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WHO medicines strategy

Revised procedure for updating WHO's Model List of Essential Drugs

Report by the Secretariat

1. In 1975, the Twenty-eighth World Health Assembly requested the Director-General to assist Member States by “advising on the selection and procurement, at reasonable cost, of essential drugs of established quality corresponding to their national health needs” (resolution WHA28.66). The first WHO Model List of Essential Drugs was prepared by a WHO Expert Committee in 1977.¹ In 1978, the Thirty-first World Health Assembly (in resolution WHA31.32) requested the Director-General, *inter alia*, “to continue to identify the drugs and vaccines which, in the light of scientific knowledge, are indispensable for primary health care and control of diseases prevalent in the population, and to update periodically this aspect of the report of the WHO Expert Committee on the Selection of Essential Drugs” and “to cooperate with Member States in formulating drug policies and management programmes that are relevant to the health needs of populations and are aimed at ensuring access of the whole population to essential drugs at a cost the country can afford”.
2. Numerous studies have documented the impact of clinical guidelines and lists of essential medicines² on the availability and proper use of medicines within health care systems.³ Careful selection of a limited range of essential medicines results in a higher quality of care, better management of medicines (including improved quality of prescribed medicines), and more cost-effective use of health resources.
3. Most countries require that a pharmaceutical product be approved on the basis of efficacy, safety and quality before it can be prescribed. In addition, the majority of health care and insurance schemes cover only the costs of medicines on a selected list. The medicines on such lists are selected after a study of the medicines used to treat particular conditions, and a comparison of the value they give in relation to their cost. The WHO Model List of Essential Medicines is an example of such a list.

¹ WHO Technical Report Series, No. 615, 1977.

² As part of the revised procedure for updating the Model List, the term “essential medicines” is used in preference to “essential drugs”. This reflects the common use of the term “medicines” to describe pharmaceutical preparations used in clinical health care practice.

³ For example, WHO medicines strategy: framework for action in essential drugs and medicines policy 2000-2003 (document WHO/EDM/2000.1) and Interventions and strategies to improve the use of antimicrobials in developing countries (document WHO/CDS/CSR/DRS/2001.9).

4. The Model List is a guide for the development of national and institutional essential medicine lists. It was not designed as a global standard. However, over the past 25 years the Model List has led to a global acceptance of the concept of essential medicines as a powerful means to promote health equity. By the end of 1999, 156 Member States had official essential medicines lists, of which 127 had been updated in the previous five years. Most countries have national lists and some have provincial or state lists as well. National lists of essential medicines usually relate closely to national guidelines for clinical health care practice which are used for the training and supervision of health workers. Lists of essential medicines also guide the procurement and supply of medicines in the public sector, schemes that reimburse medicine costs, medicine donations, and local medicine production. Many international organizations, including UNICEF and UNHCR, as well as nongovernmental organizations and international non-profit supply agencies, have adopted the essential medicines concept and base their medicine supply system mainly on the Model List.

WHO MODEL LIST OF ESSENTIAL MEDICINES

5. Every two years since 1977 the Model List has been updated by the WHO Expert Committee on the Use of Essential Drugs.¹ The current Model List (November 1999) lists 306 active ingredients, of which 250 are included in WHO clinical guidelines. Among the 306 active ingredients are vaccines, contraceptives, preventive agents such as insect repellents and some diagnostic agents.

Revised procedure for updating and disseminating the Model List

6. At its meeting in 1999, the Expert Committee proposed that the methods for updating and disseminating the Model List be revised because of (1) advances in the science of evidence-based decision-making; (2) the increasing link between essential medicines and guidelines for clinical health care; and (3) the high cost of many new and effective medicines. The Expert Committee concluded that current procedures do not define the range of conditions covered with adequate specificity, nor are the reasons for inclusion recorded with sufficient clarity.

7. In May 2001 an information document containing a proposed timetable for developing revised procedures to update the Model List was presented to the Executive Board at its 108th session.² In June 2001 all Member States were invited to comment on a discussion paper "Updating and disseminating the WHO Model List of Essential Drugs: the way forward". Comments were analysed and, in August 2001, a revised paper was sent for comments to Member States, WHO collaborating centres, members of expert advisory panels, organizations of the United Nations system, nongovernmental organizations, professional associations, national essential medicines programmes, universities, representatives of the pharmaceutical industry, and patients' organizations.

8. The issue was discussed at the 43rd Directing Council of the Pan American Health Organization (the 53rd session of the WHO Regional Committee for the Americas) in September 2001.³ It was also discussed at the Forty-eighth session of the Regional Committee for the Eastern Mediterranean in October 2001, which strongly endorsed the revised procedure for updating the WHO Model List of Essential Drugs and requested the Director-General to finalize it as soon as possible (resolution EM/RC48/R.2).

¹ In 1977 and 1979 the name of the committee was the Expert Committee on the Selection of Essential Drugs. Since 1982, the committee has been named the Expert Committee on the Use of Essential Drugs.

² Document EB108/INF.DOC./2.

³ See document CD 43/5.

KEY FEATURES OF THE NEW PROCEDURE

9. As a result of this two-stage consultation process, a new procedure for updating and disseminating the Model List has been developed (see Annex). Major features of the new procedure include:

- (1) use of the term “essential medicines” as an alternative to “essential drugs” with immediate effect, reflecting the common use of the term “medicines” to describe pharmaceutical preparations used in clinical health care practice;
- (2) a more systematic approach to encouraging and handling applications for medicines to be included in or deleted from the Model List;
- (3) a more transparent process for selecting medicines to be included in the list, including systematic analysis of medicines proposed for use in the care of different health conditions (comparing efficacy, safety and, where possible and appropriate, cost-effectiveness);
- (4) opportunities for interested parties to comment on both an application and the draft recommendations of the Expert Committee;
- (5) the full involvement of different WHO departments in the application and selection process, linking the process to clinical guidelines disseminated by WHO;
- (6) development of a new WHO essential medicines library which facilitates access to information about medicines on the Model List; and
- (7) steps to ensure that the Expert Committee operates with full scientific independence as it makes its final recommendations (in line with current practice for decisions on regulatory approval, procurement, and reimbursement within Member States).

Essential medicines concept

10. During the consultation processes, most reviewers agreed with the 1999 Expert Committee’s conclusion that: “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, and at a price that individuals and the community can afford”.¹

11. Some reviewers questioned the inclusion of the phrase on affordability and others wondered whether the expression “the majority of the population” is useful. There were other concerns that the needs for sustained financing for essential medicines, and for essential medicines of adequate quality, were not dealt with.

12. Taking this into account, a complete description of essential medicines might:

- first include a definition: Essential medicines are those that satisfy the priority health care needs of the population;

¹ WHO Technical Report Series, No. 895, 2000.

- then include the criteria for their selection: Essential medicines are selected with due regard to disease prevalence, evidence on efficacy and safety, and comparative cost-effectiveness;
- lastly, include reference to the purpose for which such a list is developed: Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality, and at a price the individual and the community can afford.

13. The definition proposed above is similar to that formulated by the first Expert Committee on the Selection of Essential Drugs in 1977: medicines that “are of utmost importance, and are basic, indispensable and necessary for the health needs of the population”.¹ The purpose for which the list has been developed was spelt out by the 1983 Expert Committee on the Use of Essential Drugs (“they should therefore be available at all times in adequate amounts and in the appropriate dosage forms”). A combination of the definition and its implications has been used to describe the essential medicines concept by all subsequent Expert Committees.

Role of treatment cost in relation to the Model List

14. The cost of medicines has been a specific concern of Member States since the concepts of national drug policies and essential medicines were first introduced in 1975.² During the consultation process, some reviewers expressed concerns about aspects of treatment costs. They questioned whether a medicine’s high cost could prevent its inclusion even if it satisfied the selection criteria on grounds of need (needed to treat a priority health problem), effectiveness (when compared with other medicines used to treat the same condition) and safety. Reviewers also questioned whether (given the wide cost variations for the same medicine) worldwide comparisons of the cost-effectiveness of different medicines in treating specific conditions would be meaningful.

15. The selection criteria proposed for the new procedure (see Annex) specify that: (1) the absolute cost of a medicine will not be a reason to exclude it from the Model List if it meets the stated selection criteria, and (2) cost-effectiveness comparisons be made among alternative medicines within the same therapeutic group (e.g., identifying the most cost-effective drug treatment to prevent mother-to-child transmission of HIV). This approach is in line with WHO’s practice of including cost considerations in the development of public health recommendation.

16. The impact of cost variations on cost-effectiveness estimates can be addressed through the use of information on indicative prices of medicines that are already available within the United Nations system, and through the rigorous identification of sources of cost information. Where available, published cost-effectiveness analyses and systematic reviews can also be used. The Expert Committee will – at all times – illustrate recommendations it makes and refer to the evidence on which each recommendation is based. The new procedure will evolve over time, drawing on Member States’ experiences with the use of cost-effectiveness analysis.

¹ WHO Technical Report Series, No. 615, 1977, p. 9.

² *Off. Rec. Wld Hlth Org.*, 226, Annex 13; resolution WHA28.66; WHO Technical Report Series, No. 615, and resolution WHA31.32 all deal with issues of pharmaceutical prices and/or costs.

WHO ESSENTIAL MEDICINES LIBRARY

17. Since 1975, WHO has been asked by Member States to provide information on medicine quality, prices,¹ and therapeutic aspects of individual pharmaceutical products within the Model List. In 1999, the Expert Committee stressed the importance of the link between selection of medicines for the Model List and clinical guidelines. It encouraged wider dissemination of the evidence used in the Expert Committee's work and recommended the careful recording of the reasons for the Expert Committee's final recommendation.

18. The revised procedure proposes the creation, by WHO, of an essential medicines library to make such information more widely available using CD-ROMs and the Internet. Links to WHO clinical guidelines, the WHO Model Formulary, existing United Nations price information services and information on international nomenclature and quality standards are also proposed.

NEXT MEETING OF THE EXPERT COMMITTEE

19. The Expert Committee meeting originally planned for October 2001 has been rescheduled for April 2002. Not all the new procedures outlined in the Annex will be fully operational by then, but those involved in consultations indicate that the Expert Committee has urgent work to do and this should not be delayed any more than is absolutely necessary.

ACTION BY THE EXECUTIVE BOARD

20. The Executive Board is invited to note the report. The Director-General will take account of comments received from the Executive Board and other Member States. She will report on the deliberations of the next meeting of the Expert Committee to the Executive Board at its 110th session.

¹ For example, resolutions WHA49.14, WHA52.19, WHA53.14 and WHA54.11.

ANNEX

PROCEDURE TO UPDATE AND DISSEMINATE THE WHO MODEL LIST OF ESSENTIAL MEDICINES¹

WHO EXPERT COMMITTEE ON THE USE OF ESSENTIAL DRUGS

1. The Model List is drawn up by the WHO Expert Committee on the Use of Essential Drugs, following the Regulations for Expert Advisory Panels and Committees.² Since 1977 the Expert Committee has been convened every two years, but could meet more often if needed.
2. The Expert Committee comprises eight to 12 members drawn from the WHO Expert Advisory Panels³ for Drug Evaluation and for Drug Policies and Management, and, where appropriate and in consultation with the relevant cluster, from other expert advisory panels. Expert Committee members are selected by the Director-General to represent a wide range of geographical and professional backgrounds, including clinical pharmacology, clinical medicine, international public health, guideline development methodology, systematic literature search methods, risk-assessment and cost-effectiveness analysis.
3. Meetings of the Expert Committee are private² and members are required to complete a WHO declaration of interest form before the meeting. Observers may be invited in accordance with Regulations for Expert Advisory Panels and Committees to attend all or parts of the meetings of the Expert Committee. Patient advocacy groups and representatives of the health care industry are invited to comment on the applications and draft recommendations (see below), but are not invited to attend decision-making parts of meetings of the Expert Committee.

APPLICATIONS FOR INCLUSION, CHANGE OR DELETION

4. Applications for inclusions, changes or deletions to the Model List are submitted by or through relevant departments in WHO to the secretary of the Expert Committee. The opinion of the relevant department in WHO is conveyed to the secretary with the application and is presented to the Expert Committee. The information that should be submitted with the application is summarized in Box 1. The application should be received at least four months before the meeting of the Expert Committee. For therapeutic categories for which no specific department exists in WHO the application can be submitted by the department of Essential drugs and medicines policy.

¹ As part of the revised procedure for updating the Model List, the term “essential medicines” is used in preference to “essential drugs”. This reflects the common use of the term “medicines” to describe pharmaceutical preparations used in clinical health care practice.

² *WHO Basic Documents*, 43rd ed., 2001, pp.101-109.

³ Members of Expert Advisory Panels are proposed by WHO and, when approved by their respective government, appointed for one or more periods of up to four years.

REVIEW OF APPLICATIONS AND DRAFT RECOMMENDATIONS

5. The step-wise approach for reviewing applications and draft recommendations is summarized in Box 2. A similar process is used periodically to review whole sections of the Model List. In that case the need for review and the selection of the reviewer(s) are considered in close collaboration with the relevant department in WHO.

Box 1. Information to be included with an application for inclusion or deletion of a medicine in the WHO Model List of Essential Medicines	
1.	Summary statement of the proposal for inclusion, change or deletion
2.	Name of the focal point in WHO submitting the application
3.	Name of the organization(s) consulted and/or supporting the application
4.	International Nonproprietary Name (INN, generic name) of the medicine
5.	Whether listing is requested as an individual medicine or as an example of a therapeutic group
6.	Information supporting the public health relevance (epidemiological information on disease burden, assessment of current use, target population)
7.	Treatment details (dosage regimen, duration; reference to existing WHO and other clinical guidelines; need for special diagnostic or treatment facilities and skills)
8.	Summary of comparative effectiveness in a variety of clinical settings: <ul style="list-style-type: none"> • Identification of clinical evidence (search strategy, systematic reviews identified, reasons for selection/exclusion of particular data) • Summary of available data (appraisal of quality, outcome measures, summary of results) • Summary of available estimates of comparative effectiveness
9.	Summary of comparative evidence on safety: <ul style="list-style-type: none"> • Estimate of total patient exposure to date • Description of adverse effects/reactions • Identification of variation in safety due to health systems and patient factors • Summary of comparative safety against comparators
10.	Summary of available data on comparative cost ¹ and cost-effectiveness within the pharmacological class or therapeutic group: <ul style="list-style-type: none"> • range of costs of the proposed medicine • comparative cost-effectiveness presented as range of cost per routine outcome (e.g. cost per case, cost per cure, cost per month of treatment, cost per case prevented, cost per clinical event prevented, or, if possible and relevant, cost per quality-adjusted life year gained)
11.	Summary of regulatory status of the medicine (in country of origin, and preferably in other countries as well)
12.	Availability of pharmacopoeial standards (British Pharmacopoeia, International Pharmacopoeia, United States Pharmacopoeia)
13.	Proposed (new/adapted) text for the WHO Model Formulary
<p>¹The information on cost and cost-effectiveness should preferably refer to average generic world market prices as listed in the <i>International Drug Price Indicator Guide</i>, an essential medicines pricing service provided by WHO and maintained by Management Sciences for Health. If this information is not available, other international sources, such as the WHO, UNICEF and <i>Médecins sans Frontières</i> price information service, can be used. All cost analyses should specify the source of the price information.</p>	

Box 2. Systematic review of applications

1. The secretary of the Expert Committee checks the application for completeness
2. A summary of the application is posted on the WHO web site¹ for review and comments
3. Specialist assessment(s) are made of the data on comparative efficacy, safety and cost-effectiveness, in close collaboration with relevant departments in WHO
4. The outcome of these assessments is summarized by an expert invited to attend the next meeting of the Expert Committee as a member ("the presenter") who formulates a draft recommendation for the Committee
5. The draft recommendation and proposed text of the WHO Model Formulary are reviewed by the relevant department in WHO and members of relevant expert advisory panels. They are also posted on the WHO web site for comments, for a minimum of 30 days
6. The presenter reviews the comments and formulates a final text for consideration by the Expert Committee
7. The Expert Committee reviews and adopts the application as a recommendation to the Director-General

¹ <http://www.who.int/medicines/>

CRITERIA FOR THE SELECTION OF ESSENTIAL MEDICINES¹

6. The choice of essential medicines depends on several factors, including the disease burden and sound and adequate data on the efficacy, safety and comparative cost-effectiveness of available treatments. Stability in various conditions, the need for special diagnostic or treatment facilities and pharmacokinetic properties are also considered if appropriate. When adequate scientific evidence is not available on current treatment of a priority disease, the Expert Committee may either defer the issue until more evidence becomes available, or choose to make recommendations based on expert opinion and experience.

7. Most essential medicines should be formulated as single compounds. Fixed-ratio combination products are selected only when the combination has a proven advantage in therapeutic effect, safety or compliance over single compounds administered separately. Examples of combination medicines that have met these criteria include new formulations for tuberculosis and malaria.

¹ Since the first meeting of the Expert Committee in 1977, criteria for selection of essential medicines have focused on disease prevalence, treatment facilities, safety, efficacy, quality, availability, and cost factors. Descriptions of selection criteria appear in the Ninth Report of the WHO Expert Committee on the Use of Essential Drugs (WHO Technical Report Series, No. 895, 2000), the Eighth Report of the WHO Expert Committee on the Use of Essential Drugs (WHO Technical Report Series, No. 882, 1998), and previous reports of the Committee.

8. In cost comparisons between medicines, the cost of the total treatment, and not only the unit cost of the medicine, is considered. Cost and cost-effectiveness comparisons may be made among alternative treatments within the same therapeutic group, but will generally not be made across therapeutic categories (for example, between treatment of tuberculosis and treatment of malaria). The absolute cost of the treatment will *not* constitute a reason to exclude a medicine from the Model List that otherwise meets the stated selected criteria. The patent status of a medicine is not considered in selecting medicines for the Model List.

9. In adapting the WHO Model List to national needs, countries often consider factors such as local demography and pattern of diseases; treatment facilities; training and experience of the available personnel; local availability of individual pharmaceutical products; financial resources; and environmental factors.

PRESENTATION OF RECOMMENDATIONS, REPORT OF THE EXPERT COMMITTEE

10. In its report the Expert Committee summarizes the reasons for each recommendation with reference to the underlying evidence. The Expert Committee may grade its recommendations depending on the nature of the underlying evidence. When insufficient evidence is available, the Expert Committee specifies that its recommendations are based on expert opinion and experience. The Committee's report also refers to existing standard clinical guidelines. The Expert Committee may specifically indicate in the list medicines for which specialized health care facilities may be needed or which meet all the selection criteria and which are cost-effective within their therapeutic group, but which are not necessarily affordable for all health systems.

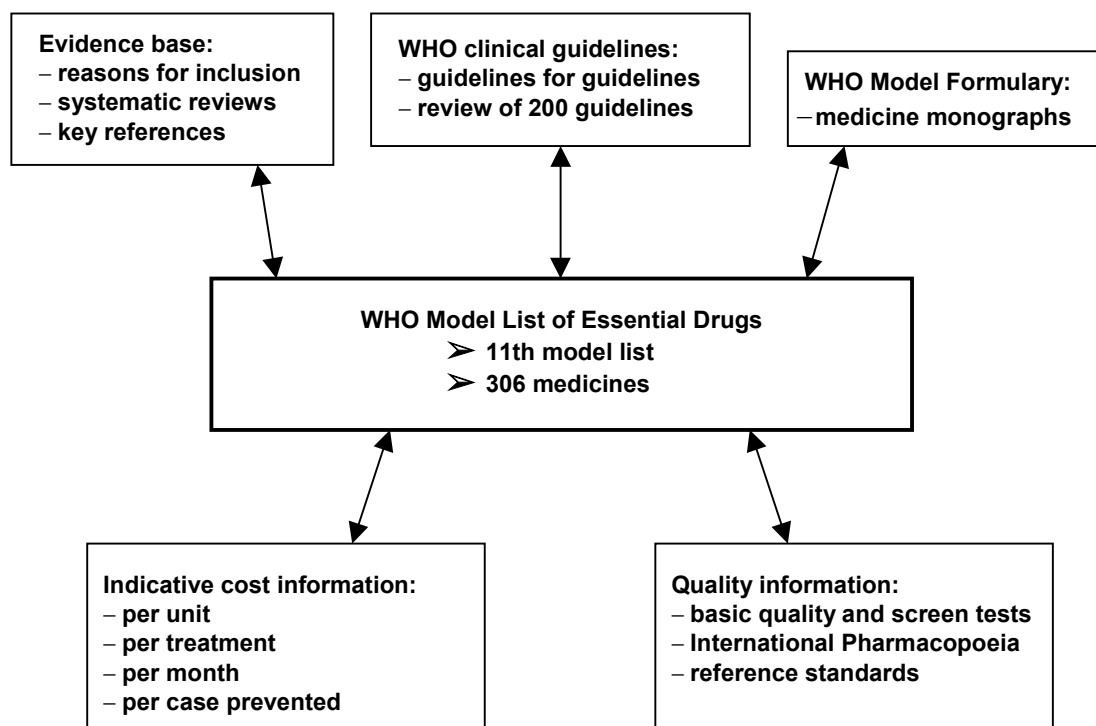
11. Presentation of the Model List will be recommended by the Expert Committee based on considerations of clarity and practicality. Previous model lists have been presented in various formats, including one in which medicines considered to be in the main list appear first under each therapeutic group, followed by medicines considered to be in a complementary list.

12. Immediately after the meeting and subject to final approval by the Director-General, the recommended changes to the Model List, the summary of the Expert Committee's considerations and other relevant information are posted on the WHO web site. The full report of the meeting is published in the WHO Technical Report Series. Translations of the report are published as soon as possible and in close collaboration with WHO regional offices.

WHO ESSENTIAL MEDICINES LIBRARY

13. In addition to the information on whether a medicine is in the Model List or not, it is important for end-users to have access to information that supports the selection, such as summaries of relevant WHO clinical guidelines, the most important systematic reviews, important references and indicative cost information. Other information is also linked to the medicines in the Model List such as the WHO Model Formulary and information on nomenclature and quality-assurance standards. All this information is presented on the WHO web site as the "WHO essential medicines library" (see figure) intended to facilitate the work of national committees.

Figure
WHO essential medicines library



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