

Acetylsalicylic acid tablets 300–500 mg and paracetamol tablets 300–500 mg are added.

Section 8. Antineoplastic and Immunosuppressive Drugs

8.2 Cytotoxic drugs: Calcium folinate (2) is moved to the complementary list and qualified by (C).

8.3 Hormones and antihormones: □Ethinylestradiol is added since it is widely used in the treatment of prostatic cancer.

Section 9. Antiparkinsonism Drugs

Levodopa is deleted since it is now used most extensively in combination with carbidopa.

Section 10. Blood, Drugs affecting the

10.2 Anticoagulants and antagonists: For □warfarin (2, 6) 1-mg and 2-mg tablets are added to provide for flexibility of dosage.

Section 12. Cardiovascular Drugs

12.1 Antianginal drugs: □Verapamil is deleted and replaced by □nifedipine since the latter has less negative inotropic effect.

12.2 Antidysrhythmic drugs: □Quinidine is moved to the complementary list and qualified by (A). Verapamil (8) is added for the treatment of supraventricular tachycardia. Isoprenaline is deleted since more effective antidysrhythmic drugs are now available.

12.3 Antihypertensive drugs: For □hydralazine a 25-mg tablet is added, as is a powder for injection for the management of hypertensive emergencies. For □hydrochlorothiazide a 25-mg tablet is added. □Nifedipine is added to the main list. Reserpine is moved to the complementary list and qualified by (A). □Sodium nitroprusside (2, 8) is moved to the complementary list and qualified by (C).

12.5 Drugs used in vascular shock: The title of the subsection is changed to provide for a more rational classification. Epinephrine is moved to section 3 as a drug used in anaphylaxis.

Section 13. Dermatological Drugs

13.2 Antiinfective drugs: Silver sulfadiazine is added for the treatment of burns.

13.5 Keratoplastic and keratolytic agents: Dithranol is added for the treatment of psoriasis. Podophyllum resin[1] is qualified by (7) and a square symbol is added to it to accommodate podophyllotoxin.

13.6 Scabicides and pediculicides: Lindane is qualified by (7) and a powder formulation is added.

Section 14. Diagnostic Agents

14.1 Ophthalmic drugs: □Tropicamide is added as a short-acting mydriatic for diagnostic ophthalmic procedures.

14.2 Radiocontrast media: A footnote is added to □propyliodone to ensure correct administration and a range of dosage strengths is included. For iohexol a range of dosage strengths and a 20 ml ampoule is added for flexibility of dosage.

Section 15. Disinfectants

Gentian violet is deleted from the complementary list in this section but is retained in section 13.2.

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[1] Podophylline in previous lists; podophyllum resin is now the International Nonproprietary Name.

Section 16. Diuretics

□Amiloride is qualified by (4, 7, 8). For □hydrochlorothiazide a 25-mg tablet is added to provide flexibility of dosage. Mannitol is moved to the complementary list and qualified by (C). Spironolactone is moved to the complementary list and qualified by (C). Chlortalidone is deleted since the differences between chlortalidone and thiazide diuretics are of minor therapeutic significance.

Section 17. Gastrointestinal Drugs

17.1 Antacids and other antiulcer drugs: Sodium citrate is added for the prevention of acid aspiration pneumonia during operative obstetrics. Calcium carbonate is deleted since it causes greater gastric secretion and acid rebound than other listed antacids.

17.4 Antiinflammatory drugs: This new subsection has been added to accommodate hydrocortisone and sulfasalazine (which is moved from section 6.2.2) for the treatment of inflammatory conditions of the lower bowel.

17.7.1 For oral rehydration: The footnote to oral rehydration salts has been revised to emphasize that the stability of sodium bicarbonate is very poor under tropical conditions.

Section 18. Hormones, Other Endocrine Drugs, and Contraceptives

The title of this section has been altered to provide for a more rational classification.

18.1 Adrenal hormones and synthetic substitutes: A 1-mg tablet of □prednisolone is added to provide flexibility of dosage in adrenal cortical insufficiency.

18.2 Androgens: Testosterone (2) is moved to the complementary list and qualified by (C). The propionate ester is deleted since the enantate has superior pharmacokinetic properties.

18.3.1 Hormonal contraceptives: For depot medroxyprogesterone acetate (7, 8) a 1-ml vial is added to provide flexibility of dosage.

18.3.2 Intrauterine devices; 18.3.3. Barrier methods: these two new subsections have been introduced since it has become important to include a range of contraceptive options including barrier methods.

18.5 Insulins and other antidiabetic agents: 100-IU/ml strengths of soluble insulin and intermediate-acting insulin are added since this is now the standardized concentration being adopted by many countries. Glibenclamide is deleted and replaced by □tolbutamide, which has a shorter half-life and is less prone to cause hypoglycaemia.

Section 19. Immunologicals

19.3.2 For specific groups of individuals: Hepatitis B vaccine and rubella vaccine are included.

Section 20. Muscle Relaxants (Peripherally Acting) and Cholinesterase Inhibitors

A powder formulation for preparing injections of suxamethonium (2) is added since this is more stable than premixed solutions.

Section 21. Ophthalmological Preparations

21.1 Antiinfective agents: □Idoxuridine is added since it is of value as a specific antiviral agent in herpetic keratitis.

Section 22. Oxytocics and Antioxytocics

22.2 Antioxytocics: This new subsection is added to accommodate □salbutamol as an antioxytocic drug.

Section 24. Psychotherapeutic Drugs

For □diazepam (1b) a 2-mg scored tablet is added to provide for flexibility of dosage during maintenance therapy and withdrawal. For □haloperidol a 5-mg tablet is added to provide for flexibility of dosage. Imipramine is deleted since □amitriptyline adequately covers this drug.

Section 25. Respiratory Tract, Drugs acting on the

25.1 Antiasthmatic drugs: For □salbutamol a 2-mg tablet is added to provide for flexibility of dosage. A square symbol is added to

cromoglicic acid (B) to accommodate ketotifen fumarate, which is used in some countries. Ephedrine is moved to the complementary list and qualified by (A).

Section 27. Vitamins and Minerals

Ascorbic acid is moved to the complementary list and qualified by (C) since it is required only for the treatment of scurvy in emergency situations. For □retinol the dosages and formulations are adjusted to provide for prophylaxis and treatment of xerophthalmia in all common clinical situations.

14. 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 indication.
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, —absorption, distribution, metabolism, and excretion of drugs and metabolites.
Therapeutic equivalence	Pharmaceutical products which, when administered to the same individuals in the same regimen, will provide essentially the same efficacy and/or toxicity.

15. ALPHABETICAL LIST OF ESSENTIAL DRUGS

(Fifth List)

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