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Report of the WHO Expert Committee, 2005
(including the 14th Model List of Essential Medicines)

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1. Introduction

The WHO Expert Committee on the Selection and Use of Essential Medicines met in Geneva from 7 to 11 March 2005. The meeting was opened on behalf of the Director-General by Dr V.K. Lepakhin, Assistant Director-General for Health Technology and Pharmaceuticals. He stated that WHO's medicines programme is very important to Member States and that the recommendations made by its Expert Committees were critical. He explained that the Department of Essential Drugs and Medicines Policy had recently been divided into two new departments. The Department of Medicines Policy and Standards would focus on policy and normative work, whereas the Department of Technical Cooperation for Essential Drugs and Traditional Medicines would concentrate on country support. Both departments would collaborate closely within one area of work, called Essential Medicines. Dr Lepakhin expressed appreciation to the staff of the Department of Essential Drugs and Medicines Policy for its hard work of the past year despite the uncertainties regarding the new structure.

Dr H.V. Hogerzeil, Director of the Department of Medicines Policy and Standards, and Secretary of the Expert Committee, also welcomed the participants. He noted that this would be the third Expert Committee operating under the new procedures approved in 2002. The full effect of these new procedures was now apparent in the careful and timely presentation of evidence-based applications for additions, changes or deletions to the WHO Model List of Essential Medicines (the Model List). Early web posting of most documents, together with the rounds of review and comments prior to the meeting ensured the transparency of the process.

The WHO Secretariat requested and received agreement from the Committee to hold an open session as part of its meeting (see section 2). The purpose of the open session was to allow all stakeholders to participate in the discussions and to comment on issues relating to the WHO Model List of Essential Medicines. Furthermore, for Expert Committee members it provides an opportunity to receive, at firsthand, additional information and opinion on matters under consideration. Discussion and consideration of the open session are reflected in the report of the meeting.

The Committee decided to maintain the reporting format adopted at previous meetings. A summary of the Committee's considerations on each of the items under discussion is presented in the main body of the report. The updated version of the Model List (the 14th Model

List), including a general introduction and explanatory notes, is presented in Annex 1. This Annex is also posted on the WHO web site and printed in hard copy in all six official languages of the Organization. A list of items on the Model List ordered by their corresponding Anatomical Therapeutical Chemical (ATC) classification code number(s) is attached as Annex 2.

The full texts of the applications for changes, additions or deletions with all the evidence and references, as well as the external reviews and comments received, are not included in the report but remain available on the WHO web site, and are accessible through the Essential Medicines Library (http://mednet3.who.int/EMLib/). Information on medicines deleted from the Model List in the past is retained in a separate section of the library.

2. Open session

The session was opened by Dr H.V. Hogerzeil, Director of the Department of Medicines Policy and Standards, and Secretary of the Expert Committee. He briefly explained some aspects regarding the procedures of the Committee. He explained that the Committee is not a representative committee, that all members participate in their personal capacity and are not allowed to take instructions from any government or any other authority. He also stated that all information submitted to the Committee in support of the evidence-based decisions would be placed in the public domain through the WHO web site. This was especially important because in one case an applicant had not allowed unpublished materials which had been referred to in the original application to be posted on the web site, although these materials had been made available to the reviewers. In this case the applicant was requested to resubmit the application on the basis of information that could be placed in the public domain.

Dr Hogerzeil reminded participants that all comments made during the open session would be noted and taken into consideration by the Committee when formulating final recommendations in subsequent private sessions.

As part of the open session, participants were briefed about various activities relating to the Model List and the rational use of medicines (see section 3.7). The new methodology used to have systematic reviews of sections of the Model List performed by experts from various national and other medicine bulletins was also summarized.

A number of issues were raised and debated during the open session. Two representatives of the World Federation of Hemophilia,

including the President, made a presentation in support of their request that factor VIII and factor IX be retained on the Model List. The core arguments were that haemophilia can easily be diagnosed, that treatment is life-saving and easy to administer, that the use of alternative products would increase the risk of transmission of blood-borne viruses, and that deleting these medicines from the Model List would seriously jeopardize global efforts to make the treatment more widely available to all who need it.

Médecins Sans Frontières called for all data supporting the application for recent antiretroviral (ARV) medicines to be made available to the Committee, and requested WHO to update its treatment protocols for human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) in developing countries. A staff member from the Quality Assurance and Safety of Medicines team, WHO, cautioned against the inclusion of methadone and buprenorphine for the treatment of drug dependence, because of the risk of diversion.

3. Update on current activities on selection and rational use

Dr H.V. Hogerzeil informed the Committee of the following recent activities.

3.1 Dissemination of the previous report of the Expert Committee (including the 13th Model List)

Members approved the report of the previous meeting of the Expert Committee for publication by the Director-General and for posting on the WHO web site within two weeks of the meeting. In 2004 the full report was issued in the WHO Technical Report Series (*1*), in English.

The 13th Model List and the general introduction (Annex 1 of the report) were posted on the WHO web site within weeks of the meeting, in all six official languages (Arabic, Chinese, English, French, Russian and Spanish). Hard copies of Annex 1 in English, French and Spanish were printed and widely distributed. Announcements of the new information on the WHO web site were made through international e-mail networks in English, French, Spanish and Russian to over 5000 experts and stakeholders worldwide.

3.2 WHO Model Formulary and WHO Essential Medicines Library

The changes to the 13th Model List of 2003 were incorporated into a second edition of the *WHO model formulary*, which was issued in January 2004 as the *WHO model formulary* 2004 (*2*). This version is now available in hard copy and as a searchable database within the WHO Essential Medicines Library on the WHO web site. The database version is also available as a CD-ROM. A brief technical manual has been developed and added to the CD-ROM version to guide national formulary committees when developing a national formulary using the *WHO model formulary* (*3*).

A Spanish-language version of the *WHO model formulary* is available in hard copy, on the web site and as a CD-ROM. Arabic and Russian translations have been completed and will soon be issued on the web site and as CD-ROMs. A special software program is being used for tracking any changes made in updating the original English text of the *WHO model formulary*, to facilitate updating the translations.

The WHO Medicines Library on the WHO web site has been further developed. It now incorporates the Model List, the *WHO model formulary*, references and electronic links to most clinical guidelines developed by WHO, price information, nomenclature and links to information on quality and standards. The "Medicines Bookshelf", a CD-ROM containing more than 250 key WHO publications on pharmaceuticals in all available language versions, also contains a digital version of the Essential Medicines Library.

3.3 Plans for further revisions of the Model List and *WHO model formulary*

In view of the considerable time and resources needed to organize the Expert Committee, produce the report and the Model List, and adapt and translate the *WHO model formulary* into various languages, a two-year production cycle has been chosen, the early experience with which is very positive. This approach implies that the Expert Committee will meet in Spring in alternate years (starting from Model List 2003). The report and the new Model List are then issued in the course of the same year. At the same time, the necessary changes are reflected in the next edition of the *WHO model formulary*, which is issued in January of the following year. Translations of the *WHO model formulary* follow as soon as possible, using the system to track the changes made, and focusing on electronic publication, which is both inexpensive and rapid. In early 2005 the revision of the Model List takes place, followed by the update of the *WHO model formulary* in 2006.

3.4 Review of essential medicines for reproductive health

The overall objective of the Quality Medicines for Reproductive Health Project is to improve access to essential reproductive health (RH) medicines and commodities by promoting global standards, developing guidance on assured quality suppliers and products, and building procurement capacity in resource-limited countries. In the past year, interagency consultations had been held between United Nations (UN) agencies and nongovernmental organizations (NGOs) working in the field of RH to finalize jointly the Essential List for RH medicines and commodities. Discrepant medicines[1] on UN RH lists were identified and decisions made (based on preliminary reviews) either to delete them from all RH lists and guidelines or to review them formally for possible addition to the Model List. For example, tinidazole will be deleted from the clinical guidelines as metronidazole is the first-line treatment for trichomoniasis. Other medicines, such as cefixime and misoprostol, were formally submitted and reviewed for possible addition to the WHO Model List of Essential Medicines. Sixteen RH medicines were reviewed during the 14th Expert Committee Meeting on the Selection and Use of Essential Medicines.

Discrepancies in terminology and content of non-medicine items in existing RH lists have also been documented and a workplan towards finalization of the harmonized UN Reproductive Health Medicines and Devices List has been formulated. As soon as the lists of essential RH medicines and of essential RH devices are finalized, RH standard treatment guidelines will be updated accordingly. These model treatment guidelines and the list of essential RH items will be made available to national programmes with guidelines to help national RH programme officers increase inclusion of RH medicines on national lists of essential medicines.

3.5 Review of the Interagency Emergency Health Kit

Review of the New Emergency Health Kit 1998 is in progress. Three interagency meetings have been held and decisions have been made to change the name of the kit and to maintain the structure of 10 basic units and a single supplementary unit. As the default position it has been decided that kits should contain treatment for malaria and for

[1] A discrepant medicine is a medicine listed on one list but not on another. The three lists reviewed to check for discrepancies were: The 13th WHO Model List of Essential Medicines, 2003 (EML), the draft United Nations Population Fund (UNFPA)/WHO List of Essential Drugs and Commodities for Reproductive Health Services, 2003 (UNFPA list) and the Draft Interagency UNFPA/United Nations Population Fund (UNAIDS)/WHO Reproductive Health Medicines and Commodities List, 2002 (RHMCL).

the presumptive treatment of victims of sexual violence unless specific requests are made by purchasers not to provide them. Basic units will contain artemether + lumefantrine with rapid diagnostic tests for malaria. Other additions, changes and deletions have been agreed. The place of sulfamethoxazole + trimethoprim in the basic units is under discussion because of increasing reports of resistance to this combination. It is anticipated that there will be interagency agreement on the contents of the kit, which will be posted on the Medicines web site and will be followed by a document later in 2006.

3.6 Report of the WHO Advisory Committee on Safety of Medicinal Products

The aims of pharmacovigilance are to promote patient care and patient safety, especially with regard to the prevention of unintended harm from the use of medicines. It also aims to improve public health and safety by the provision of reliable, balanced information, which will contribute to the assessment of the risk–benefit profile of medicines, and, in turn, encourage safer and more effective use of medicines.

To promote these aims of pharmacovigilance, WHO has established a high-level Advisory Committee on Safety of Medicinal Products (ACSoMP). The second meeting of this Committee was held in October 2004. Major items on the agenda were the recent establishment of the International Alliance for Patient Safety, the safety of medicines for children, pharmacovigilance in various public health programmes, and in relation to several specific medicines. The Advisory Committee expressed a strong interest in contributing to the work of the Expert Committee.

3.7 Update on current activities in the field of rational use of medicines

WHO continues to develop and expand the medicine use database, which now contains more than 550 studies. The database provides useful data to track use of medicines over time, and between sectors and prescriber types in developing and transitional countries. The data will be used for planning, evaluation and advocacy.

The manual *Drug and therapeutics committees: a practical guide* was published in April 2004, and French and Spanish versions are due for publication in 2006. Four international and seven national courses have been conducted in Africa, Asia and Latin America, during which 361 people from 56 countries have been trained in drug and therapeutics committee activities. Such committees can be promoted

in developing countries through a combination of training and follow-up support.

In April 2004, as part of a global effort to improve the use of medicines, 472 leading policy-makers, researchers and other stakeholders representing 70 countries gathered again in Chiang Mai, Thailand, for the Second International Conference on Improving Use of Medicines (ICIUM 2004). This conference was supported by WHO and other partners. Evidence presented made it clear that despite examples of progress, misuse of medicines continues to be widespread and has serious health and economic implications, especially in resource-poor settings. Participants called upon governments to implement policies and programmes in the priority areas discussed at the conference. (All conference presentations, posters and abstracts are available at http://www.icium.org.)

Many promising and successful interventions were presented at ICIUM 2004, yet global progress so far, has been confined primarily to demonstration projects. There are few reports of effective national efforts to improve the use of medicines on a large scale and in a sustainable manner. The conference therefore highlighted the need to move from small-scale research projects to implementing programmes that achieve large-scale and sustained improvements within health systems.

WHO has also been working towards containing antimicrobial resistance (AMR) through advocacy at the country, regional and global levels. Five operational research projects in India and South Africa are being supported to develop community-based surveillance systems. The initial results were presented at ICIUM 2004, where it was concluded that it is possible to have a locally-based multidisciplinary approach to contain AMR in a resource-poor setting. There is an urgent need for further research and other activities in this area. A resolution on AMR is being submitted to the 2005 World Health Assembly.

3.8 Report of the Critically Important Antibiotics for Human Health Meeting, Canberra, Australia, 15–17 February 2005

Antibiotic resistance arising from non-human use of antibacterial agents contributes to the resistance burden in humans. WHO is participating in efforts to establish a list of antibacterial agents, for which loss of efficacy resulting from bacterial resistance would be disastrous to human medicine. This list will subsequently be used by the Codex Alimentarius Commission in defining risk management strategies for non-human use of antibacterial agents. Two criteria were used to

categorize antibacterials: (1) the antibacterial is the sole therapy, or one of few alternatives, available to treat serious human disease, or (2) the antibacterial is used to treat diseases caused by bacteria that may be transmitted, or acquire resistance genes, from non-human sources. Antibacterials that met both criteria were categorized as critically important; antibacterials that met one criterion were categorized as highly important and antibacterials that met neither criterion were categorized as important. The great majority of the antibacterials on the Model List were considered to be critically important. The sulfonamides, doxycycline and spectinomycin were considered highly important. Cloxacillin, chloramphenicol, clindamycin, metronidazole and nitrofurantoin were considered important.

3.9 Update on the Priority Medicines Project

In response to a request and support provided by the Government of the Netherlands, WHO has produced a report on *Priority medicines for Europe and the world* (*4*). This report reviewed the global and European burden of diseases; assessed where pharmaceutical gaps existed; suggested areas in which pharmaceutical innovation was required; and attempted to identify future essential medicines. In addition, the report addressed the particular needs of children, women, the elderly and those suffering from rare diseases. A section of the report addressed barriers to innovation in relation to regulatory and pricing issues, and the need for comparative clinical trials. A series of conclusions and recommendations was also provided. The report was presented at a major meeting of the European Union in The Hague on 18 November 2004 and will be used as a resource for the seventh framework programme of the European Community for research, technological development and demonstration activities.

3.10 Collaboration with the International Society of Drug Bulletins

A report was given by the Chair of the International Society of Drug Bulletins (ISDB) on a WHO/ISDB pilot project to write three section reviews and to review 21 single medicines previously identified for possible deletion from the Model List at the Expert Committee meeting of 2003. The completed reviews were posted on the WHO web site as part of the documentation to be used by the Expert Committee in its deliberations.

3.11 Discussion

The Committee considered that there was great potential for collaboration with the WHO Advisory Committee on Safety of Medicinal

Products. One issue noted was the potential difficulty in accessing data on adverse reactions from the WHO Collaborating Centre for International Drug Monitoring because of the Centre's need to raise resources for its work on a "user-pays" basis. The Committee noted the importance of ensuring sufficient resources to support the work of the Advisory Committee and the Collaborating Centre. The Committee looked forward to further collaboration with the Advisory Committee in relation to medicines on the Model List.

The Committee noted the report by the Secretariat entitled "Rational use of medicines by prescribers and patients" provided for the provisional agenda of the 115th Session of the Executive Board and the Executive Board Resolution "Antimicrobial resistance: a threat to global health security". The Committee considered that the Resolution, although it addresses a critically important public health issue, was focused on antimicrobial resistance and did not address the equally critical issues of developing strategies to improve the use of medicines in general. The Committee therefore strongly recommended that WHO encourage and support Member States in developing and implementing effective strategies (*5*) and national programmes to improve access to and quality use of medicines. Furthermore, the Committee recommended that WHO urgently identify potential sources of funding and donor support to develop a workplan for this key area.

4. Changes made in revising the Model List

4.1 Applications for deletions

4.1.1 *Aminophylline and theophylline*

During its meeting in 2003, the Committee recommended that aminophylline and theophylline be reviewed for fast-track deletion at the meeting in 2005. An application to retain these items was received from the Department of Chronic Respiratory Disease and Arthritis. Reviews were undertaken by ISDB and comments were received from the WHO Department of Chemical Safety and Médecins Sans Frontières.

The Committee noted that as theophylline and aminophylline have limited efficacy in comparison with the other bronchodilators, their relative toxicity becomes a major issue. As noted in the reviews, both products have very narrow therapeutic margins and case reports, case series and studies on theophylline toxicity have been well-documented. One study estimated the overall mortality rate associated with theophylline poisoning to be approximately 10% (*6*).

A Cochrane review (*7*) indicated that use of intravenous aminophylline in acute asthma did not result in any additional bronchodilatation when compared with standard care, and the frequency of adverse events was higher with aminophylline. In the treatment of exacerbations of chronic obstructive pulmonary disease, the efficacy of methylxanthines was unclear, whereas adverse effects increased significantly (*8*).

The Committee recommended that aminophylline and theophylline be deleted from the Model List because of the availability of safer and more effective alternatives on the Model List.

4.1.2 *Atropine*

During its meeting in 2003, the Committee recommended that atropine (as an antispasmodic in the gastrointestinal section) be reviewed for possible fast-track deletion at the meeting in 2005. A review was prepared by the ISDB.

The Committee noted that the ISDB review indicated that there had been no systematic review or good clinical trial to support the efficacy of atropine as an antispasmodic. Atropine has a high potential for adverse effects; it offers little help to patients with irritable bowel syndrome and has no proven benefit in diverticular disease or dyspepsia.

The Committee therefore recommended that atropine (as an antispasmodic) together with the whole section on antispasmodic medicines be deleted from the Model List because of lack of evidence of efficacy and safety.

4.1.3 *Calcium gluconate*

During its meeting in 2003, the Committee recommended that calcium gluconate be reviewed for possible fast-track deletion at the meeting in 2005. Calcium gluconate is listed in the Model List in Section 4 (Antidotes and other substances used in poisoning) and in Section 27 (Vitamins and minerals, complementary list) in the form of 100 mg/ml in a 10-ml ampoule. A review was received from the ISDB.

The ISDB review stated that calcium gluconate injection is important for the treatment of acute hypocalcaemic tetany, and consideration should be given to the inclusion in the Model List of other forms of calcium supplementation both for the treatment of less acute hypocalcaemic tetany and as part of the management of bone diseases such as osteoporosis. A Cochrane review indicates that calcium supplementation alone has a small positive effect on bone density. The data

show a trend towards reduction in vertebral fractures, but it is unclear if calcium supplementation reduces the incidence of non-vertebral fractures (*9*).

The Committee recommended that calcium gluconate injection be retained in Section 4 for magnesium sulfate poisoning, and in the complementary list of Section 27 for hypocalcaemia and hypocalcaemic tetany, and that the footnote on fast-track deletion be removed from Section 27. The Committee also recommended that an application for the inclusion on the Model List of oral calcium (plus vitamin D) in the treatment of oesteoporosis be invited for its next meeting, and that a review of the section on antidotes be made together with suggestions for deletion and applications for medicines suggested for addition.

4.1.4 *Clonazepam*

During its meeting in 2003, the Committee recommended that clonazepam be reviewed for possible fast-track deletion at the meeting in 2005. A detailed review was provided by the ISDB.

The Committee noted that there was inadequate evidence to support the efficacy of clonazepam in the treatment of myoclonic epilepsy. The ISDB review indicated that valproate is the therapy of first choice. This review also indicated that clonazepam may have a place as a second-line drug for the treatment of refractory myoclonic seizures, but no clinical trial is available to support the retention of this item in the Model List.

The Expert Committee recommended that clonazepam be deleted because of the lack of evidence of better efficacy or safety when compared with valproate.

4.1.5 *Codeine*

At its meeting in 2003, the Committee recommended that codeine (as an antimotility medicine in the gastrointestinal section) be reviewed for possible fast-track deletion at the meeting in 2005. A review was undertaken by the ISDB.

The Committee noted the ISDB review which indicated that there had been no systematic review or good clinical trial to support the efficacy of codeine in the treatment of diarrhoea. It mentioned that the value of antimotility medicines in the treatment of acute diarrhoea (including traveller's diarrhoea) was not clear. There had been no systematic reviews of the effects of codeine on the duration and severity of symptoms or of its unwanted effects in acute diarrhoea. There was evidence that it could worsen conditions causing toxic

megacolon, prolonging fever (in shigellosis), and in children with Shiga toxin-producing *Escherichia coli*, causing haemolytic–uraemic syndrome. It was contraindicated in patients with bloody or suspected inflammatory diarrhoea. However, the Committee also noted that there was a need for symptomatic treatment of diarrhoea in adults with certain conditions, such as HIV/AIDS.

The Committee recommended that the heading of the section be changed to "Antidiarrhoeal (symptomatic) medicines for adults", and that codeine be retained on the list at this time. A review of this subsection, including the potential benefit of loperamide and diphenoxylate and the dangers of their use in children (*10*), should be presented at its next meeting, especially taking account of the need for symptomatic treatment of diarrhoea in people with HIV/AIDS. A footnote on possible deletion should be added.

4.1.6 *Colchicine*

During its meeting in 2003, the Committee recommended that colchicine be reviewed for possible fast-track deletion at the meeting in 2005. A detailed review was undertaken by the ISDB.

The Committee noted that colchicine is the oldest available treatment for gout, but that there are very few systematic reviews or good clinical trials to prove its efficacy in the treatment of gout. Its usefulness for treating acute attacks is limited by its dose-dependent toxicity and the therapeutic margin is narrow. Patients often experience gastrointestinal adverse effects such as diarrhoea, before relief of gout symptoms. At high doses, colchicine is bone-marrow suppressive and it cannot be dialysed (*11*). Rarely, its long-term use can result in myopathy. With the availability of other agents, there is a limited special role for colchicine for treatment of acute attacks. The Committee also noted that colchicine is not cheaper than ibuprofen; it has a Median Agency Price (MAP) of US$ 0.1760/defined daily dosage (DDD) compared with US$ 0.0318/DDD for ibuprofen (*12*). Colchicine has not been procured to any great extent by international suppliers over the last five years.

The Committee recommended that colchicine be deleted from the Model List because of its unfavourable benefit–risk ratio when compared with non-steroidal anti-inflammatory drugs (NSAIDs) for most people with gout.

4.1.7 *Cromoglycic acid*

During its meeting in 2003, the Committee recommended that cromoglycic acid be reviewed for possible fast-track deletion at the

meeting in 2005. Responses were received from the WHO Department of Chronic Respiratory Disease and Arthritis and the Japan Institute of Pharmacovigilance, Osaka. A review was undertaken by the ISDB. The Committee noted that there is inadequate evidence to support the inclusion of cromoglycic acid in the Model List. A Cochrane systematic review of trials involving more than 1000 patients aged up to 18 years indicated no evidence that the efficacy of sodium cromoglycate is greater than that of a placebo (*13*).

The Committee recommended that cromoglycic acid be deleted from the Model List because of the availability of more effective and safer alternatives on the Model List.

4.1.8 *Diethyltoluamide*

During its meeting in 2003, the Committee recommended that diethyltoluamide be reviewed for possible fast-track deletion at the meeting in 2005. Comments were received from Médecins Sans Frontières and the Roll Back Malaria programme of WHO.

The Committee noted that there is inadequate evidence to establish the efficacy of diethyltoluamide in preventing malaria. Médecins Sans Frontières indicated that case reports on young children had described serious adverse effects. The WHO Roll Back Malaria Partnership supported the deletion of this item from the Model List, as diethyltoluamide is not on the WHO list of pesticides recommended for use in public health programmes.

The Committee therefore recommended that diethyltoluamide be deleted from the Model List.

4.1.9 *Ergotamine*

During its meeting in 2003, the Committee recommended that ergotamine be reviewed for possible fast-track deletion at the meeting in 2005. A review was received from the ISDB, and support for deletion was received from the Global Campaign to Reduce the Burden of Headache.

The Committee noted that the available evidence does not support the use of oral ergotamine in the treatment of acute migraine attack. A meta-analysis of placebo-controlled trials of ergotamine was not able to demonstrate a benefit from treatment with oral ergotamine (*14*).

The Committee recommended that ergotamine be deleted from the Model List because of lack of evidence of efficacy and the availability of effective and safe alternatives. The Committee also recommended

that a full application for inclusion of a $5HT_1$ agonist (triptan) for migraine be submitted at its next meeting in 2007.

4.1.10 *Ergometrine*

During its meeting in 2003, the Committee recommended that ergometrine be reviewed for possible fast-track deletion at the meeting in 2005. Comments were received from the WHO Department of Reproductive Health and Research.

A review of the evidence found that there was no robust clinical evidence to establish the effectiveness and safety of ergometrine used alone for active management of labour. A Cochrane review (*15*) of trials of oxytocin alone showed that it reduced postpartum haemorrhage, and that the combination of ergometrine with oxytocin was slightly superior for this outcome. Maternal side-effects were more frequent in women treated with the combination regimen. There was no clinical trial evidence to support the efficacy and safety of ergometrine used alone or in combination with oxytocin for the treatment of postpartum haemorrhage.

The Committee recommended that ergometrine injection for the treatment of acute postpartum haemorrhage be retained on the Model List, mainly due to the potential benefits offered by its different pharmacological action (tonic versus periodic contractions that occur with oxytocin). The Committee also recommended that more clinical studies be performed in this area. The Committee saw no indication for ergometrine tablets and recommended that these be deleted from the Model List.

4.1.11 *Ether*

During its meeting in 2003, the Committee recommended that ether be reviewed for possible fast-track deletion at the meeting in 2005. A detailed review was received from the ISDB and a comment was received from the World Federation of Societies of Anaesthesiologists (WFSA).

The Committee noted that halothane is the medicine of choice rather than ether as regards unwanted effects and it enables better precision in controlling the anaesthetic state. This was supported by the ISDB report which recommended that halothane should be used in preference to ether where cost, training, equipment and patient susceptibilities permit. Yet both the ISDB and WFSA suggested that ether be retained on the Model List because of its low cost and relative safety when used by inexperienced staff, in the absence of oxygen, and when patients have contraindications to halothane. The Commit-

tee also noted that ether has not been procured to any great extent by the large non-profit international suppliers over the last five years and that its use is generally declining and limited to rural areas. In addition, ether is an explosive chemical with special storage and transport requirements, which places extra demands on national procurement agencies.

The Committee recommended that ether be deleted from the Model List in view of its cumbersome storage and transport requirements, its declining use and the availability of alternative fluorinated inhalational anaesthetic agents; and that a square box be added to the entry for halothane in the Model List.

4.1.12 *Factors VIII and IX concentrates*

During its meeting in 2003, the Committee recommended that factors VIII and IX concentrates be reviewed for possible fast-track deletion at the meeting in 2005. This decision was based on the fact that haemophilia is a rare disease. An application to retain these items on the Model List was received from the European Plasma Fractionation Association (EPFA), Plasma Protein Therapeutic Association (PPTA), and the World Federation of Hemophilia, with support from a number of individuals as well as haemophilia associations from Argentina, Australia, Dominican Republic, Finland, India, Ireland, People's Republic of China, Portugal, Sri Lanka, Switzerland, the United Kingdom and the USA.

The Committee noted from the application that the approximate estimated prevalence rate of haemophilia in the USA was between 97 and 205 cases per million in the male population, or approximately 75 cases per million in the total population. There were approximately 0.20–0.26 million males with haemophilia in the People's Republic of China, and the incidence rate of the disease in India was 1 in 10 000 live male births. The application also indicated that the cost of treatment with factor VIII concentrate was approximately US$ 4000 (20 000 units × US$ 0.20/unit) per patient per year, and that of treatment with factor IX concentrate was similar.

The Committee noted that factors VIII and IX concentrates are life-saving in the treatment for haemophilia, and that the alternative (cryoprecipitate of whole blood) is less safe and more expensive. In addition, use of the concentrates avoids the risk of acquiring HIV and hepatitis. Another argument was that national blood transfusion services were often built around the production of plasma fractions. However, the Committee also noted that the cost of the treatment is

relatively high, and that the prevalence of the disease is very low, suggesting low public health relevance.

The Committee recommended that factors VIII and IX concentrates be retained on the Model List, accepting the inherent inconsistency caused by the fact that haemophilia is a rare disease. The Committee also recommended that a policy advisory group on rare diseases be established to determine a more general approach to their management.

4.1.13 *Imipenem + cilastatin*

The public health relevance of imipenem + cilastatin was questioned at the 2003 meeting and this item was proposed for possible deletion. Comment was received from the WHO official responsible for AMR strategy, and numerous letters of support for retention were received from Austria, Eastern European countries, the Russian Federation and Sweden. The ISDB produced an extensive review with an annex on comparative costs.

The ISDB review pointed out that this medicine has wide activity against both Gram-negative and Gram-positive organisms as well as anaerobes, but because of its expense when compared with other medicines on the Model List, the reviewers suggested that imipenem + cilastatin be deleted. In a detailed fully referenced response, the company which developed the product suggested that deleting this medicine would limit the choice of medicines available to clinicians to treat life-threatening infections, put increased pressure on cheaper antibacterials to develop resistance and eliminate the drug of choice for treating disease caused by extended spectrum beta-lactamase-producing organisms. In addition imipenem + cilastatin has a good safety record, with more than 20 years of experience.

The Committee noted that recent reports have highlighted the threat of antibacterial resistance. The Committee noted the minimal cross-resistance of imipenem + cilastatin with other antibiotics, and that this medicine is now off patent and is becoming more widely available as a generic product.

The Committee recommended that imipenem + cilastatin be retained on the complementary list, for the treatment of life-threatening hospital-based infections due to suspected or proven multidrug-resistant infection, and that the existing footnote to that effect should be retained.

4.1.14 *Isoprenaline*

During its meeting in 2003, the Committee recommended that isoprenaline be reviewed for possible fast-track deletion at the meeting in 2005. The Committee noted that there was no published evidence to support the efficacy of isoprenaline in the emergency treatment of bradycardia. This was supported by the ISDB review which also concluded that cardiac pacing and other drug therapies provide effective, safer alternatives. The Japan Institute of Pharmacovigilance proposed that isoprenaline be retained because it is needed in the treatment of transient and reversible severe bradycardia where cardiac pacing is unavailable, and in the treatment of beta-blocker overdose. Unfortunately, no data were submitted to support these assertions, and the Committee could not find good clinical studies to support its efficacy and safety.

The Committee therefore recommended that isoprenaline be deleted from the Model List because of the lack of evidence and the very limited indications for its use.

4.1.15 *Levofloxacin*

Levofloxacin has been a complementary medicine for the treatment of multi-drug resistant tuberculosis (MDR-TB) since 1999. It was suggested for deletion at the 2003 meeting of the Committee because of concern for the public health relevance of the product. The Stop TB Department had suggested that fluoroquinolones have emerged as an important class of drugs in the treatment of MDR-TB. They suggested that levofloxacin is the treatment of choice for MDR-TB. They quoted from a recent review article (*16*) which supported their position.

The Committee recommended that levofloxacin be retained as a complementary medicine for the treatment of MDR-TB, and the footnote signalling the restriction of use for this specific indication be retained. The Committee did not recommend the use of a square box symbol to encompass both levofloxacin and ofloxacin, as this might be taken to include gatifloxacin or moxifloxacin for which no review has been undertaken.

The Committee also recommended that the evidence for all medicines for the treatment of MDR-TB be reviewed at its next meeting, in the light of increasing experience with their use.

4.1.16 *Local anaesthetic, astringent or anti-inflammatory as antihaemorrhoidal medicines*

During its meeting in 2003, the Committee recommended that antihaemorrhoidal medicines be reviewed for possible fast-track deletion at the meeting in 2005. A review was received from the ISDB.

The Committee noted that there is no strong evidence to support the efficacy of topical products containing local anaesthetics, astringents or anti-inflammatory medicines in the treatment of haemorrhoids, as was also concluded in the ISDB review.

Therefore the Committee recommended that antihaemorrhoidal medicines (ointment or suppository) and the section on antihaemorrhoidal medicines be deleted from the Model List because of lack of evidence of efficacy and safety, and because of uncertainty as to the real burden of disease caused by this condition.

4.1.17 *Medroxyprogesterone acetate (depot injection 150 mg/ml)*

During its meeting in 2003, the Committee recommended that medroxyprogesterone acetate (depot injection 150 mg/ml) be reviewed for possible fast-track deletion at the meeting in 2005. Comments in support of retention were received from the WHO Department of Reproductive Health and Research, Médecins Sans Frontières and the Expert Committee on the Essential Drugs List of Sri Lanka.

The Committee noted that medroxyprogesterone acetate depot injection (DMPA) is the only three-monthly injectable contraceptive currently available and widely used in developing countries, and that the efficacy of this item has been reviewed and is well-documented. It was reported that the risk of unintended pregnancy during the first year of usage was 3% among typical users and 0.3% among perfect users (*17*). The applicant suggested that DMPA be upgraded from the complementary to the core list. However, the Committee also noted that this medicine has been reported to reduce bone density in comparison with estrogens, but the long-term overall clinical implications of this finding have not yet been determined.

The Committee noted that there is no alternative three-monthly injectable contraceptive. While noting the safety concerns, the Committee recommended that DMPA be retained on the Model List, moved from the complementary list to the core list as requested by the WHO Department of Reproductive Health and Research, and that the footnote on possible fast-track deletion be removed.

4.1.18 *Medroxyprogesterone acetate (tablet 5 mg)*

During its meeting in 2003 medroxyprogesterone acetate (MPA) tablet, 5 mg, was marked for possible fast-track deletion of the meeting in 2005, due to the concerns about adverse effects, including risk of decreased bone mineral density (BMD). A review was carried out that evaluated negative effects of oral formulations of MPA on BMD, as well as clinical outcomes such as fractures.

The Committee noted that the MPA 5-mg tablet is generally used for short-term treatment of dysfunctional metrorrhagia and endometriosis. The review of effects on BMD suggested that only long-term use of MPA may be associated with significant changes in BMD and therefore the Committee decided to retain this product on the Model List at this time. However, the Committee recommended that a further review on the efficacy, safety and public health relevance of norethisterone, medroxyprogesterone acetate and also of ethinylestradiol be presented at its next meeting, and that a footnote to this effect be added in the Model List.

4.1.19 *Nalidixic acid*

During its meeting in 2003 the Committee recommended that nalidixic acid be reviewed for possible fast-track deletion at the meeting in 2005. Reviews were received from the ISDB and Médecins Sans Frontières, and a comment was received from the WHO Department of Child and Adolescent Health and Development, all supporting the deletion of this item from the Model List.

The Committee noted that there was no strong evidence on the efficacy of nalidixic acid in the treatment of urinary tract infections. Both ISDB and Médecins Sans Frontières indicated that antibacterial resistance to nalidixic acid developed quickly, and this may induce resistance to other quinolones such as ciprofloxacin (*18*). The WHO Department of Child and Adolescent Health and Development stated that ciprofloxacin is now the recommended first-line antibiotic for treating shigellosis, and that the use of nalidixic acid should be discontinued even in areas where it is still effective against *Shigella* (*19*). The Committee also noted that the cost/DDD of nalidixic acid is higher than that of ciprofloxacin (MSP US$ 0.3488 and MAP US$ 0.4488 for nalidixic acid versus MSP US$ 0.0618 and MAP US $0.0890 for ciprofloxacin) (*12*).

The Committee recommended that nalidixic acid be deleted from the Model List because of lack of evidence of efficacy in current practice and the availability of better alternatives.

4.1.20 *Niclosamide*

During its meeting in 2003, the Committee recommended that niclosamide be reviewed for possible fast-track deletion at the meeting in 2005. Submissions supporting the retention of niclosamide were received from the WHO Department of Communicable Diseases, Surveillance and Response.

The Committee noted that niclosamide is effective for the treatment of cestode infections. It was estimated that in Latin America 75 million people live in areas where cysticercosis is endemic and approximately 400 000 people have symptomatic disease (*20*). Niclosamide is not absorbed from the gastrointestinal tract.

A review sponsored by the WHO Quality Assurance and Safety of Medicines team confirmed that no major safety concerns have been raised in relation to the use of this item. Niclosamide is not contraindicated in children and pregnant women. Its efficacy and safety in treating *Taenia solium* carriers in the presence of (neuro) cysticercosis has an advantage over praziquantel because it does not increase the likelihood of seizures.

The Committee recommended that niclosamide be retained on the Model List as a reserve medicine, and also for treatment of patients in endemic areas presenting with epileptic seizures which could be caused by cysticercosis and in whom the use of praziquantel is not possible.

4.1.21 *Nifedipine*

During its meeting in 2003, the Committee recommended that long-acting nifedipine be reviewed for possible fast-track deletion at the meeting in 2005. A review was prepared by the WHO Collaborating Centre for Research and Training in Pharmaco-epidemiology in Barcelona, Spain, and comments were received from Médecins Sans Frontières.

The Committee noted that the presentation of nifedipine in the 13th Model List was slightly ambiguous and confirmed that only slow-release tablets of 10 mg were listed. The Committee also noted that short-acting nifedipine is not recommended in the treatment of hypertension due to its relative lack of safety when compared with other antihypertensive medicines. The review prepared by the Collaborating Centre identified that the clinical trial evidence showing benefits of dihydropyridine calcium-channel blockers was strongest for amlodipine.

On the basis of the review, the Committee recommended that sustained-release nifedipine be replaced with amlodipine (5 mg tablet) with a square box as the representative long-acting dihydropyridine calcium channel blocker. The Committee also recommended a review of the continued use of the square box at its next meeting.

4.1.22 *Oxamniquine*

During its meeting in 2003, the Committee recommended that oxamniquine be reviewed for possible fast-track deletion at the meeting in 2005. Submissions recommending the retention of oxamniquine were received from the WHO Department of Communicable Diseases, Surveillance and Response. A review sponsored by the WHO Quality Assurance and Safety of Medicines team confirmed that no major safety concerns have been raised in relation to the use of this item.

The Committee noted that although praziquantel is the medicine of choice for treating *Schistosomiasis mansoni*, oxamniquine can be used in cases when praziquantel may be contraindicated or in the case of resistance. A Cochrane review reported that oxamniquine has equal efficacy to praziquantel in the treatment of *S. mansoni* although lower doses of oxamniquine (<30 mg/kg) may not be as effective in some areas (*21*). The safety review reported a relatively high incidence of minor gastrointestinal and central nervous system side-effects, but these have not limited its widespread use. Oxamniquine is generally more expensive than praziquantel.

Despite some of the comparative disadvantages mentioned above, the Committee recommended that oxamniquine be maintained on the Model List for use in case of failure of treatment with praziquantel.

4.1.23 *Polygeline*

In 2003 the Expert Committee recommended reviewing polygeline for possible fast-track deletion at the meeting in 2005. One review was received from the ISDB and one from Médecins Sans Frontières.

A Cochrane review (*22*) of 57 trials involving 3659 patients compared the effects of different colloid solutions in patients thought to need blood volume replacement. It showed that there is no evidence that one colloid solution is more effective or safer than any other. Another Cochrane review (*23*) indicated that there is no evidence from randomized controlled trials that resuscitation with colloids, compared with resuscitation with crystalloids, reduces the risk of death in patients with trauma or burns or following surgery. The Committee also

noted that the cost of polygeline (US$ 0.0126/ml) is twice that of dextran 70 in normal saline (US$ 0.0056/ml) (*12*).

The Committee concluded that polygeline and dextran 70 are similar in safety and efficacy. The Committee decided that, in view of its lower price, dextran 70 should be retained on the Model List, with a square box to cover polygeline. The choice made will depend on national circumstances. A full review of colloids compared with crystalloids would be welcome at the next meeting of the Committee.

4.1.24 *Procainamide*

During its meeting in 2003, the Committee recommended that procainamide be reviewed for possible fast-track deletion at the meeting in 2005. A review was received from the ISDB.

The Committee noted that there is evidence that calls into question the continued use of procainamide in the treatment of arrhythmias. However, because of the limited choice of antiarrhythmics available on the current Model List, the Committee recommended that procainamide be retained on the Model List at this time, that the subsection of antiarrhythmic medicines (12.2) be fully reviewed at the next meeting of the Expert Committee in 2007, including full applications for amiodarone and sotalol, and that a footnote be added to this effect.

4.1.25 *Pyrantel*

During its meeting in 2003, the Committee recommended that pyrantel be reviewed for possible fast-track deletion at the meeting in 2005. Submissions recommending the retention of pyrantel were received from the WHO Department of Communicable Disease Surveillance and Response. A comprehensive safety review was also prepared.

The Committee noted that, in adults, pyrantel was equally effective and as safe as the benzimidazoles, but that a previous price advantage no longer existed as benzimidazoles were now generally cheaper. Whereas benzimidazoles are therefore the medicines of choice for treating nematode infections, pyrantel can still be used when benzimidazoles are contraindicated, as in the case of resistance, or in the treatment of children under one year old (*24*), although the latter need is rare.

The Committee recommended that pyrantel be retained on the Model List as an alternative to benzimidazoles. At country level the choice between the two medicines would depend on the local cost.

4.1.26 *Quinidine*

During its meeting in 2003, the Committee recommended that quinidine be reviewed for possible fast-track deletion at the meeting in 2005. A review was received from the ISDB.

The Committee noted that there is evidence that calls into question the continued use of quinidine in the treatment of arrhythmias. It was reported that quinidine was effective in the treatment of atrial fibrillation or sustained ventricular arrhythmias. Due to the limited choices of anti-arrhythmics available on the current Model List, the Committee recommended that quinidine be retained on the List at this time, that the subsection of anti-arrhythmic medicines (12.2) be fully reviewed at the next meeting of the Expert Committee in 2007, including full applications for amiodarone and sotalol and that a footnote should be added to this effect.

4.1.27 *Salbutamol*

During its meeting in 2003, the Committee recommended that salbutamol (as a tocolytic) be reviewed for possible fast-track deletion at the meeting in 2005. Comments were received from the WHO Department of Reproductive Health and Research, Médecins Sans Frontières and BMJ-Clinical Evidence.

The Committee noted that there is inadequate evidence to support the efficacy of salbutamol as a tocolytic agent. No systematic review is available relating to salbutamol specifically, but a Cochrane review concluded that terbutaline is ineffective as a tocolytic (*25*). Betamimetics are effective in facilitating external cephalic version, but one small randomized controlled trial showed that salbutamol did not significantly reduce failed cephalic version. There is also inadequate evidence to support the use of betamimetics in impaired fetal growth, placenta praevia and fetal distress.

The Committee therefore recommended that salbutamol (as a tocolytic) be deleted from the Model List.

4.1.28 *Silver nitrate eye solution*

During its meeting in 2003, the Committee recommended that silver nitrate eye solution be reviewed for possible fast-track deletion at the meeting in 2005. A review was received from the ISDB, and a comment was received from the WHO Department of Chronic Diseases, Prevention and Management.

The Committee noted that there was inadequate evidence on the safety of silver nitrate eye solution in the prevention of neonatal

gonococcal conjunctivitis. The ISDB and the WHO Department of Chronic Diseases, Prevention and Management both raised safety concerns and supported the deletion of this item from the Model List. The aqueous solutions had caused chemical conjunctivitis due to the evaporation of the solvent over time, especially in tropical conditions, and such conjunctival irritation hampered eye contact of the neonate with the mother, which was claimed to hinder bonding. The Committee also noted that tetracycline ointment, which is already in the Model List, can be used for the same indications with fewer unwanted effects.

The Committee therefore recommended that silver nitrate eye solution be deleted from the Model List.

4.1.29 *Sodium fluoride*

During its meeting in 2003, the Committee recommended that sodium fluoride (in any appropriate formulation) be reviewed for possible fast-track deletion at the meeting in 2005. Responses were received from the WHO Oral Health Programme and the World Dental Federation which argued for the retention of sodium fluoride on the Model List. Comments on safety issues were received from Fluoride Action Network and Medwatcher, Japan. The Committee also received a review by the ISDB on this item.

The Committee noted that the efficacy of topical fluoride formulations in preventing dental caries is firmly established (*26–30*). The Committee also noted that the selection of a suitable preparation should take into account local circumstances, including the fluoride content of drinking-water. Fluoride tablets are no longer recommended because of the risk of fluorosis when they are used in excess.

The Committee therefore recommended that sodium fluoride be retained on the Model List, but that the description be changed to "in any appropriate topical formulation", and that the square box and the footnote regarding fast-track deletion be removed.

4.1.30 *Spectinomycin*

During its meeting in 2003, the Committee recommended that spectinomycin be reviewed for possible fast-track deletion at the meeting in 2005. A response was received from the WHO Department of Reproductive Health and Research, and reviews were received from Médecins Sans Frontières and the ISDB.

All responses argued for the retention of spectinomycin on the Model List. Spectinomycin was recommended in the WHO *Guidelines for the management of sexually transmitted infections* (*31*) as one of the

first-line treatment options for uncomplicated ano-genital gonococcal infections, disseminated gonococcal infection, adult gonococcal conjunctivitis and pelvic inflammatory disease. The Committee noted that spectinomycin can be used in patients who are intolerant to cefalosporins or quinolones.

The Committee recommended that spectinomycin continue to be listed in the WHO Model List, as an alternative to cephalosporins in the treatment of gonorrhoea and chancroid in adults.

4.1.31 *Sun protection agents*

During its meeting in 2003, the Committee recommended that sun protection agents be reviewed for possible fast-track deletion at the meeting in 2005. A review was received from the ISDB.

The Committee noted that the use of topical sun protection agents (sunscreen products) containing substances that protect the skin against ultraviolet radiation (UVA and UVB) prevents squamous-cell skin cancer in susceptible people (*32*).

The Committee also noted that although the public health relevance of this item for the prevention of skin cancer is high, sunscreens are normally not provided by public facilities and that provision through such sources was not needed.

The Committee therefore recommended that topical sun protection agents be deleted from the Model List.

4.1.32 *Thioacetazone + isoniazid*

Thioacetazone in combination with isoniazid has been a complementary medicine since 1990. It was suggested for possible fast-track deletion by the Committee at its meeting in 2003 because of concern for the public health relevance of thioacetazone. The WHO Stop TB Department undertook a comprehensive review of the use of this medicine and the attitudes of the world's major TB service providers. Comments were received from the Damien Foundation, the International Union against Tuberculosis and Lung Disease (IUATLD), the Deutsche Lepra- und Tuberkulosehilfe e.V. (DAHW), the Centers for Disease Control, USA (CDC) and Médecins Sans Frontières.

Thioacetazone has been used in combination with isoniazid for the treatment of tuberculosis since the 1960s, to prevent the development of resistance to isoniazid. Thioacetazone has always been associated with adverse cutaneous reactions. However, if a patient is co-infected with HIV, the frequency and severity of these reactions is increased, sometimes leading to death. As a result the use of thioacetazone in

HIV-positive patients has been discouraged. Ethambutol and rifampicin are effective alternatives to thioacetazone (*33–35*). In a survey undertaken by the Stop TB Department, thioacetazone was being used in only seven countries, and in many of these its use was being phased out. These countries carry 1.5% of the global TB burden.

Of the agencies that responded to queries about the position of the medicine, support for retention was very mixed. CDC suggested that the risks outweigh the benefits; DAHW strongly suggested removing the product from the Model List. Conversely, the IUATLD supported its retention on the basis of safety for category 1 patients, low price, and concern that in view of the limited number of products available to treat TB, losing one of them would be a serious matter. The Damien Foundation supported retention based on their experience of using this medicine in Bangladesh. Médecins Sans Frontières suggested that thioacetazone be retained for the treatment of pregnant women who are HIV-negative and who require retreatment. In terms of comparative cost-effectiveness, thioacetazone + isoniazid costs US$ 1.24 to US$ 1.71 as compared with a cost of US$ 2.93 (MAP) per person for isoniazid + ethambutol. This costing does not take into account the cost of HIV testing and counselling to preclude the presence of HIV.

The conclusion of the WHO Stop TB Department was to recommend keeping thioacetazone + isoniazid on the complementary list of the Model List for the next two years pending further assessment. This was on the grounds that this medicine continues to be used in a few Member States and because of its potential in prevention of emergence of resistance. However, the Stop TB Department recommended adding a box, after the text on thioacetazone + isoniazid in the Model List and the *WHO model formulary*, containing the following note: *Thioacetazone may be used only where HIV-infection has been excluded because of the risk of serious skin reactions.*

While giving due weight to the proposal by the Stop TB Department and the suggestions from IUATLD, Médecins Sans Frontières and the Damien Foundation, the Committee recommended that thioacetazone + isoniazid be removed from the Model List because it does not fulfil the definition of a complementary product. It cannot be considered as needing specialized diagnostic or monitoring facilities, and/or specialist medical care, and/or specialist training. In addition, the strong association of HIV with TB means that all patients being considered for treatment with thioacetazone should receive HIV testing, which makes thioacetazone + isoniazid less cost-effective than

alternative products such as isoniazid + ethambutol or rifampicin + isoniazid. Removing thioacetazone + isoniazid from the Model List does not preclude individual countries or programmes continuing to use the combination nor does it preclude returning the combination to the Model List if changing needs in relation to the treatment of MDR-TB require it.

4.1.33 *Triclabendazole*

During its meeting in 2003, the Committee recommended that triclabendazole be reviewed for possible fast-track deletion at the meeting in 2005. Submissions recommending the retention of triclabendazole were received from the WHO Department of Communicable Disease Surveillance and Response. A comprehensive safety review was also considered.

The Committee noted that approximately 2.5 million people worldwide are affected by fascioliasis. Triclabendazole is more efficacious than praziquantel in treating paragonimiasis but it is also more expensive (*12*). There are also reports of the successful use of triclabendazole in treating praziquantel-ineffective fascioliasis. A review sponsored by the WHO Quality Assurance and Safety of Medicines team confirmed that triclabendazole appears to be very well tolerated; fewer side-effects were recorded when triclabendazole was used than when praziquantel was used. The small number of reports in the WHO database could be a reflection of its safety, though lack of pharmacovigilance systems in several of the countries where the medicine is used may also be a factor.

In view of the above information the Committee recommended that triclabendazole be retained on the Model List, as the medicine of choice for treatment of fascioliasis and paragonimiasis.

4.2 Applications for additions

4.2.1 *Caffeine citrate*

An application was submitted by the Royal Children's Hospital, Melbourne, Australia, with the support of the WHO Department of Child and Adolescent Health and Development, for the inclusion in the Model List of caffeine citrate, oral solution 20 mg/ml, and IV injection 20 g/ml, for the treatment of apnoea of prematurity in neonates, as an example of the therapeutic class of methylxanthines, with the alternatives being aminophylline and theophylline.

The Committee noted that evidence is available to support the efficacy of caffeine citrate in the treatment of apnoea in preterm neonates. Reviews (*36*) indicated that caffeine appears to have similar

short-term effects on apnoea/bradycardia, with fewer cardiovascular adverse effects than theophylline. However, there are insufficient data to evaluate adequately the side-effects and no data to determine its effects in different gestational age groups. Reviews also indicated that the safety of therapy with methylxanthines was uncertain, especially regarding long-term growth and development.

The Committee noted that caffeine is considerably more expensive than theophylline and that the evidence on the effectiveness and safety of methylxanthines in the treatment of apnoea in preterm neonates is not robust because the number of trials and patients is limited.

The Committee noted that a large clinical trial is about to be completed and therefore decided to defer its decision until its next meeting pending the outcome of this trial.

4.2.2 *Cefixime*

An application was received from the WHO Department of Reproductive Health and Research, Controlling Sexually Transmitted and Reproductive Tract Infections team, to include cefixime, oral tablet 400 mg, for the treatment of uncomplicated gonorrhoea infection.

The Committee noted that cefixime is well tolerated and that most adverse drug reactions are related to the gastrointestinal system. The costs of single dose oral cefixime and ceftriaxone injection are comparable. Cefixime is listed in the WHO *Guidelines for the management of sexually transmitted infections* (*31*) and the European Sexually Transmitted Disease Guidelines as one of the recommended options. However, the Committee also noted that concerns have been raised about the emerging resistance of *Neisseria gonorrhoeae* (*37*).

The Committee recommended that cefixime be added to the Model List for the treatment of uncomplicated ano-genital gonorrhoea only, and the addition of a footnote to that effect.

4.2.3 *Clotrimazole*

An application was received from UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction, the WHO Department of Reproductive Health and Research and BMJ Knowledge, BMJ Publishing Group, London, England, to include clotrimazole (1% and 10% vaginal creams, and 100 mg and 500 mg vaginal tablets) for the treatment of uncomplicated candidiasis.

The Committee noted that there has been adequate clinical evidence to support the efficacy and safety of topical and intravaginal clotrimazole in the treatment of vulvovaginal candidiasis. The efficacy of clotrimazole in uncomplicated candidiasis in non-pregnant women was demonstrated by four clinical trials comparing clotrimazole with placebo (*38*). A Cochrane review (*39*), based on five trials, indicated that imidazole drugs were clearly more effective than nystatin in treating vaginal candidiasis in pregnancy. Topical administration of clotrimazole is recommended by Médecins Sans Frontières and in the *WHO Guidelines for the management of sexually transmitted diseases* (*31*).

The Committee therefore recommended that clotrimazole (1%, 10% vaginal cream; 100 mg, 500 mg vaginal tablets) be included in the Model List for the treatment of vulvovaginal candidiasis.

4.2.4 *Combination injectable contraceptives*

With the support of the Geneva Foundation for Medical Education and Research, an application was submitted by UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction and the WHO Department of Reproductive Health and Research, to include two combination injectable contraceptives, medroxyprogesterone acetate 25 mg + estradiol cypionate 5 mg (MPA/E_2C) and norethisterone enanthate 50 mg + estradiol valerate 5 mg (NET-EN/E_2V) on the Model List. The Committee also noted the information contained in a new Cochrane review which is in press (*40*).

The evidence provided to the Committee showed that the efficacy of combination injectable contraceptives (CICs) for contraception was equivalent to that of progestogen-only and combined oral contraceptives. The Committee noted that CICs had some advantages in relation to more regular bleeding patterns and convenience of use, but there was a lack of data on long-term safety.

Although the Committee recognized the drive towards greater patient choice of contraceptives, it also questioned the public health need for this preparation in view of the lack of compelling evidence of better efficacy, convenience and safety. The Committee therefore recommended that the application be rejected.

4.2.5 *Emtricitabine*

Emtricitabine had been proposed for addition to the list of antiretroviral products by the company developing the product. This medicine was approved by the US Food and Drug Administration on

2 July 2003 and in Europe on 24 October 2003. A full application was submitted. A report on safety was submitted by the WHO Advisory Committee on Safety of Medicinal Products.

The reviewer noted that most of the data provided were unpublished study reports from the sponsor or papers available in abstract only. Most were cited as poster publications only and these data could not be independently evaluated. In addition the safety data appeared to be based on a limited number of patients participating in the efficacy trials. The WHO Advisory Committee on Safety of Medicinal Products noted that use of emtricitabine had been low and therefore limited safety data were available. They expressed concern about the acceptability and tolerability of adverse effects.

The Committee noted that it could not make a recommendation to include a medicine on the Model List on the basis of data which could not be made publicly available afterwards. The Committee therefore decided to defer its decision because of the lack of publicly available data that would allow for an independent assessment of comparative effectiveness and safety in populations likely to use the medicine.

4.2.6 *Emtricitabine + tenofovir fixed-dose combination*

Emtricitabine + tenofovir had been proposed as a fixed-dose combination for addition to the list of antiretroviral products by the company developing the medicine. The company had also submitted applications for the individual components to be added to the list.

The Committee noted that the fixed-dose combination had only recently been approved by the US Food and Drug Administration, but that it is increasingly being used in national programmes. However, it would be illogical to consider the combination so long as the individual medicines had not been added to the Model List. The Committee concluded that listing of the combination at this stage would be premature, and decided to defer its decision because of the lack of information, for example, in comparison with lamivudine.

4.2.7 *Etonogestrel-releasing implant*

An application was submitted by UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction and the WHO Department of Reproductive Health and Research, with support from the Geneva Foundation for Medical Education and Research, to include etonogestrel-releasing implant as a contraceptive on the Model List.

The Committee noted that etonogestrel is an effective and safe contraceptive. However, it also noted that the insertion of the implant

should be undertaken only by specially trained personnel, and that the nature of removal depends on the correctness of the implant insertion. Etonogestrel implant was expensive.

The Committee recognized the potential value of an implantable progestogen. The advantages were the clear evidence of efficacy, the prolonged effect, and therefore the suitability for women wanting long periods of protection. The disadvantages noted were the difficulties associated with insertion and, especially with removal, and the training required for this purpose, and the relatively high acquisition cost.

After consideration of the balance of benefits, harms, suitability, and the need for the additional choice and the relatively high cost, the Committee decided to reject the application.

4.2.8 *Ibuprofen paediatric suspension*

An application for the inclusion of ibuprofen paediatric suspension 20 mg/ml on the Model List was reviewed by the Expert Committee at its meeting in 2003. The Committee rejected that application on the basis that there was insufficient evidence to conclude that ibuprofen provides an antipyretic effect superior to that of paracetamol, and because data on the comparative safety and cost-effectiveness of ibuprofen and paracetamol were lacking. A full application was submitted to the Expert Committee in 2005 by the International Ibuprofen Foundation (IIF), Marlborough, England, with support from Boots Healthcare International, Wyeth Consumer Health, and several clinicians from Australia, the Netherlands, the United Kingdom and the USA. A detailed review was provided by the Cochrane Pain and Palliative Care Group. The WHO Department of Child and Adolescent Health and Development recommended rejection of the application.

The Committee noted that ibuprofen has comparable efficacy to paracetamol in reducing body temperature. However, paracetamol is safer. A randomized controlled study involving 27 065 febrile children confirmed this view (*41*). The Committee also noted that ibuprofen is more expensive than paracetamol; the MAP of ibuprofen is US$ 0.0105/ml and that for paracetamol syrup US$ 0.0008–0.0032/ml (*12*).

The Committee recommended that ibuprofen paediatric suspension not be added to the Model List in view of its unfavourable benefit–risk ratio when compared to paracetamol, and its higher cost. The Committee also recommended that no further application be considered without substantial new data.

4.2.9 *Levonorgestrel-releasing implant*

An application was submitted by the United Nations Development Programme/United Nations Population Fund (UNDP/UNFPA)/ WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction and the WHO Department of Reproductive Health and Research, with support from the Geneva Foundation for Medical Education and Research, to include levonorgestrel-releasing implant as a contraceptive on the Model List.

The Committee noted that levonorgestrel is an effective and safe contraceptive. However, it also noted that the insertion of the implant should be undertaken only by specially trained personnel, and that the nature of removal depends on the correctness of the implant insertion. Levonorgestrel implant was expensive.

The Committee recognized the potential value of an implantable progestogen. The advantages were the clear evidence of efficacy, the prolonged effect, and therefore the suitability for women wanting long periods of protection. The disadvantages noted were the difficulties associated with insertion, and especially with removal, and the training required for this purpose, and the relatively high acquisition cost.

After consideration of the balance of benefits, harms, suitability, and the need for the additional choice and the relatively high cost, the Committee decided to reject the application.

4.2.10 *Levonorgestrel-releasing IUD*

An application was submitted by the UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction and the WHO Department of Reproductive Health and Research, with support from the Geneva Foundation for Medical Education and Research, to include levonorgestrel-releasing IUD as a contraceptive on the Model List.

The Committee noted that levonorgestrel-releasing IUD (LNG-20 IUD) is an effective contraceptive. The results of a Cochrane review (*42*) indicated that LNG-20 IUD is as effective as non-hormonal IUDs > 250 mm^2. However its discontinuation rate is significantly higher than that of copper IUDs, with amenorrhoea as the main reason given for discontinuing use of LNG-20 IUD. The Committee also noted that LNG-20 IUD is more expensive than copper IUDs.

The Committee recommended rejection of the application for inclusion of the levonorgestrel-releasing IUD for contraception because of

the lack of evidence for better efficacy, its higher discontinuation rate and because it is more expensive than the copper IUD already in the Model List.

4.2.11 *Methadone and buprenorphine*

An application was received from the WHO Department of Mental Health and Substance Abuse and Department of HIV/AIDS with support from the WHO Collaborating Center/College on Problems of Drug Dependence, Philadelphia, Virginia Commonwealth University Institute for Drug and Alcohol Studies, Alcohol and other Drugs Control of Australia, European AIDS Treatment Group, Central and Eastern European Harm Reduction Network, and more than 10 individuals and other organizations. Comment was received from the Islamic Republic of Iran.

The Committee noted that the most widely used illicit opioid is heroin, mainly through intravenous injecting. It is estimated that there are 12.6 million injecting drug users (IDUs) worldwide, approximately 10% of HIV infections are associated with injecting drug use. Intravenous drug users are also at a high risk of exposure to hepatitis B and C. Treatment of heroin dependence is therefore of high public health relevance. Both buprenorphine and methadone are effective for the treatment of heroin dependence (*43*, *44*). However, methadone maintenance therapy at appropriate doses is the most effective in retaining patients in treatment and suppressing heroin use (*45*). Methadone is less costly than buprenorphine. It was reported that the cost of buprenorphine per patient per year varied from US$ 300–600 for the generic product to approximately US$ 1750–3500 for a branded product in India. The cost of methadone per patient per year in developing countries was reported as US$ 29 for the Slovak Republic, US$ 60 as a generic product from the Netherlands and US$ 180 in the Islamic Republic of Iran. The Committee also noted that misuse of buprenorphine by IDUs is reported from the Islamic Republic of Iran.

The Committee noted that the quality of the data will be inherently weaker than in other therapeutic areas because of the type of disorder and the situations in which it occurs. In addition to conventional randomized controlled trials with abstinence rate as an outcome, the evidence of effectiveness in various societal effects (such as a reduction in criminality) should also be taken into consideration. The Committee noted evidence that the use of methadone reduces seroconversion of HIV/AIDS (*46*). It has also been noted that methadone interacts with antiretroviral medicines, but that this only affects the serum level of methadone, which needs to be adjusted according

to the patient response. The Committee noted that there is less clinical experience with buprenorphine than with methadone, but that there is more pharmacological evidence and evidence of favourable societal outcomes. The Committee recommended that the treatment should be initiated and monitored by specially trained staff within an established support structure, but recognized that this would not necessarily require a tertiary hospital setting.

The Committee recommended that methadone (oral solution 5 mg/5ml, 10 mg/5ml; or concentrate for oral solution 5 mg/ml, 10 mg/ml) be added to the complementary list of the Model List, with a square box to cover buprenorphine only, within a new subsection "Medicines used in substance dependence programmes" and that a footnote be added that these products should be used only within an established programme.

4.2.12 *Methoxyflurane*

An application was received from Medical Development International Ltd, Springvale, Australia, to include methoxyflurane, inhaled 3-ml preparation (Penthrox® Inhaler), as an example of preoperative medication and sedation for short-term procedures, and as an analgesic (section 2).

The Committee noted that there was inadequate evidence to support the inclusion of methoxyflurane on the Model List, either for analgesia or for short-term anaesthesia. A list of 12 randomized clinical studies (conducted between 1966 and 1975) and two more recent studies (conducted in 2002) was provided in the application, mostly conducted with small numbers of patients. It was reported that a study involving 1257 women in labour (*47*) indicated that methoxyflurane had equal analgesic effect to trichloroethylene and nitrous oxide, and another study involving 1616 women in labour (*48*) indicated that methoxyflurane provided an analgesic effect equal to that of nitrous oxide and cyclopropane. However, no detailed information on the methodology of the trials was provided. No compelling evidence was provided to show that, in clinical practice, methoxyflurane is more efficacious or safer than the alternative. Concern about its efficacy and safety was further heightened by the fact that it is registered in only two countries despite having been available for over 30 years.

The Committee recommended that methoxyflurane not be added to the Model List in view of the lack of evidence that it is more efficacious or safer than its alternatives.

4.2.13 *Miltefosine*

An application was received from the manufacturer to include miltefosine 10 mg and 50 mg capsules for the treatment of leishmaniasis. Comments on safety were received from Médecins Sans Frontières and the Department of Communicable Disease Surveillance and Response.

The Committee recognized the importance of encouraging applications for medicines for neglected diseases. The Committee noted that oral miltefosine shows equal efficacy to amphotericin B in the treatment of visceral leishmaniasis in adults (*49*). However, the observation that many patients discontinued miltefosine due to adverse reactions indicates that more data need to be generated about its safety, especially keeping in mind the risk of teratogenicity. Very little is known about the pharmacokinetic profile of miltefosine in humans, and the dosage schedule for adults with visceral leishmaniasis is not very clear. The Committee also noted that miltefosine is registered in India (in 2002) only for the treatment of visceral leishmaniasis, and its availability is restricted. In addition, miltefosine has not been sufficiently tested for treatment of cutaneous leishmaniasis.

The Committee considered that miltefosine may be of potential value for the treatment of visceral leishmaniasis. However, from the evidence currently available, the Committee recommended rejection of the application for miltefosine. Any future application should include data demonstrating comparative effectiveness, including for cutaneous leishmaniasis; evidence for safety particularly in relation to the question of teratogenicity; and an evaluation of the comparative cost-effectiveness, including in comparison with liposomal amphotericin B.

4.2.14 *Nifedipine*

During its meeting in 2003, the Committee recommended that long-acting nifedipine be reviewed for possible fast-track deletion at the meeting in 2005. A review was prepared by the WHO Collaborating Centre for Research and Training in Pharmacoepidemiology in Barcelona, Spain, and comments were received from Médecins Sans Frontières.

The Committee noted that the presentation of nifedipine in the 13th Model List was slightly ambiguous and confirmed that only slow release tablets of 10 mg were listed. The Committee also noted that short-acting nifedipine is not recommended in the treatment of hypertension due to its relative lack of safety when compared with other antihypertensive medicines. The review prepared by the

Collaborating Centre identified that the clinical trial evidence showing benefits of dihydropyridine calcium-channel blockers was strongest for amlodipine.

Based on the review, the Committee recommended that sustained-release nifedipine be replaced with amlodipine (5 mg tablet) with a square box as the representative long-acting dihydropyridine calcium channel blocker. The Committee also recommended a review of the continued use of the square box at its next meeting.

4.2.15 *Mifepristone with misoprostol*

An application was received from the UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), the WHO Department of Reproductive Health and Research and the Geneva Foundation for Medical Education and Research to include in the Model List sequential administration of oral mifepristone and intravaginal misoprostol for induction of medical abortion.

The Committee noted a Cochrane review of 39 trials (*50*) which showed that sequential administration of a single-dose mifepristone oral 200-mg tablet followed by a vaginal single dose of misoprostol, 800 micrograms in 36 to 48 hours is effective, safe and convenient in inducing medical abortion until nine weeks of pregnancy. Major complications appeared to be rare, the most common complication being the need for blood transfusion (about 0.2%). It was reported that the side-effects (nausea, vomiting and diarrhoea) were mainly due to prostaglandins. Higher doses were associated with increased incidence of side-effects. The risks of bleeding, abdominal pain, fever and dizziness in the medical abortion population were higher than those in the surgical abortion population (*51*). In addition, the duration of bleeding caused by medical abortion was longer than that caused by surgical abortion.

The Committee noted from the application that the mifepristone/misoprostol regimen for medical abortion in the first nine weeks of pregnancy has been registered in the following countries in Europe: Austria, Belgium, Finland, France, Germany, Greece, Luxembourg, the Netherlands, Norway, Romania, Spain, Sweden, Switzerland and the United Kingdom. The regimen has also been registered in Azerbaijan, Georgia, India, Israel, New Zealand, the People's Republic of China, the Russian Federation, South Africa, Tunisia, Ukraine, the USA, Uzbekistan and Viet Nam.

The Committee noted that the use of this medication in medical abortion should be undertaken under close medical supervision, and

that its efficacy decreases if used after nine weeks of gestation. The Committee therefore recommended that mifepristone (200-mg tablet) followed by misoprostol (200-microgram tablet) be included on the complementary list of the Model List for medical abortion within nine weeks of the start of pregnancy, and that the following footnote be added:

> Requires close medical supervision.

Note from the Secretariat: In reviewing the recommendation relating to this combination of products, the Director-General decided to add a note adjacent to the combination in the WHO Model List stating:

> Where permitted under national law and where culturally acceptable.

4.2.16 *Misoprostol, low dose*

An application was received from the UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction, the WHO Department of Reproductive Health and Research and BMJ Knowledge, to include misoprostol, 25–50-microgram intravaginal tablets, for induction of at-term labour.

The Committee was informed that induction of labour is sometimes needed because of safety concerns for the mother or child. Methods of preparing the uterine cervix and inducing labour include: administration of oxytocin, prostaglandins, prostaglandin analogues, mifepristone, extra-amniotic saline solution infusion or mechanical procedures. When the condition of the cervix is unfavourable in the third trimester or when uterine evacuation is needed in the first or second trimesters, oxytocin has a high failure rate for labour induction. In those cases, prostaglandin preparations have proved beneficial, but most of them are expensive and unstable at room temperature. Misoprostol, dinoprostone and carboprost are used in the induction and augmentation of labour.

The Committee noted that current evidence indicates that misoprostol is effective in cervical ripening and labour induction (*52*, *53*). In an initial dose of 25 micrograms every four or six hours, vaginal misoprostol is more effective than oral and sublingual misoprostol. On the other hand, intravaginal misoprostol increases uterine hyperstimulation with or without changes in fetal heart rate. There are anecdotal reports of uterine rupture following treatment with prostaglandin analogues in women with or without previous caesarean section, but this is a very rare outcome. The Committee also noted that vaginal administration of misoprostol seems to be cost-effective, mainly because it reduces the incidence of operative deliveries which could lead

to further cost savings. The Committee recommended that misoprostol be administered as low-dose vaginal tablets, and be used only in organized health services with facilities to manage negative outcomes. The Committee stressed that vaginal use of the 200-microgram oral tablet for the same purpose is dangerous and should be discouraged.

In view of the evidence of its efficacy and safety, the Committee recommended that misoprostol vaginal tablet (25-microgram intravaginal tablet) be included on the complementary list of the Model List for the induction of at-term labour.

4.2.17 *Nifedipine*

An application was received from the UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction, the WHO Department of Reproductive Health and Research and BMJ Knowledge for the inclusion of nifedipine tablet and capsule 10 mg and 20 mg, as a tocolytic on the Model List. Comments were received from Médecins Sans Frontières.

The Committee noted that there is strong evidence to support the use of nifedipine to inhibit preterm labour. Nifedipine was studied in 10 randomized controlled trials in a Cochrane review (*54*). The results indicated that, compared with any other tocolytic agent (mainly betamimetics), nifedipine or nicardipine reduced the frequency of neonatal respiratory distress syndrome, necrotizing enterocolitis, intraventricular haemorrhage and neonatal jaundice.

The Committee concluded that nifedipine is effective and safe for this indication, and noted that the sublingual route is pharmacologically equivalent to the conventional oral route (*54*) because the medicine is absorbed low in the gastrointestinal tract. The Committee recommended that nifedipine (10-mg immediate release capsules) be included on the Model List in the subsection of tocolytics.

4.2.18 *Tenofovir*

Tenofovir had been proposed for addition to the Model List of antiretrovirals by the company developing the medicine. The applicant submitted additional information that the US Department of Health and Human Services had updated their guidelines for the use of antiretroviral agents to recommend the use of tenofovir as part of the nucleoside reverse transcriptase inhibitor (NRTI) backbone for both NRTI- and protease inhibitor (PI)-based regimens. Tenofovir was approved by the US Food and Drug Administration on 26 October 2001 and in Europe on 5 February 2002. A full application has been submitted. A report was submitted by the WHO Advisory Committee

on Safety of Medicines. The Committee also reviewed public statements by the European Agency for the Evaluation of Medicinal Products (EMEA) made on 30 July 2003 and 22 October 2003.

The Committee noted that the data provided in the application were generally the sponsor's summaries of the unpublished study reports that had been used as the basis of the regulatory review in the USA. References were not provided with the application and most of those cited were posters. An independent literature search carried out for this review identified several reports published over the last year that appear to include relevant information not provided in the application. These included case reports in relation to renal toxicity, a systematic review of the use of tenofovir in children and at least two observational studies of adverse effects and interactions. The safety data submitted in the application appeared to be based on a limited number of patients participating in the efficacy trials.

The WHO Advisory Committee on Safety of Medicinal Products expressed concern about the acceptability and tolerability of adverse effects related to renal toxicity, interactions, lactic acidosis, bone problems and liver problems. In addition the EMEA had issued two public statements about tenofovir, concerning high rates of virologic failure with combinations of tenofovir and didanosine or lamivudine (*55*). On the basis of evidence available to the Agency at that time they advised against initiating new patients on a regimen containing tenofovir with didanosine or lamivudine.

The Committee noted that tenofovir is mentioned in the WHO Guidelines on *Scaling-up antiretroviral therapy in resource-limited settings: treatment guidelines for a public health approach 2003 revision*, and that possible adverse effects and virologic failures are recognized. The guidelines state:

> As experience, availability and cost issues in resource-limited settings become clarified the inclusion of tenofovir (TDF) in WHO-recommended first-line regimens should be reconsidered.

The Committee noted a lack of publicly available data to allow for an independent assessment of comparative effectiveness and safety. In particular there appear to be no published studies in highly relevant populations likely to use the product. As more complete data are likely to become available in the near future the Committee decided to defer its final recommendation to the next meeting in 2007.

4.2.19 *Zinc sulfate*

An application was submitted by the WHO Department of Child and Adolescent Health and Development and UNICEF to include zinc

sulfate (tablets 10 mg, 20 mg) on the Model List for supplementation of treatment of childhood diarrhoea with oral rehydration salts (ORS).

The Committee noted that there is adequate evidence to support the efficacy of zinc sulfate supplementation as an adjunctive therapy in the treatment of acute and persistent non-dysenteric diarrhoea in children (*56*). Pooled analyses of trials showed that in children with acute diarrhoea who received zinc supplementation, the probability of continuing an episode of diarrhoea was 15% lower, and the probablility of persistent symptoms of chronic diarrhoea was 24% lower than in children who received no zinc supplementation.

The Committee recommended that zinc sulfate (tablet or syrup in 10 mg per unit dosage) be included on the Model List in the section on antidiarrhoeal drugs as a new subsection, with a footnote that in the treatment of children with acute diarrhoea, the product should only be used as an adjunct to ORS.

4.3 Other changes

4.3.1 *Alcuronium and vecuronium*

The Committee noted that no systematic review is available to validate the comparative efficacy and safety of alcuronium and vecuronium. The ISDB reviewer indicated that vecuronium offers advantages over alcuronium (*57*), and is therefore a better representative of neuromuscular blocking agents than alcuronium. However, the Committee noted that vecuronium is relatively expensive compared with the other alternatives.

In view of the above considerations the Expert Committee recommended that alcuronium and vecuronium be retained with a square box on the Model List, and that a footnote should be added to alcuronium stating that alternative medicines for its possible replacement will be reviewed at its next meeting in 2007.

4.3.2 *Antiretroviral medicines*

The Committee received a proposal from Médecins Sans Frontières to include specific pharmaceutical preparations better adapted to the situations in developing countries, such as non-refrigerated formulations, other improved dosage forms such as enteric-coated tablets; and once-a-day, time-released antiretroviral formulations in the antiretroviral section. The Committee recommended that the description in the Model List 2003 be revised as follows:

> In order to simplify treatment, facilitate storage and distribution, and improve patients' adherence to the treatment plan, the Committee

recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations, including modified dosage forms, non-refrigerated formulations and paediatric formulations with assured pharmaceutical quality and interchangeability with single products as approved by the relevant medicine regulatory authority.

4.3.3 *Ceftriaxone 1 g injection*

An application was received from the WHO Department of Communicable Disease Surveillance and Response, to add a dosage strength of 1 g ceftriaxone for the treatment of epidemic meningococcal meningitis.

The Committee noted that ceftriaxone 1 g injection is at least therapeutically equivalent to oily chloramphenicol for the immediate treatment of cases of meningococcal infection during an epidemic period and also in the treatment of children aged more than 2 months. However, the Committee also noted that widespread availability of low-cost ceftriaxone could lead to rapid emergence of resistance, given that this medicine can be used for several other indications.

The Committee recommended that the dosage form of 1 g ceftriaxone injection be included with the existing 250-mg injection on the complementary list.

4.3.4 *Immunoglobulin, human normal*

During the Expert Committee Meeting in 2003, the Committee noted that there was no need for immunoglobulin in view of the availability of suitable vaccines, that there are no WHO clinical guidelines recommending its use, and that quality control of this blood product poses a problem. This assessment was based on the fact that immunoglobulin had been used in protection against hepatitis A, measles and, to a lesser extent, rubella. The Committee recommended that this item be deleted from the Model List.

Applications for reinstatement were received, as immunoglobulin is used in the replacement and treatment of primary and secondary immunodeficiency syndromes. Full applications were received from the Plasma Protein Therapeutic Association (PPTA), the European Plasma Fractionation Association (EPFA) and the Immune Deficiency Foundation (IDF), with the WHO Department of Blood Transfusion Safety as the focal point. Brief applications for reinstatement were received from many international unions and societies. A list of organizations supporting the reinstatement was submitted, consisting of groups from Canada, France, Ireland, Italy, the Netherlands, New Zealand and Spain.

The Committee noted Cochrane reviews which indicated that the efficacy of intravenous immunoglobulin was equal to that of plasma exchange for the treatment of Guillain-Barré syndrome (*58*), and the efficacy was equal to that of plasma exchange and prednisolone in the treatment of chronic inflammatory demyelinating polyradiculoneuropathy (*59*). A study involving 46 subjects who received 12 months of treatment for primary immunodeficiency showed that the use of immunoglobulin resulted in an estimated serious infection rate of 0.1 per subject per year (*60*). No data were submitted on the incidence rate of immunodeficiency diseases, but it was mentioned that the estimated prevalence rate in the USA of the total conditions needing immunoglobulin as replacement therapy and immunomodulation was approximately 3658 per million people (3.6/10 000). No data were available from other parts of the world.

The Committee noted that immunoglobulin is needed in the treatment of primary immunodeficiency, and is an alternative treatment to plasma exchange for secondary immunodeficiency. However, the Committee also noted that the individual and total prevalence of these diseases is very rare, that there is insufficient evidence of the efficacy of immunoglobulin despite its reported use, and that the cost of treatment is very high. On the basis of the above considerations, the Committee recommended that human immunoglobulin not be reinstated on the Model List.

4.3.5 *Labetalol*

The starting point for this discussion was the discrepancy in the choice of beta-blockers between the 13th Model List and WHO clinical guidelines for the treatment of hypertension in pregnancy. A review was received from the Department of Reproductive Health and Research. The Committee noted that insufficient information was available on the efficacy of labetalol in the treatment of chronic hypertension in pregnancy (*61*). In the treatment of mild to moderate hypertension in pregnancy no significant difference in efficacy was found between the various antihypertensive medicines (*62*). Beta-blockers seem to be well tolerated by pregnant women.

The Committee recommended no action at this stage, in view of the lack of evidence of better efficacy and safety of labetalol in the treatment of hypertension in pregnancy. The Committee also recommended that a full review of all medicines for the treatment of hypertension in pregnancy be discussed at the next meeting in 2007.

4.3.6 *Prostaglandins for postpartum haemorrhage*

A statement on the status of prostaglandins for postpartum haemorrhage was received from the WHO Department of Reproductive Health and Research.

The Committee noted that none of the prostaglandin analogues have been evaluated rigorously to identify benefits and harms when used in the treatment of postpartum haemorrhage. A Cochrane review (*63*) of 24 trials of misoprostol and eight of prostaglandin involving a total of 34 203 participants indicated that neither intramuscular prostaglandins nor misoprostol is preferable to conventional injectable uterotonics as part of the active management of the third stage of labour, especially for low-risk women. A trial on the efficacy of prostaglandins in treatment of primary postpartum haemorrhage (*64*) showed that rectal misoprostol at a dose of 800 micrograms could be a useful first-line medicine. However, further randomized controlled trials are required to identify the best combinations of medicines, route of administration and dose for the treatment of postpartum haemorrhage.

The Committee welcomed the fact that research is being undertaken on oral medicines to treat postpartum haemorrhage, and expressed its interest in reviewing future applications pertaining to medicines for treating this condition. In view of the lack of evidence presented in the current application, the Committee recommended that prostaglandins (i.e. misoprostol) for the treatment of postpartum haemorrhage should not be included in the Model List at this time.

5. Reviews of sections of the Model List

5.1 Beta-lactam medicines

During its meeting in 2003, the Committee noted that there was a need to review the cefalosporins on the Model List. An extensive review was undertaken by the ISDB. The review proposed that ceftazidime and ceftriaxone be retained on the Model List, and also that cefalexin and cefazolin be included on the Model List. Cefalexin was proposed as an alternative to amoxicillin/ampicillin and cefazolin as an alternative for surgical prophylaxis.

Following the procedures of the Expert Committee prior to 2002, cefazolin and cefalexin would probably have been added to the 14th Model List based on the information in this section review and the opinion of the Committee. In keeping with the importance of its procedures, which require that full information be included in an

application for addition, and recognizing the resulting lack of balance in the list with the current inclusion of cefixime (see section 4.2.2), the Committee accepted the recommendation of the reviewer and requested that a formal application for these two medicines be submitted for the next meeting, and that a footnote to this effect be added to the Model List.

5.2 General anaesthetics and oxygen

During its meeting in 2003, the Expert Committee noted that there was a need to review the anaesthetics section of the Model List. A review was undertaken by the ISDB. Based on the review, the Committee recommended that ether be deleted (see section 4.1.11) while all other medicines in this section be retained on the Model List. A short-acting intravenous agent, propofol, is now cheaper than sodium thiopentone and is included on the essential medicines lists of many countries. The Expert Committee recommended that an application for propofol be submitted for its meeting in 2007.

5.3 Muscle relaxants

During its meeting in 2003, the Committee noted that there was a need to review the muscle relaxants section. Based on a detailed review by the ISDB, the Committee recommended that suxamethonium chloride and neostigmine metilsulfate be retained on the Model List, and requested that applications for atracurium and pancuronium, which could possibly replace alcuronium, be submitted to its meeting in 2007 (see below). In this application due regard should be given to the relative lack of heat stability of atracurium and to comparative cost information.

5.4 Ophthalmological preparations

During its meeting in 2003, the Committee noted that there was a need to review the ophthalmology section. Unfortunately the review had not been completed and was therefore not discussed. The Committee requested that this section be reviewed at the next meeting.

6. Rare diseases

The Committee considered the issue of rare diseases as a result of concerns expressed about the possible deletion of factor VIII and factor IX and medicines for other rare diseases also known as "orphan diseases". The Committee reviewed the discussion paper entitled *Rare essentials? Drugs for rare diseases on the Essential*

Medicines List (*65*). The Committee made a distinction between "neglected diseases" which may not be rare in some geographical areas[1] and rare diseases which have a prevalence of fewer than 5 per 10 000 worldwide. Medicines for neglected diseases may be considered as essential medicines.

The Committee acknowledged that the recognition of rare diseases may increase in importance as diagnostics improve, access to health systems increases and communicable diseases decline in importance. Countries are likely to seek advice from WHO as to how to address this issue. The Committee suggested that there was a need for WHO to establish a policy advisory group on rare diseases to study this issue.

7. Future priorities

The Committee recommended that full applications for addition of the following items be submitted to the Committee for consideration at its next meeting in 2007: (1) propofol, (6.2.1) cefalexin, cefazolin; (6.4.2) emtricitabine, tenofovir and combination; (7.1) 5 HT_1 agonist (triptan(s)); (12.2) amiodarone, sotalol; (20) atracurium, pancuronium; (27) oral calcium.

The Committee recommended that the following section reviews be prepared and submitted for discussion at its next meeting in 2007: Section 4: antidotes; Section 6.4: medicines for MDR-TB; Section 11.1: colloids versus crystalloids; Section 12.2: anti-arrhythmic medicines; Section 12.3: medicines for hypertension in pregnancy, and also the continued use of the square box for amlodipine; Section 12.4: medicines used for cardiac failure; Section 17.7.2: antidiarrhoeals in adults; Section 18.3: contraceptives; Section 21: ophthalmological preparations.

7.1 Summary of recommendations — additions, changes and deletions to the Model List

1. The Committee recommended that the following medicines be deleted from the Model List:
   (1.1) ether

[1] This definition is derived from orphan drug legislation in the European Union and the USA.

(2.3) colchicine
(5) clonazepam
(6.2.2) nalidixic acid
(6.2.5) thioacetazone + isoniazid
(6.6) diethyltoluamide
(7.1) ergotamine
(11.1) polygeline
(12.2) isoprenaline
(13.7) sun protection agents
(17.3) local anaesthetics, astringent, anti-inflammatory as anti-haemorrhoidal
(17.4) atropine as spasmolytic
(21.1) silver nitrate eye solution
(22.1) ergometrine tablet
(22.2.2) salbutamol as tocolytic
(25) theophylline, aminophylline, cromoglicic acid.

2. The Committee recommended that the following changes be made in items already on the Model List:
(6.1.1) niclosamide: remove footnote on future review
(6.1.1) pyrantel: remove footnote on future review
(6.1.3) oxamniquine: remove footnote on future review; triclabendazole: remove footnote on future review
(6.2.1) ceftriaxone: add 1 g injection
(6.2.1) imipenem + cilastatin: remove footnote on future review
(6.2.2) spectinomycin: remove footnote on future review
(6.2.4) levofloxacin: remove footnote on future review
(11.1) dextran 70: add square box
(11.2) factors VIII and IX concentrates: remove footnote on future review
(12.2) antiarrhythmic medicines: add footnote that section will be reviewed at next meeting
(12.3) nifedipine: replace with amlodipine with square box
(12.4) heart failure: add furosemide (tablet and injection, as under diuretics)
(17.7) change section name to: "Antidiarrhoeal (symptomatic) medicines for adults"
(18.3.1) subsection "hormonal" to be divided into two subsections: oral, injectable medroxyprogesterone acetate (depot injection): move to core list, remove footnote on future review;
(18.4) ethinyloestradiol: add footnote on future review
(18.7) norethisterone: add footnote on future review; medroxyprogesterone acetate: add footnote on future review

(20) alcuronium: add footnote that potential alternatives will be reviewed in 2007
(27) sodium fluoride: change description to "in any appropriate topical formulation"; remove square box and remove footnote on future review, calcium gluconate: remove footnote on future review.

3. The Committee recommended that the following medicines be added to the 14th Model List:
(6.2.1) cefixime tablet 400 mg
(6.3) clotrimazole 1%, 10% vaginal cream; 100 mg, 500 mg vaginal tablets
(17.5.2) zinc sulfate tablet or syrup in 10 mg per unit dosage
(22.1) misoprostol 25 microgram intravaginal tablet on complementary list; mifepristone 200 mg oral tablet — misoprostol 200 microgram vaginal tablet on the complementary list with the footnote "Requires close medical supervision": in reviewing the recommendation relating to this combination of products, the Director-General decided to add a note adjacent to the combination in the WHO Model List stating "*Where permitted under national law and where culturally acceptable*".
(22.2) nifedipine 10 mg capsule as tocolytic
(24.5) methadone oral solution 5 mg/5 ml, 10 mg/5 ml, or concentrate for oral solution 5 mg/ml, 10 mg/ml on complementary list, with square box to cover buprenorphine, within a new subsection "Medicines used in substance dependence programmes" and a footnote that these products should be used only within an established support programme.

4. The Committee decided to defer its recommendations on the following items, and requested that more information be submitted at its next meeting in 2007:
(6.4.2) tenofovir, emtricitabine, tenofovir + emtrictabine
(25) caffeine citrate.

5. The Committee recommended that the following applications be rejected:
(2.1) ibuprofen paediatric suspension
(2.1) methoxyflurane
(6.5.2) miltefosine
(12.3) labetalol
(18.3.1) combination injectable contraceptives, etonogestrel-releasing implant, levonorgestrel-releasing implant, levonorgestrel-releasing IUD
(19.2) immunoglobulin, human normal.

6. The Committee recommended that full applications for addition of the following items be submitted to the Committee for consideration at its next meeting in 2007: (1) propofol, (6.2.1) cefalexin, cefazolin; (6.4.2) emtricitabine + tenofovir; (7.1) 5 HT_1 agonist (triptan(s)); (12.2) amiodarone, sotalol; (20) atracurium, pancuronium; (27) oral calcium.

7. The Committee recommended that the following section reviews be prepared and submitted for discussion at its next meeting in 2007:
   Section 4: antidotes
   Section 6.2.4: medicines for MDR-TB
   Section 11.1: colloids versus crystalloids
   Section 12.2: anti-arrhythmic medicines
   Section 12.3: medicines for hypertension in pregnancy and also the continued use of the square box for amlodipine
   Section 12.4: medicines used for cardiac failure
   Section 17.7.2: antidiarrhoeals in adults
   Section 18.3: contraceptives
   Section 21: ophthalmological preparations.

7.2 Methodological issues

1. The Committee recommended that section reviews should, as far as possible, be performed in the first year after a Committee meeting, so that full applications for new additions, if suggested by the section review, can be prepared in time for submission to the Committee meeting at the same time as the section review.
2. The Committee recommended that a policy advisory group on rare disease be established to study the issue of effective medicines for life-threatening rare diseases.
3. The Committee recommended that the original applications and other supporting documents for the Expert Committee published on the WHO web site be maintained on the web site for readers of the report who wish to see these materials, and that a permanent record be created as well.

7.3 Rational medicine use

The Committee recommended that WHO encourages and supports Member States in developing and implementing effective strategies and national programmes to improve access to and use of quality medicines, and that WHO urgently identify potential sources of funding and donor support to develop a workplan for this key area.

References

1. The selection and use of essential medicines. *Report of the WHO Expert Committee, 2003 including the 13th Model List of Essential Medicines.* Geneva, World Health Organization, 2004 (WHO Technical Report Series, No. 920).
2. Mehta DK, Ryan RSM, Hogerzeil HV (eds). *WHO model formulary 2004.* Geneva*:* World Health Organization, 2004.
3. *WHO model formulary 2004.* CD-ROM. Geneva, World Health Organization, 2004.
4. Kaplan W, Laing R. *Priority medicines for Europe and the world.* Geneva, World Health Organization, 2004 (available at:http://mednet3.who.int/prioritymeds/report/index.htm).
5. Http://www.who.int/gb/ebwha/pdf-files/EB115-REC1/e/Resolutions.pdf
6. Dawson AH, Whyte IM. The assessment and treatment of theophylline poisoning. *Medical Journal of Australia*, 1989, **151**:689–693.
7. Parameswaran K, Belda J, Rowe BH. Addition of intravenous aminophylline to beta2-agonists in adults with acute asthma. *Cochrane Database of Systematic Reviews* 2000, (4):CD002742 (http://www.cochrane.org/cochrane/revabstr/AB002742.htm, accessed 18 January 2005).
8. Barr RG, Rowe BH, Camargo CA Jr. Methylxanthines for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* 2003, (2):CD002168 (http://www.cochrane.org/cochrane/revabstr/AB002168.htm, accessed 18 January 2005).
9. Shea B, et al, the Osteoporosis Methodology Group, and the Osteoporosis Research Advisory Group. Calcium supplementation on bone loss in postmenopausal women (Cochrane Review). In: *The Cochrane Library*, issue 4. Chichester, John Wiley & Sons, 2004 (http://www.cochrane.org/cochrane/revabstr/AB004526.htm, accessed 10 January 2005).
10. Anonymous. Loperamide. In: *The rational use of drugs in the management of diarrhoea in children.* Geneva, World Health Organization, 1990, pp.17–22.
11. Rott KT, Agudelo CA. Gout. *Journal of the American Medical Association*, 2003, **289**:2857–2860.
12. MSH. *International drug price indicator guide, 2003* (http://erc.msh.org/dmpguide/, accessed 30 January 2005).
13. van der Wouden JC et al. Inhaled sodium cromoglycate for asthma in children (Cochrane Review). In: *Cochrane Library*, issue 4. Chichester, John Wiley & Sons, 2004. (http://www.cochrane.org/cochrane/revabstr/AB002173.htm, accessed 22 November 2004).
14. Treatment of acute migraine headaches. *Therapeutics Letter*. Vancouver, Therapeutics Initiative. 1997.
15. McDonald S. Abbot JM, Higgins SP. Prophylactic ergometrine-oxytocin versus oxytocin for the third stage of labour (Cochrane Review). In *Cochrane Library*, issue 2. Chichester, John Wiley & Sons, 2005 (http://www.cochrane.org/cochrane/revabstr/AB000201.htm).

16. **Ginsburg AS, Grosset JH, Bishai W.** Fluoroquinolones, tuberculosis and resistance. *Lancet Infectious Diseases* 2003, **3**:432–442.

17. Reproductive Health and Research. *Medical eligibility criteria for contraceptive use*, third ed. Geneva, World Health Organization, 2004 (http://www.who.int/reproductive-health/publications/MEC_3/mec.pdf, accessed 2 February 2005).

18. **Sack et al.** *Antimicrobial resistance in shigellosis, cholera, and campylobacteriosis*. Geneva, World Health Organization, 2001.

19. Antibiotics in the management of shigellosis. *WHO Weekly Epidemiological Record*, 2004, **79**:355–356.

20. **Bern C et al.** Magnitude of the disease burden from neurocysticercosis in a developing country. *Clinical Infectious Diseases*, 1999, **29**:1203–1209.

21. **Saconato H, Atallah A.** Interventions for treating *Schistosomiasis mansoni*. *Cochrane Database of Systematic Reviews* 1999, Issue 3 (http://www.cochrane.org/cochrane/revabstr/AB000528.htm, accessed 3 December 2004).

22. **Bunn F, Alderson P, Hawkins V.** Colloid solutions for fluid resuscitation. *Cochrane Database of Systematic Reviews* 2003, (1) (http://www.cochrane.org/cochrane/revabstr/ AB001319.htm, accessed 12 October 2004).

23. **Roberts I et al.** Colloids versus crystalloids for fluid resuscitation in critically ill patients. *Cochrane Database of Systematic Reviews* 2004, (4) (http://www.cochrane.org/cochrane/revabstr/AB002045.htm, accessed 10 January 2005).

24. World Health Organization. *Report of the WHO Informal Consultation on the use of praziquantel during pregnancy/lactation and albendazole/mebendazole in children under 24 months. Geneva, 8–9 April, 2002.* Geneva, World Health Organization, 2002 (WHO/CDS/CPE/PVC/2002.4).

25. **Nanda K et al.** Terbutaline pump maintenance therapy after threatened preterm labor for preventing preterm birth (Cochrane Review). In: *Cochrane Library,* issue 4. Chichester, John Wiley & Sons, 2004 (http://www.cochrane.org/cochrane/revabstr/ABoo3933.htm, accessed 4 December 2004).

26. **Marinho VCC et al.** Fluoride toothpastes for preventing dental caries in children and adolescents (Cochrane Review). In: *Cochrane Library*, issue 4. Chichester, John Wiley & Sons, 2004 (http://www.cochrane.org/cochrane/revabstr/AB002278.htm, accessed October 2004).

27. **Marinho VCC.** Fluoride varnishes for preventing dental caries in children and adolescents (Cochrane Review). In: *Cochrane Library*, issue 4. Chichester, John Wiley & Sons, 2004 (http://www.cochrane.org/cochrane/revabstr/AB002279.htm, accessed October 2004).

28. **Marinho VCC.** Fluoride gels for preventing dental caries in children and adolescents (Cochrane Review). In: *Cochrane Library*, issue 4. Chichester, John Wiley & Sons, 2004 (http://www.cochrane.org/cochrane/revabstr/AB002280.htm, accessed October 2004).

29. Marinho VCC et al. Fluoride mouthrinses for preventing dental caries in children and adolescents (Cochrane Review). In: *Cochrane Library*, issue 4. Chichester, John Wiley & Sons, 2004 (http://www.cochrane.org/cochrane/revabstr/AB002284.htm, accessed October 2004).

30. Marinho VCC et al. Combinations of topical fluoride (toothpastes, mouthrinses, gels, varnishes) versus single topical fluoride for preventing dental caries in children and adolescents (Cochrane Review). In: *Cochrane Library*, issue 4. Chichester, John Wiley & Sons, 2004 (http://www.cochrane.org/cochrane/revabstr/AB002781.htm, accessed Oct. 2004).

31. *Guidelines for the management of sexually transmitted infections*. Geneva, World Health Organization, 2003.

32. Green A et al. Daily sunscreen application and betacarotene supplementation in prevention of basal cell and squamous-cell carcinomas of the skin: a randomised controlled trial. *Lancet*, 1999, **35**:723–729.

33. Nunn P et al. Cutaneous hypersensitivity reactions due to thioacetazone in HIV-1 seropositive patients treated for TB. *Lancet*, 1991, **337**:627–630.

34. Kelly P et al. Cutaneous reactions to thiocetazone in Zambia. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1994, **88**:113–115.

35. Nunn P, Porter J, Winstanley P. Thioacetazone: avoid like poison. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1993, **87**:578–582.

36. Steer PA, Henderson-Smart DJ. Caffeine versus theophylline for apnea in preterm infants. *Cochrane Database of Systematic Reviews* 1998, (2):CD000273 (http://www.cochrane.org/cochrane/ revabstr/AB000273.htm, accessed 3 February 2005).

37. Wang SA et al. Multidrug-resistant *Neisseria gonorrhoeae* with decreased susceptibility to Cefixime – Hawaii, 2001. *Clinical Infectious Diseases*, 2003, **37**:849–852.

38. Spence D. Candidiasis (vulvovaginal). *Clinical Evidence*, 2004,**12**:2490–2508.

39. Young GL, Jewell D. Topical treatment for vaginal candidiasis (thrush) in pregnancy. *Cochrane Database of Systematic Reviews* 2001(3):CD000225 (http://www.cochrane.org/cochrane/revabstr/AB000225.htm, accessed 1 February 2005).

40. Gallo MF et al. Combination injectable contraceptives for contraception. *Cochrane Database of Systematic Reviews* 2005, issue 4. Chichester, John Wiley & Sons (http://www.cochrane.org/reviews/en/AB004568.html).

41. Lesko SM, Mitchell AA. The safety of acetaminophen and ibuprofen among children younger than two years old. *Pediatrics* 1999, **104**:39.

42. French R et al. Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy. *Cochrane Database of Systematic Reviews* 2004, (3) (http://www.cochrane.org/cochrane/revabstr/AB001776.htm, accessed 10 February 2005).

43. Mattick RP et al. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database of Systematic*

Reviews 2003, (2) (http://www.cochrane.org/cochrane/revabstr/AB002207.htm, accessed 27 November 2004).

44. **Mattick RP et al.** Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database of Systematic Reviews* 2003, (2) (http://www.cochrane.org/cochrane/revabstr/AB002209.htm, accessed 27 November 2004).
45. **Amato L et al.** Effectiveness of opiate maintenance therapies: an overview of systematic reviews. *Cochrane Colloquia*, Ottawa 2004 (http://www.cochrane.org/colloquia/abstracts/ottawa/P-004.htm, accessed 27 November 2004).
46. **Metzger DS, Woody GE, McLellan AT.** Human immunodeficiency virus seroconversion among intravenous drug users in- and out-of-treatment: an 18-month prospective follow-up. *Journal of Acquired Immune Deficiency Syndromes*, 1993, **6**:1049–1056.
47. **Rosen M et al.** Field trial of methoxyflurane, nitrous oxide, and trichloroethylene as obstetric analgesics. *British Medical Journal*, 1969, **3**:263–267.
48. **Smith BE, Moya F.** Inhalational analgesia with methoxyflurane for vaginal delivery. *Southern Medical Journal*, 1968, **61**:386–390.
49. **Sundar S et al.** Oral miltefosine for Indian visceral leishmaniasis. *New England Journal of Medicine*, 2002, **347**:1739–1746.
50. **Kulier R et al.** Medical methods for first trimester abortion. *Cochrane Database of Systematic Reviews*, 2004, (2) (http://www.cochrane.org/cochrane/revabstr/AB002855.htm, accessed 31 January 2005).
51. **Zou Y et al.** Side effect of mifepristone in combination with misoprostol for medical abortion. *Zhonghua Fu Chan Ke Za Zhi*, 2004, **39**:39–42.
52. **Hofmeyr GJ, Gülmezoglu AM.** Vaginal misoprostol for cervical ripening and induction of labour. *Cochrane Database of Systematic Reviews* 2002, (4):CD000941 (http://www.cochrane.org/cochrane/revabstr/AB000941.htm, accessed 13 February 2005).
53. **Alfirevic Z.** Oral misoprostol for induction of labour. *Cochrane Database of Systematic Reviews* 2001, (2):CD001338 (http://www.cochrane.org/cochrane/revabstr/AB001338.htm, accessed 13 February 2005).
54. **King JF et al.** Calcium channel blockers for inhibiting preterm labour. *Cochrane Database of Systematic Reviews* 2003, (1):CD002255 (http://www.cochrane.org/cochrane/revabstr/AB002255.htm, accessed 10 January 2005).
55. EMEA Public Statement. *High rates of virologic failure in patients with HIV infection treated with a once-daily triple nucleoside/nucleotide reverse transcriptase inhibitors combination containing didanosine, lamivudine and tenofovir*. London, European Agency for the Evaluation of Medicinal Products, 2003 (EMEA/CPMP/5094/03).
56. **Bhutta ZA et al.** Therapeutic effects of oral zinc in acute and persistent diarrhoea in children in developing countries: pooled analysis of randomized controlled trials. *American Journal of Clinical Nutrition*, 2000, **72**:1516–1522.

57. Alcuronium dichloride. In: Dollery C, ed. *Therapeutic drugs*. 2nd ed. Vol. 1. Edinburgh, Churchill Livingstone, 1999:A63–A64.

58. Hughes RAC et al. Intravenous immunoglobulin for Guillain-Barré syndrome. *Cochrane Database of Systematic Reviews* 2004, (1) (http://www.cochrane.org/cochrane/revabstr/AB002063.htm, accessed 10 October 2004).

59. Van Schaik IN et al. Intravenous immunoglobulin for chronic inflammatory demyelinating polyradiculoneuropathy. *Cochrane Database of Systematic Reviews* 2002, (2) (http://www.cochrane.org/cochrane/revabstr/AB001797.htm, accessed 10 October 2004).

60. Ochs HD, Pinciaro PJ, and the Octagam Study Group. Octagam® 5%, an intravenous IgG product, is efficacious and well tolerated in subjects with primary immunodeficiency diseases. *Journal of Clinical Immunology,* 2004, **24**:308–313.

61. Duley L, Henderson-Smart DJ. Drugs for treatment of very high blood pressure during pregnancy. *Cochrane Database of Systematic Reviews* 2002, (4).

62. Magee L, Duley L. Oral beta-blockers for mild to moderate hypertension during pregnancy. *Cochrane Database of Systematic Reviews* 2003, (3).

63. Gülmezoglu AM et al. Prostaglandins for prevention of postpartum haemorrhage. *Cochrane Database of Systematic Reviews,* 2004, (1) (http://www.cochrane.org/cochrane/revabstr/AB000494.htm, accessed 12 February 2005).

64. Mousa Mousa HA, Alfirevic Z. Treatment for primary postpartum haemorrhage. *Cochrane Database of Systematic Reviews* 2003, (1) (http://www.cochrane.org/cochrane/revabstr/AB003249.htm, accessed 12 February 2005).

65. Stolk P, Willemen M, Leufkens HG. Rare essentials? Drugs for rare diseases on the Essential Medicines List. Discussion Paper for the WHO Expert Committee on the Selection and Use of Essential Medicines. Utrecht Institute for Pharmaceutical Sciences. The Netherlands, 1 March 2005.

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Annex 1
The 14th WHO Model List of Essential Medicines

Introduction

The concept of essential medicines

Essential medicines are those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness. 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 adequate information, and at a price the individual and the community can afford. The implementation of the concept of essential medicines is intended to be flexible and adaptable to many different situations; exactly which medicines are regarded as essential remains a national responsibility. Experience has shown that 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 a more cost-effective use of available health resources.

The WHO Model List of Essential Medicines

Most countries require that a pharmaceutical product be approved on the basis of efficacy, safety and quality before it can be prescribed. The majority of health care and insurance schemes will only cover the cost of medicines on a given list of approved medicines. Medicines on such lists are selected after careful study of the medicines used to treat particular conditions and a comparison of the value they provide in relation to their cost. The WHO Model List of Essential Medicines (the Model List) is an example of such a list.

The first WHO Model List was drawn up in 1977 in response to a request from the World Health Assembly (resolution WHA28.66) to the Director-General of WHO to provide Member States with advice on the selection and procurement, at reasonable costs, of essential medicines of established quality corresponding to their national health needs. The Model List has since been revised and updated at intervals of approximately two years. Over the past two decades, the

regular updating of the Model List has not only been at the heart of WHO's revised drug strategy but has also formed a key component of the information required by Member States in relation to their medicine procurement and supply programmes.

The Model List was originally intended as a guide for the development of national and institutional essential medicine lists. It was not designed as a global standard. Nevertheless, since its introduction the Model List has led to a global acceptance of the concept of essential medicines as a powerful tool for promoting health equity. By the end of 2003, 156 Member States had official essential medicines lists, of which 99 had been updated in the previous five years. Most countries have national lists; some have provincial or state lists as well.

The concept of essential medicines has also been adopted by many international organizations, including the United Nations Children's Fund (UNICEF) and the Office of the United Nations High Commissioner for Refugees (UNHCR), as well as by nongovernmental organizations and international non-profit supply agencies. Many of these organizations base their medicine supply system on the Model List. 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, and, furthermore, are widely used as informational and educational tools by health professionals. Health insurance schemes too are increasingly using national lists of essential medicines for reference purposes.

The way in which national lists of essential medicines are developed and used has evolved over time. Initially, lists were drawn up primarily as a means to guide the procurement of medicines. More recently, however, greater emphasis has been placed on the development of treatment guidelines as the basis for medicine selection and supply, and on the evidence underlying the development of those treatment guidelines. Consequently, there has been an increasing demand for information on why a particular medicine is included in the Model List and also for references to the underlying evidence. Activities are now underway to strengthen the links between the Model List and the treatment guidelines developed by WHO.

In its present form, the Model List aims to identify cost-effective medicines for priority conditions, together with the reasons for their inclusion, linked to evidence-based clinical guidelines and with special emphasis on public health aspects and considerations of value for money. Information that supports the selection of essential medicines, such as relevant WHO clinical guidelines, systematic reviews, key references and indicative cost information is being made

available via the WHO web site as the WHO Essential Medicines Library. The latter provides links to other relevant sources of information, including the *WHO model formulary* and information on nomenclature and quality assurance standards. The Essential Medicines Library is under construction and will be expanded over time. Its primary function is to facilitate the work of national and institutional committees in developing national and institutional lists of essential medicines.

Medicines on the Model List are classified as either "core" list or "complementary" list medicines. The core list presents a list of minimum medicine needs for a basic health care system, listing the most efficacious, safe and cost-effective medicines for priority conditions. Priority conditions are selected on the basis of current and estimated future public health relevance, and potential for safe and cost-effective treatment. The complementary list presents essential medicines for priority diseases, for which specialized diagnostic or monitoring facilities and/or specialist medical care and/or specialist training are needed. In case of doubt, medicines may also be listed as complementary on the basis of consistently higher costs or less attractive cost-effectiveness in a variety of settings.

A number of medicines are labelled with a square box symbol. This symbol is primarily intended to indicate similar clinical performance within a pharmacological class. The listed medicine should be the example of the class for which there is the best evidence for effectiveness and safety. In some cases, this may be the first medicine that is licensed for marketing; in others, subsequently licensed compounds may be safer or more effective. Where there is no difference in terms of the efficacy and safety data, the listed medicine should be the one that is generally available at the lowest price, based on international drug price information sources. Therapeutic equivalence is only indicated on the basis of reviews of efficacy and safety and when consistent with WHO clinical guidelines. National lists should not use a similar symbol and should be specific in their final selection, which would depend on local availability and price. Examples of alternatives for the medicines with a square box symbol are not included in the Model List, but such information is provided in the *WHO model formulary* and in the Essential Medicines Library.

Procedures for updating the Model List

The procedures for updating the Model List are in line with the WHO recommended process for developing clinical practice guidelines. The key components are a systematic approach to collecting and review-

ing evidence and a transparent development process with several rounds of external review. The procedures are intended to serve as a model for developing or updating national and institutional clinical guidelines and lists of essential medicines. Further information on the procedures for updating the Model List, including descriptions of the applications and details of the review process, is available from the WHO web site.

Selection criteria

The choice of essential medicines depends on several factors, including public health relevance and the availability of data on the efficacy, safety and comparative cost-effectiveness of available treatments. Factors such as stability in various conditions, the need for special diagnostic or treatment facilities and pharmacokinetic properties are also considered if appropriate. In adapting the Model List to their own needs, countries often consider factors such as local demography and the pattern of prevalent diseases; treatment facilities; training and experience of available personnel; local availability of individual pharmaceutical products; financial resources; and environmental factors.

The selection of essential medicines must be based on valid scientific evidence; only medicines for which sound and adequate data on efficacy and safety are available should be selected. In the absence of adequate scientific evidence on current treatment of a priority disease, the WHO Expert Committee on the Selection and Use of Essential Medicines may either defer its decision regarding selection until more evidence becomes available, or choose to make recommendations based on expert opinion and experience.

Most essential medicines should be formulated as single compounds. Fixed-dose combination products are selected only when the combination has a proven advantage over single compounds administered separately in therapeutic effect, safety, adherence or in delaying the development of drug resistance in malaria, tuberculosis and HIV/AIDS.

When making cost comparisons between medicines, the cost of the total treatment, not just 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 are generally not made across therapeutic categories (e.g. between the treatment of tuberculosis and the treatment of malaria). The absolute cost of the treatment does 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 when selecting medicines for the Model List.

Quality assurance

Priority should be given to ensuring that available medicines have been made according to good manufacturing practices and are of assured quality. Factors that need to be considered include:

— knowledge of, and confidence in, the origin of the product;
— the pharmaceutical stability of the product, particularly in the environment that it will be used;
— where relevant, bioavailability and bioequivalence information.

It is recommended that all medicines be purchased from known manufacturers, their duly accredited agents, or recognized international agencies known to apply high standards in selecting their suppliers.

Promoting rational use of essential medicines

The selection of essential medicines is only one step towards the improvement of the quality of health care; selection needs to be followed by appropriate use. Each individual should receive the right medicine, in an adequate dose for an adequate duration, with appropriate information and follow-up treatment, and at an affordable cost. Within different countries and settings, this is influenced by a number of factors, such as regulatory decisions, procurement, information, training, and the context in which medicines are prescribed or recommended.

Training, education and the provision of medicines information

To ensure the safe, effective and prudent use of essential medicines, access to relevant, reliable and independent information on medicines is vital. Health care professionals should receive education about the use of medicines not only during their training but also throughout their careers. The more highly trained individuals should be encouraged to assume responsibility for educating those with less training. Health care providers and pharmacists who are responsible for dispensing medicines should take every opportunity to inform consumers about the rational use of products, including those for self-medication, at the time they are dispensed.

Governments, universities and professional associations have a critical role to play with regard to the improvement of undergraduate, postgraduate and continuing education in clinical pharmacology,

therapeutics and medicines information issues. Problem-based pharmacotherapy teaching has been shown to be a particularly effective strategy in this area.

Well presented and appropriate information about medicines not only ensures that they are used properly but also decreases the inappropriate use of medicines. Health ministries have a responsibility to arrange for the provision of such information. Independent medicines information activities should also be properly funded and, if necessary, financed through health care budgets. Electronic, readily accessible sources of medicines information are becoming more widely available and can form the basis of reliable medicines information systems in many settings.

Standard clinical guidelines

Standard clinical guidelines are an effective tool for assisting health professionals to choose the most appropriate medicine for a given patient with a given condition. They should be developed at national and local levels and updated on a regular basis. In order to be effective, however, standard clinical guidelines require the support of appropriate education and training programmes aimed at encouraging their use.

Drug and therapeutics committees

Drug and therapeutics committees can play an important role in the development and implementation of effective essential medicines programmes. Such committees should be encouraged to select products for local use from a national essential medicines list, to measure and monitor the use of these products in their own environments and to undertake interventions to improve their rational use. There is good evidence to suggest that involving both drug and therapeutics committees and prescribers in guideline development can contribute to improved prescribing behaviour.

Measuring and monitoring medicine use

The purpose of drug utilization studies is to examine the development, regulation, marketing, distribution, prescription, dispensing and use of medicines within a society, with special emphasis on the medical, social and economic consequences. Studies of this type consider all levels of the therapeutic chain, from the development of medicines to their use by consumers. Drug utilization studies can be medicine-oriented (i.e. focused on the use of a particular medicine or group of medicines) or problem-oriented (i.e. focused on the treatment of a particular condition or disease)

and can provide consumption indicators for a given country, area or institution.

Consumption can be measured in terms of economic expenditure (either in absolute terms or as a percentage of the total health budget), the number of units, or as Defined Daily Doses (DDDs). However, it is generally recommended that drug utilization studies be conducted using the Anatomical Therapeutic Chemical (ATC) classification and the DDD as the measuring unit, especially when making international comparisons on the use of medicines.

The efficacy of a medicine is best assessed on the basis of randomized clinical trials, which, if well conducted, provide reliable estimates of the treatment effect of a new medicine. However, clinical trials cannot be conducted in all possible populations or settings and therefore their results must be translated into routine clinical practice with care. Given that drug utilization studies generally provide evidence on the use and the effects of medicines in routine conditions, they can provide additional evidence for the evaluation of the effectiveness of a medicine.

Drug utilization studies and clinical trials are important tools for identifying those factors or elements of the therapeutic chain in need of improvement or change. The results of such studies should be taken into consideration when taking regulatory action, selecting medicines, or designing information, training and teaching programmes.

Monitoring of medicine safety and pharmacovigilance

Safety monitoring is an important part of the overall surveillance of medicine use. The aims of the various forms of pharmacovigilance are to identify new, previously unrecognized adverse effects of medicines, to quantify their risks, and to communicate these to drug regulatory authorities, health professionals, and, when relevant, the public. Voluntary reporting of adverse effects of medicines, on which the International WHO Programme for Drug Monitoring is based, has been effective in identifying a number of previously undescribed effects. Voluntary reporting schemes, together with other methods for assembling case series, can identify certain local safety problems, and thus form the basis for specific regulatory or educational interventions. The magnitude of the risk of adverse effects is generally evaluated using observational epidemiological methods, such as case–control, cohort and case–population studies. Each country and institution should set up simple schemes aimed at identifying problems related to the safety of medicines.

Explanatory notes

The **core list** presents a list of minimum medicine needs for a basic health care system, listing the most efficacious, safe and cost-effective medicines for priority conditions. Priority conditions are selected on the basis of current and estimated future public health relevance, and potential for safe and cost-effective treatment.

The **complementary list** presents essential medicines for priority diseases, for which specialized diagnostic or monitoring facilities, and/or specialist medical care, and/or specialist training are needed. In case of doubt medicines may also be listed as complementary on the basis of consistently higher costs or less attractive cost-effectiveness in a variety of settings.

When the strength of a medicine 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".

The square box symbol (□) is primarily intended to indicate similar clinical performance within a pharmacological class. The listed medicine should be the example of the class for which there is the best evidence for effectiveness and safety. In some cases, this may be the first medicine that is licensed for marketing; in other instances, subsequently licensed compounds may be safer or more effective. Where there is no difference in terms of efficacy and safety data, the listed medicine should be the one that is generally available at the lowest price, based on international drug price information sources. Therapeutic equivalence is only indicated on the basis of reviews of efficacy and safety and when consistent with WHO clinical guidelines. National lists should not use a similar symbol and should be specific in their final selection, which would depend on local availability and price.

Medicines are listed in alphabetical order, within sections.

1. Anaesthetics

1.1 *General anaesthetics and oxygen*

□ halothane	inhalation
ketamine	injection, 50 mg (as hydrochloride)/ml in 10-ml vial
nitrous oxide	inhalation
oxygen	inhalation (medicinal gas)
□ thiopental	powder for injection, 0.5 g, 1.0 g (sodium salt) in ampoule

1.2 *Local anaesthetics*

□ bupivacaine	injection, 0.25%, 0.5% (hydrochloride) in vial
	injection for spinal anaesthesia, 0.5% (hydrochloride) in 4-ml ampoule to be mixed with 7.5% glucose solution
□ lidocaine	injection, 1%, 2% (hydrochloride) in vial
	injection for spinal anaesthesia, 5% (hydrochloride) in 2-ml ampoule to be mixed with 7.5% glucose solution
	topical forms, 2–4% (hydrochloride)
lidocaine + epinephrine (adrenaline)	injection 1%, 2% (hydrochloride) + epinephrine 1 : 200 000 in vial
	dental cartridge 2% (hydrochloride) + epinephrine 1 : 80 000
Complementary list	
ephedrine	injection, 30 mg (hydrochloride)/ml in 1-ml ampoule (for use in spinal anaesthesia during delivery, to prevent hypotension)

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

atropine	injection, 1 mg (sulfate) in 1-ml ampoule
□ diazepam	injection, 5 mg/ml in 2-ml ampoule
	tablet, 5 mg
morphine	injection, 10 mg (sulfate or hydrochloride) in 1-ml ampoule
promethazine	elixir or syrup, 5 mg (hydrochloride)/5 ml

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

2. Analgesics, antipyretics, non-steroidal anti-inflammatory medicines, medicines used to treat gout and disease modifying agents used in rheumatoid disorders

2.1 *Non-opioids and non-steroidal anti-inflammatory medicines*

acetylsalicylic acid	tablet, 100–500 mg
	suppository, 50–150 mg
ibuprofen	tablet, 200 mg, 400 mg
paracetamol[a]	tablet, 100–500 mg
	suppository, 100 mg
	syrup, 125 mg/5 ml

2.2 *Opioid analgesics*

codeine	tablet, 30 mg (phosphate)
morphine	injection, 10 mg (sulfate or hydrochloride) in 1-ml ampoule
	oral solution, 10 mg (hydrochloride or sulfate)/5 ml
	tablet, 10 mg (sulfate)

2.3 *Medicines used to treat gout*

allopurinol	tablet, 100 mg

2.4 *Disease-modifying agents used in rheumatoid disorders*

chloroquine	tablet, 100 mg, 150 mg (as phosphate or sulfate)
Complementary list	
azathioprine	tablet, 50 mg
methotrexate	tablet, 2.5 mg (as sodium salt)
penicillamine	capsule or tablet, 250 mg
sulfasalazine	tablet, 500 mg

3. Antiallergics and medicines used in anaphylaxis

□ chlorphenamine	tablet, 4 mg (hydrogen maleate)
	injection, 10 mg (hydrogen maleate) in 1-ml ampoule
dexamethasone	injection, 4 mg dexamethasone phosphate (as disodium salt) in 1-ml ampoule

[a] Not recommended for anti-inflammatory use due to lack of proven benefit to that effect.
□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

3. Antiallergics and medicines used in anaphylaxis (*continued*)	
epinephrine (adrenaline)	injection, 1 mg (as hydrochloride or hydrogen tartrate) in 1-ml ampoule
hydrocortisone	powder for injection, 100 mg (as sodium succinate) in vial
□ prednisolone[a]	tablet, 5 mg, 25 mg
4. Antidotes and other substances used in poisonings	
Section 4 will be reviewed at the next meeting of the Expert Committee.	
4.1 ***Non-specific***	
charcoal, activated	powder
4.2 ***Specific***	
acetylcysteine	injection, 200 mg/ml in 10-ml ampoule
atropine	injection, 1 mg (sulfate) in 1-ml ampoule
calcium gluconate	injection, 100 mg/ml in 10-ml ampoule
deferoxamine	powder for injection, 500 mg (mesilate) in vial
dimercaprol	injection in oil, 50 mg/ml in 2-ml ampoule
DL-methionine	tablet, 250 mg
methylthioninium chloride (methylene blue)	injection, 10 mg/ml in 10-ml ampoule
naloxone	injection, 400 micrograms (hydrochloride) in 1-ml ampoule
penicillamine	capsule or tablet, 250 mg
potassium ferric hexacyanoferrate(II)·$2H_20$ (Prussian blue)	powder for oral administration
sodium calcium edetate	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. Anticonvulsants/antiepileptics	
carbamazepine	scored tablet, 100 mg, 200 mg
□ diazepam	injection, 5 mg/ml in 2-ml ampoule (intravenous or rectal)
magnesium sulfate[b]	injection, 500 mg/ml in 2-ml ampoule, 500 mg/ml in 10-ml ampoule

[a] There is no evidence for complete clinical similarity between prednisolone and dexamethasone at high doses.
[b] For use in eclampsia and severe pre-eclampsia and not for other convulsant disorders.
□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

5. Anticonvulsants/antiepileptics (*continued*)	
phenobarbital	tablet, 15–100 mg
	elixir, 15 mg/5 ml
phenytoin	capsule or tablet, 25 mg, 50 mg, 100 mg (sodium salt)
	injection, 50 mg/ml in 5-ml vial (sodium salt)
valproic acid	enteric coated tablet, 200 mg, 500 mg (sodium salt)
Complementary list	
ethosuximide	capsule, 250 mg
	syrup, 250 mg/5 ml
6. Anti-infective medicines	
6.1 *Anthelminthics*	
6.1.1 *Intestinal anthelminthics*	
albendazole	chewable tablet, 400 mg
levamisole	tablet, 50 mg, 150 mg (as hydrochloride)
□ mebendazole	chewable tablet, 100 mg, 500 mg
niclosamide[a]	chewable tablet, 500 mg
praziquantel	tablet, 150 mg, 600 mg
pyrantel	chewable tablet, 250 mg (as embonate)
	oral suspension, 50 mg (as embonate)/ml
6.1.2 *Antifilarials*	
ivermectin	scored tablet, 3 mg, 6 mg
Complementary list	
diethylcarbamazine	tablet, 50 mg, 100 mg (dihydrogen citrate)
suramin sodium	powder for injection, 1 g in vial
6.1.3 *Antischistosomals and other antitrematode medicine*	
praziquantel	tablet, 600 mg
triclabendazole	tablet, 250 mg

[a] Niclosamide is listed for use when praziquantel treatment fails.
□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

6. Anti-infective medicines (*continued*)

Complementary list	
oxamniquine[a]	capsule, 250 mg
	syrup, 250 mg/5 ml

6.2 *Antibacterials*

6.2.1 *β-Lactam medicines*[b]	
amoxicillin	capsule or tablet, 250 mg, 500 mg (anhydrous)
	powder for oral suspension, 125 mg (anhydrous)/5 ml
amoxicillin + clavulanic acid	tablet, 500 mg + 125 mg
ampicillin	powder for injection, 500 mg, 1 g (as sodium salt) in vial
benzathine benzylpenicillin	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) (sodium or potassium salt) in vial
cefixime[c]	capsule 400 mg
□ cloxacillin	capsule, 500 mg, 1 g (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
procaine benzylpenicillin	powder for injection, 1 g (= 1 million IU), 3 g (= 3 million IU) in vial
Complementary list	
ceftazidime	powder for injection, 250 mg (as pentahydrate) in vial

[a] oxamniquine is listed for use when praziquantel treatment fails.
[b] Applications for cefalexin and cefazolin are anticipated for the next meeting of the Expert Committee.
[c] Only listed for single-dose treatment of uncomplicated ano-genital gonorrhoea.
□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

6. Anti-infective medicines (*continued*)

□ *ceftriaxone*	powder for injection, 250 mg, 1 g (as sodium salt) in vial
imipenem[a] + *cilastatin*[a]	powder for injection 250 mg (as monohydrate) + 250 mg (as sodium salt), 500 mg (as monohydrate) + 500 mg (as sodium salt) in vial
6.2.2 *Other antibacterials*	
azithromycin[b]	capsule, 250 mg or 500 mg
	suspension 200 mg/5 ml
chloramphenicol	capsule, 250 mg
	oral suspension, 150 mg (as palmitate)/5 ml
	powder for injection, 1 g (sodium succinate) in vial
	oily suspension for injection, 0.5 g (as sodium succinate)/ml in 2-ml ampoule
ciprofloxacin[c]	tablet 250 mg (as hydrochloride)
doxycycline[c]	capsule or tablet, 100 mg (hydrochloride)
□ erythromycin	capsule or tablet, 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[c]	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
nitrofurantoin	tablet, 100 mg
spectinomycin	powder for injection, 2 g (as hydrochloride) in vial

[a] Only listed for the treatment of life-threatening hospital-based infection due to suspected or proven multidrug-resistant infection.
[b] Only listed for single-dose treatment of genital *Chlamydia trachomatis* and of trachoma.
[c] Final selection depends on indication for use.
□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

6. Anti-infective medicines (*continued*)

sulfamethoxazole + trimethoprim	tablet, 100 mg + 20 mg, 400 mg + 80 mg
	oral suspension, 200 mg + 40 mg/5 ml
	injection, 80 mg + 16 mg/ml in 5-ml and 10-ml ampoules
trimethoprim	tablet, 100 mg, 200 mg
Complementary list	
clindamycin	capsule, 150 mg
	injection, 150 mg (as phosphate)/ml
sulfadiazine	tablet, 500 mg
	injection, 250 mg (sodium salt) in 4-ml ampoule
vancomycin	powder for injection, 250 mg (as hydrochloride) in vial

6.2.3 *Antileprosy medicines*

Medicines used in the treatment of leprosy should never be used except in combination. Combination therapy is essential to prevent the emergence of drug resistance. Colour-coded blister packs (multidrug therapy (MDT) blister packs) containing standard two-medicine (paucibacillary leprosy) or three-medicine (multibacillary leprosy) combinations for adult and childhood leprosy should be used. MDT blister packs can be supplied free of charge through WHO.

clofazimine	capsule, 50 mg, 100 mg
dapsone	tablet, 25 mg, 50 mg, 100 mg
rifampicin	capsule or tablet, 150 mg, 300 mg
6.2.4 *Antituberculosis medicines*	
ethambutol	tablet, 100–400 mg (hydrochloride)
isoniazid	tablet, 100–300 mg
isoniazid + ethambutol	tablet, 150 mg + 400 mg
pyrazinamide	tablet, 400 mg
rifampicin	capsule or tablet, 150 mg, 300 mg
rifampicin + isoniazid	tablet, 60 mg + 30 mg; 150 mg + 75 mg; 300 mg + 150 mg; 60 mg + 60 mg;[a] 150 mg + 150 mg[a]

[a] For intermittent use three times weekly.

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

6. Anti-infective medicines (*continued*)

rifampicin + isoniazid + pyrazinamide	tablet, 60 mg + 30 mg + 150 mg; 150 mg + 75 mg + 400 mg
	150 mg + 150 mg + 500 mg[a]
rifampicin + isoniazid + pyrazinamide + ethambutol	tablet, 150 mg + 75 mg + 400 mg + 275 mg
streptomycin	powder for injection, 1 g (as sulfate) in vial
Complementary list	
amikacin[b]	powder for injection, 1000 mg in vial
p-*aminosalicylic acid*[b]	tablet, 500 mg; granules, 4 g in sachet
capreomycin[b]	powder for injection, 1000 mg in vial
ciprofloxacin[b]	tablet, 250 mg, 500 mg
cycloserine[b]	capsule or tablet, 250 mg
ethionamide[b]	tablet, 125 mg, 250 mg
kanamycin[b]	powder for injection, 1000 mg in vial
levofloxacin[b]	tablet, 250 mg, 500 mg
ofloxacin[b]	tablet, 200 mg, 400 mg

6.3 *Antifungal medicines*

clotrimazole	vaginal tablet, 100 mg, 500 mg
	vaginal cream, 1%, 10%
□ fluconazole	capsule, 50 mg
	injection, 2 mg/ml in vial
	oral suspension, 50 mg/5 ml
griseofulvin	capsule or tablet, 125 mg, 250 mg
nystatin	tablet, 100 000 IU, 500 000 IU
	lozenge 100 000 IU
	pessary, 100 000 IU
Complementary list	
amphotericin B	powder for injection, 50 mg in vial

[a] For intermittent use three times weekly.
[b] Reserve second-line medicine for the treatment of multidrug-resistant tuberculosis (MDR-TB) should be used in specialized centres adhering to WHO standards for TB control. These medicines will be reviewed at the next meeting of the Expert Committee.
□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

6. Anti-infective medicines (*continued*)

flucytosine	capsule, 250 mg
	infusion, 2.5 g in 250 ml
potassium iodide	saturated solution

6.4 *Antiviral medicines*

6.4.1 *Antiherpes medicines*

□ aciclovir	tablet, 200 mg; powder for injection, 250 mg (as sodium salt) in vial

6.4.2 *Antiretroviral medicines*

The antiretroviral medicines do not cure the HIV infection, they only temporarily suppress viral replication and improve symptoms. They have various adverse effects and patients receiving these medicines require careful monitoring by adequately trained health professionals. For these reasons, continued rigorous promotion of measures to prevent new infections is essential and the need for this has not been diminished in any way by the addition of antiretroviral medicines to the Model List. Adequate resources and trained health professionals are a prerequisite for the introduction of this class of medicines. Effective therapy requires commencement of three or four medicines simultaneously, and alternative regimens are necessary to meet specific requirements at start-up, to substitute for first-line regimens in the case of toxicity, or to replace failing regimens. In order to simplify treatment, facilitate storage and distribution, and improve patients' adherence to the treatment plan, the Committee recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations. These include modified dosage forms, non-refrigerated formulations and paediatric formulations with assured pharmaceutical quality and interchangeability with the single products as approved by the relevant drug regulatory authority.

6.4.2.1 Nucleoside reverse transcriptase inhibitors

abacavir (ABC)	tablet, 300 mg (as sulfate)
	oral solution, 100 mg (as sulfate)/5 ml
didanosine (ddI)	buffered chewable, dispersible tablet, 25 mg, 50 mg, 100 mg, 150 mg, 200 mg
	buffered powder for oral solution, 100 mg, 167 mg, 250 mg packets
	unbuffered enteric coated capsule, 125 mg, 200 mg, 250 mg, 400 mg
lamivudine (3TC)	tablet, 150 mg
	oral solution, 50 mg/5 ml
stavudine (d4T)	capsule 15 mg, 20 mg, 30 mg, 40 mg
	powder for oral solution, 5 mg/5 ml

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

6. Anti-infective medicines (*continued*)

zidovudine (ZDV or AZT)	tablet, 300 mg
	capsule 100 mg, 250 mg
	oral solution or syrup, 50 mg/ 5ml
	solution for IV infusion injection, 10 mg/ml in 20-ml vial

6.4.2.2 Non-nucleoside reverse transcriptase inhibitors

efavirenz (EFV or EFZ)	capsule, 50 mg, 100 mg, 200 mg
	oral solution, 150 mg/5 ml
nevirapine (NVP)	tablet, 200 mg
	oral suspension, 50 mg/5 ml

6.4.2.3 Protease inhibitors

Selection of two or three protease inhibitors from the Model List will need to be determined by each country after consideration of local treatment guidelines and experience, as well as the comparative costs of available products. Ritonavir is recommended for use in combination with indinavir, lopinavir and saquinavir as a booster, and not as a medicine in its own right.

indinavir (IDV)	capsule, 200 mg, 333 mg, 400 mg (as sulfate)
lopinavir + ritonavir (LPV/r)	capsule, 133.3 mg + 33.3 mg
	oral solution, 400 mg + 100 mg/5 ml
nelfinavir (NFV)	tablet, 250 mg (as mesilate)
	oral powder, 50 mg/g
ritonavir	capsule, 100 mg
	oral solution, 400 mg/5 ml
saquinavir (SQV)	capsule, 200 mg

6.5 *Antiprotozoal medicines*

6.5.1 *Antiamoebic and antigiardiasis medicines*

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

6.5.2 *Antileishmaniasis medicines*

□ meglumine antimoniate	injection, 30%, equivalent to approximately 8.1% antimony in 5-ml ampoule

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

6. Anti-infective medicines (*continued*)

Complementary list	
amphotericin B	powder for injection, 50 mg in vial
pentamidine	powder for injection, 200 mg, 300 mg (isetionate) in vial

6.5.3 *Antimalarial medicines*

6.5.3.1 For curative treatment

Medicines for the treatment of *Plasmodium falciparum* malaria cases should be used in combination.

amodiaquine[a]	tablet, 153 mg or 200 mg (base)
artemether + lumefantrine[b]	tablet, 20 mg + 120 mg
chloroquine	tablet 100 mg, 150 mg (as phosphate or sulfate)
	syrup, 50 mg (as phosphate or sulfate)/5 ml
	injection, 40 mg (as hydrochloride, phosphate or sulfate)/ml in 5-ml ampoule
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
Complementary list	
artemether	injection, 80 mg/ml in 1-ml ampoule
artesunate	tablet, 50 mg
doxycycline	capsule or tablet, 100 mg (hydrochloride)
	(for use only in combination with quinine)
mefloquine	tablet, 250 mg (as hydrochloride)
sulfadoxine + pyrimethamine	tablet, 500 mg + 25 mg

6.5.3.2 For prophylaxis

chloroquine	tablet, 150 mg (as phosphate or sulfate)
	syrup, 50 mg (as phosphate or sulfate)/5 ml

[a] Amodiaquine should preferably be used as part of combination therapy.
[b] Recommended for use in areas with significant drug resistance and not in pregnancy or in children below 10 kg.
□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

6. Anti-infective medicines (*continued*)	
doxycycline	capsule or tablet, 100 mg (hydrochloride)
mefloquine	tablet, 250 mg (as hydrochloride)
proguanil[a]	tablet, 100 mg (hydrochloride)
6.5.4 *Anti-pneumocystosis and antitoxoplasmosis medicines*	
pyrimethamine	tablet, 25 mg
sulfamethoxazole + trimethoprim	injection, 80 mg + 16 mg/ml in 5-ml ampoule
	80 mg + 16 mg/ml in 10-ml ampoule
Complementary list	
pentamidine	tablet, 200 mg, 300 mg
6.5.5 *Antitrypanosomal medicines*	
6.5.5.1 African trypanosomiasis	
melarsoprol	injection, 3.6% solution
suramin sodium	powder for injection, 1 g in vial
Complementary list	
eflornithine	injection, 200 mg (hydrochloride)/ml in 100-ml bottle
pentamidine	powder for injection, 200 mg, 300 mg (isetionate) in vial
6.5.5.2 American trypanosomiasis	
benznidazole	tablet, 100 mg
nifurtimox	tablet, 30 mg, 120 mg, 250 mg
7. Antimigraine medicines	
7.1 *For treatment of acute attack*	
acetylsalicylic acid	tablet, 300–500 mg
paracetamol	tablet, 300–500 mg
7.2 *For prophylaxis*	
□ propranolol	tablet, 20 mg, 40 mg (hydrochloride)

[a] For use only in combination with chloroquine.
□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

8. Antineoplastic, immunosuppressives and medicines used in palliative care

8.1 *Immunosuppressive medicines*

Complementary list

azathioprine	tablet, 50 mg
	powder for injection, 100 mg (as sodium salt) in vial
ciclosporin	capsule, 25 mg
	concentrate for injection, 50 mg/ml in 1-ml ampoule for organ transplantation

8.2 *Cytotoxic medicines*

Complementary list

asparaginase	powder for injection, 10 000 IU in vial
bleomycin	powder for injection, 15 mg (as sulfate) in vial
calcium folinate	tablet, 15 mg
	injection, 3 mg/ml in 10-ml ampoule
chlorambucil	tablet, 2 mg
chlormethine	powder for injection, 10 mg (hydrochloride) in vial
cisplatin	powder for injection, 10 mg, 50 mg in vial
cyclophosphamide	tablet, 25 mg
	powder for injection, 500 mg in vial
cytarabine	powder for injection, 100 mg in vial
dacarbazine	powder for injection, 100 mg in vial
dactinomycin	powder for injection, 500 micrograms in vial
daunorubicin	powder for injection, 50 mg (as hydrochloride)
doxorubicin	powder for injection, 10 mg, 50 mg (hydrochloride) in vial
etoposide	capsule, 100 mg
	injection, 20 mg/ml in 5-ml ampoule
fluorouracil	injection, 50 mg/ml in 5-ml ampoule
levamisole	tablet, 50 mg (as hydrochloride)
mercaptopurine	tablet, 50 mg

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

8. Antineoplastic, immunosuppressives and medicines used in palliative care (*continued*)

methotrexate	tablet, 2.5 mg (as sodium salt)
	powder for injection, 50 mg (as sodium salt) in vial
procarbazine	capsule, 50 mg (as hydrochloride)
vinblastine	powder for injection, 10 mg (sulfate) in vial
vincristine	powder for injection, 1 mg, 5 mg (sulfate) in vial

8.3 ***Hormones and antihormones***

Complementary list	
dexamethasone	injection, 4 mg dexamethasone phosphate (as disodium salt) in 1-ml ampoule
hydrocortisone	powder for injection, 100 mg (as sodium succinate) in vial
□ *prednisolone*[a]	tablet, 5 mg, 25 mg
tamoxifen	tablet, 10 mg, 20 mg (as citrate)

8.4 ***Medicines used in palliative care***

The WHO Expert Committee on the Selection and Use of Essential Medicines recommended that all the medicines mentioned in the WHO publication *Cancer pain relief: with a guide to opioid availability*, 2nd ed., be considered essential (*1*). The medicines are included in the relevant sections of the Model List, according to their therapeutic use, e.g. as analgesics.

9. Antiparkinsonism medicines

biperiden	tablet, 2 mg (hydrochloride)
	injection, 5 mg (lactate) in 1-ml ampoule
levodopa + □carbidopa	tablet, 100 mg + 10 mg; 250 mg + 25 mg

10. Medicines affecting the blood

10.1 ***Antianaemia medicines***

ferrous salt	tablet, equivalent to 60 mg iron
	oral solution, equivalent to 25 mg iron (as sulfate)/ml
ferrous salt + folic acid[b]	tablet, equivalent to 60 mg iron + 400 micrograms folic acid

[a] There is no evidence for complete clinical similarity between prednisolone and dexamethasone at high doses.
[b] Nutritional supplement for use during pregnancy.
□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

10. Medicines affecting the blood (*continued*)

folic acid	tablet, 1 mg, 5 mg
hydroxocobalamin	injection, 1 mg in 1-ml ampoule

10.2 *Medicines affecting coagulation*

heparin sodium	injection, 1000 IU/ml, 5000 IU/ml, 20 000 IU/ml in 1-ml ampoule
phytomenadione	injection, 10 mg/ml in 5-ml ampoule
	tablet, 10 mg
protamine sulfate	injection, 10 mg/ml in 5-ml ampoule
□ warfarin	tablet, 1 mg, 2 mg, 5 mg (sodium salt)

11. Blood products and plasma substitutes

11.1 *Plasma substitutes*

□ dextran 70[a]	injectable solution, 6%

11.2 *Plasma fractions for specific use*

All plasma fractions should comply with the *Requirements for the collection, processing and quality control of blood, blood components, and plasma derivatives* (Revised 1992) as published in the forty-third report of the WHO Expert Committee on Biological Standardization (*2*).

Complementary list

□ *factor VIII concentrate*	dried
□ *factor IX complex (coagulation factors, II, VII, IX, X) concentrate*	dried

12. Cardiovascular medicines

12.1 *Antianginal medicines*

□ atenolol	tablet, 50 mg, 100 mg
glyceryl trinitrate	tablet (sublingual), 500 micrograms
□ isosorbide dinitrate	tablet (sublingual), 5 mg
verapamil	tablet, 40 mg, 80 mg (hydrochloride)

12.2 *Antiarrhythmic medicines*

This subsection will be reviewed at the next meeting of the Expert Committee when it is anticipated that applications for amiodarone and sotalol will be received.

[a] Polygeline, injectable solution, 3.5% is considered as equivalent.
□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

12. Cardiovascular medicines (*continued*)

□ atenolol	tablet, 50 mg, 100 mg
digoxin	tablet, 62.5 micrograms, 250 micrograms
	oral solution, 50 micrograms/ml
	injection, 250 micrograms/ml in 2-ml ampoule
epinephrine (adrenaline)	injection, 1 mg (as hydrochloride)/ml in ampoule
lidocaine	injection, 20 mg (hydrochloride)/ml in 5-ml ampoule
verapamil	tablet, 40 mg, 80 mg (hydrochloride)
	injection, 2.5 mg (hydrochloride)/ml in 2-ml ampoule
Complementary list	
□ *procainamide*	injection, 100 mg (hydrochloride)/ml in 10-ml ampoule
□ *quinidine*	tablet, 200 mg (sulfate)

12.3 *Antihypertensive medicines*

□ amlodipine	tablet, 5 mg
□ atenolol	tablet, 50 mg, 100 mg
□ enalapril	tablet, 2.5 mg
hydralazine[a]	tablet, 25 mg, 50 mg (hydrochloride)
	powder for injection, 20 mg (hydrochloride) in ampoule
hydrochlorothiazide	scored tablet, 25 mg
methyldopa[b]	tablet, 250 mg
Complementary list	
sodium nitroprusside	powder for infusion, 50 mg in ampoule

[a] Hydralazine is listed for use in the acute management of severe pregnancy-induced hypertension only. Its use in the treatment of essential hypertension is not recommended in view of the availability of more evidence of efficacy and safety of other medicines.

[b] Methyldopa is listed for use in the management of pregnancy-induced hypertension only. Its use in the treatment of essential hypertension is not recommended in view of the availability of more evidence of efficacy and safety of other medicines.

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

12. Cardiovascular medicines (*continued*)

12.4 *Medicines used in heart failure*

This subsection will be reviewed at the next meeting of the Expert Committee.

digoxin	tablet, 62.5 micrograms, 250 micrograms
	oral solution, 50 micrograms/ml
	injection, 250 micrograms/ml in 2-ml ampoule
□ enalapril	tablet, 2.5 mg
□ furosemide	tablet, 40 mg
	injection, 10 mg/ml in 2-ml ampoule
□ hydrochlorothiazide	scored tablet, 25 mg
Complementary list	
dopamine	injection, 40 mg (hydrochloride) in 5-ml vial

12.5 *Antithrombotic medicines*

acetylsalicylic acid	tablet, 100 mg
Complementary list	
streptokinase	*powder for injection, 1.5 million IU in vial*

12.6 *Lipid-lowering agents*

The WHO Expert Committee on the Selection and Use of Essential Medicines recognizes the value of lipid-lowering medicines in treating patients with hyperlipidaemia. β-Hydroxy-β-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors, often referred to as "statins", are a family of potent and effective lipid-lowering medicines with a good tolerability profile. Several of these medicines have been shown to reduce the incidence of fatal and non-fatal myocardial infarction, stroke and mortality (all causes), as well as the need for coronary by-pass surgery. All remain very costly but may be cost-effective for secondary prevention of cardiovascular disease as well as for primary prevention in some very high-risk patients. Since no single medicine has been shown to be significantly more effective or less expensive than others in the group, none is included in the Model List; the choice of medicine for use in patients at highest risk should be decided at the national level.

13. Dermatological medicines (topical)

13.1 *Antifungal medicines*

benzoic acid + salicylic acid	ointment or cream, 6% + 3%
□ miconazole	ointment or cream, 2% (nitrate)
sodium thiosulfate	solution, 15%

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

13. Dermatological medicines (topical) (*continued*)

13.2 *Anti-infective medicines*

Complementary list

selenium sulfide	detergent-based suspension, 2%
□ methylrosanilinium	aqueous solution, 0.5%
chloride (gentian violet)	tincture, 0.5%
neomycin sulfate + □ bacitracin	ointment, 5 mg neomycin sulfate + 500 IU bacitracin zinc/g
potassium permanganate	aqueous solution, 1 : 10 000
silver sulfadiazine	cream, 1%, in 500-g container

13.3 *Anti-inflammatory and antipruritic medicines*

□ betamethasone	ointment or cream, 0.1% (as valerate)
□ calamine lotion	lotion
□ hydrocortisone	ointment or cream, 1% (acetate)

13.4 *Astringent medicines*

aluminium diacetate	solution, 13% for dilution

13.5 *Medicines affecting skin differentiation and proliferation*

benzoyl peroxide	lotion or cream, 5%
coal tar	solution, 5%
dithranol	ointment, 0.1%–2%
fluorouracil	ointment, 5%
□ podophyllum resin	solution, 10–25%
salicylic acid	solution, 5%
urea	ointment or cream, 10%

13.6 *Scabicides and pediculicides*

□ benzyl benzoate	lotion, 25%
permethrin	cream, 5%
	lotion, 1%

14. Diagnostic agents

14.1 *Ophthalmic medicines*

fluorescein	eye drops, 1% (sodium salt)
□ tropicamide	eye drops, 0.5%

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

14. Diagnostic agents (*continued*)	
14.2 *Radiocontrast media*	
□ amidotrizoate	injection, 140–420 mg iodine (as sodium or meglumine salt)/ml in 20-ml ampoule
barium sulfate	aqueous suspension
□ iohexol	injection, 140–350 mg iodine/ml in 5-ml, 10-ml or 20-ml ampoule
□ iopanoic acid	tablet, 500 mg
□ propyliodone	oily suspension, 500–600 mg/ml in 20-ml ampoule[a]
Complementary list	
□ *meglumine iotroxate*	*solution, 5–8 g iodine in 100–250 ml*
15. Disinfectants and antiseptics	
15.1 *Antiseptics*	
□ chlorhexidine	solution, 5% (digluconate) for dilution
□ ethanol	solution, 70% (denatured)
□ polyvidone iodine	solution, 10%
15.2 *Disinfectants*	
□ chlorine base compound	powder (0.1% available chlorine) for solution
□ chloroxylenol	solution, 4.8%
glutaral	solution, 2%
16. Diuretics	
amiloride	tablet, 5 mg (hydrochloride)
□ furosemide	tablet, 40 mg
	injection, 10 mg/ml in 2-ml ampoule
□ hydrochlorothiazide	scored tablet, 25 mg
mannitol	injectable solution, 10%, 20%
spironolactone	tablet, 25 mg
17. Gastrointestinal medicines	
17.1 *Antacids and other antiulcer medicines*	
aluminium hydroxide	tablet, 500 mg
	oral suspension, 320 mg/5 ml

[a] For administration only into the bronchial tree.

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

17. Gastrointestinal medicines (*continued*)

magnesium hydroxide	oral suspension, equivalent to 550 mg magnesium oxide/10 ml
□ ranitidine	tablet, 150 mg (as hydrochloride)
	oral solution, 75 mg/5 ml
	injection, 25 mg/ml in 2-ml ampoule

17.2 *Antiemetic medicines*

metoclopramide	tablet, 10 mg (hydrochloride)
	injection, 5 mg (hydrochloride)/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 *Anti-inflammatory medicines*

□ sulfasalazine	tablet, 500 mg
	suppository, 500 mg
	retention enema
Complementary list	
□ *hydrocortisone*[a]	suppository, 25 mg (acetate)
	retention enema

17.4 *Laxatives*

□ senna	tablet, 7.5 mg (sennosides) (or traditional dosage forms)

17.5 *Medicines used in diarrhoea*

17.5.1 *Oral rehydration*

oral rehydration salts (for glucose–electrolyte solution)	powder, 20.5 g/l	
	Components (for 1 litre of glucose–electrolyte solution)[b]	
	glucose:	13.5 g/l
	sodium chloride:	2.6 g/l
	potassium chloride:	1.5 g/l

[a] The square box symbol (□) only applies to hydrocortisone retention enema.
[b] In cases of cholera a higher concentration of sodium may be required.
□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

17. Gastrointestinal medicines (*continued*)

trisodium citrate dihydrate[a]:	2.9 g/l
These components provide a glucose–electrolyte solution with the following molar concentrations:	
glucose:	75 mEq
sodium:	75 mEq or mmol/l
chloride:	65 mEq or mmol/l
potassium:	20 mEq or mmol/l
citrate:	10 mmol/l
osmolarity:	245 mOsm/l

17.5.2 *Medicines for diarrhoea in children*

zinc sulfate[b]	tablet or syrup in 10 mg per unit dosage forms

17.5.3 *Antidiarrhoeal (symptomatic) medicines for adults*

codeine[c]	tablet, 30 mg (phosphate)

18. Hormones, other endocrine medicines and contraceptives

18.1 *Adrenal hormones and synthetic substitutes*

Addison disease is a rare condition; adrenal hormones for the treatment of this condition are already included in section 3.

18.2 *Androgens*

Complementary list

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

18.3 *Contraceptives*

This subsection will be reviewed at the next meeting of the Expert Committee.

18.3.1 *Oral hormonal contraceptives*

□ ethinylestradiol + □ levonorgestrel	tablet, 30 micrograms + 150 micrograms

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

[b] In acute diarrhoea, zinc sulfate should be used as an adjunct to oral rehydration salts.

[c] The therapeutic efficacy of this item has been questioned and its continued inclusion on the list will be reviewed at the next meeting of the Expert Committee.

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

18. Hormones, other endocrine medicines and contraceptives (*continued*)

□ ethinylestradiol + □ norethisterone	tablet, 35 micrograms + 1.0 mg
levonorgestrel	tablet, 30 micrograms, 750 micrograms (pack of two), 1.5 mg
18.3.2 *Injectable hormonal contraceptives*	
medroxyprogesterone acetate	depot injection, 150 mg/ml in 1-ml vial
norethisterone enantate	oily solution, 200 mg/ml in 1-ml ampoule
18.3.3 *Intrauterine devices*	
copper-containing device	
18.3.4 *Barrier methods*	
condoms	
diaphragms	
18.4 *Estrogens*	
□ ethinylestradiol[a]	tablet, 10 micrograms, 50 micrograms
18.5 *Insulins and other antidiabetic agents*	
glibenclamide	tablet, 2.5 mg, 5 mg
insulin injection (soluble)	injection, 40 IU/ml in 10-ml vial, 100 IU/ml in 10-ml vial
intermediate-acting insulin	injection, 40 IU/ml in 10-ml vial
	100 IU/ml in 10-ml vial (as compound insulin zinc suspension or isophane insulin)
metformin	tablet, 500 mg (hydrochloride)
18.6 *Ovulation inducers*	
Complementary list	
clomifene	tablet, 50 mg (citrate)
18.7 *Progestogens*	
norethisterone[a]	tablet, 5 mg

[a] The public health relevance and/or comparative efficacy and/or safety of this item has been questioned and its continued inclusion on the Model List will be reviewed at the next meeting of the Expert Committee.

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

18. Hormones, other endocrine medicines and contraceptives (*continued*)

Complementary list

medroxyprogesterone acetate[a]	tablet, 5 mg

18.8 *Thyroid hormones and antithyroid medicines*

levothyroxine	tablet, 50 micrograms, 100 micrograms (sodium salt)
potassium iodide	tablet, 60 mg
□ propylthiouracil	tablet, 50 mg

19. Immunologicals

19.1 *Diagnostic agents*

All tuberculins should comply with the WHO Requirements for Tuberculins (Revised 1985). WHO Expert Committee on Biological Standardization, Thirty-sixth report (WHO Technical Report Series, No. 745, 1987, Annex 1) (*3*).

tuberculin, purified protein derivative (PPD)	injection

19.2 *Sera and immunoglobulins*

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

anti-D immunoglobulin (human)	injection, 250 micrograms in single-dose vial
antitetanus immunoglobulin (human)	injection, 500 IU in vial
antivenom serum[b]	injection
diphtheria antitoxin	injection, 10 000 IU, 20 000 IU in vial
□ rabies immunoglobulin	injection, 150 IU/ml in vial

19.3 *Vaccines*

All vaccines should comply with the WHO requirements for biological substances, as published in the reports of the WHO Expert Committee on Biological Standardization. BCG vaccines should comply with the Requirements for Dried BCG Vaccine (Revised 1985), as published in the thirty-sixth report of the WHO

[a] The public health relevance and/or comparative efficacy and/or safety of this item has been questioned and its continued inclusion on the list will be reviewed at the next meeting of the Expert Committee.
[b] Exact type to be defined locally.
□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

19. Immunologicals (*continued*)

Expert Committee on Biological Standardization (*4*) and subsequent Amendment 1987 as published in the thirty-eighth report of the WHO Expert Committee on Biological Standardization (*5*). Diphtheria, pertussis and tetanus vaccines should comply with the Requirements for Diphtheria, Tetanus, Pertussis and Combined Vaccines (Revised 1989), as published in the fortieth report of the WHO Expert Committee on Biological Standardization (*6*). Hepatitis B vaccines should comply with the Requirements for Hepatitis B Vaccine Prepared from Plasma (Revised 1994), as published in the forty-fifth report of the WHO Expert Committee on Biological Standardization (*7*). Measles, mumps and rubella vaccines should comply with the Requirements for Measles, Mumps and Rubella Vaccines and Combined Vaccine (Live) (Revised 1992), as published in the forty-third report of the WHO Expert Committee on Biological Standardization (*8*) and subsequent Note, as published in the forty-fourth report of the WHO Expert Committee on Biological Standardization (*9*). Poliomyelitis vaccines should comply with the Requirements for Poliomyelitis Vaccine (Oral) (Revised 1989) as published in the fortieth report of the WHO Expert Committee on Biological Standardization (*10*) or the Requirements for Poliomyelitis Vaccine (Inactivated) (Revised 1981), as published in the report of the WHO Expert Committee on Biological Standardization (*11*) and subsequent Addendum 1985, as published in the thirty-sixth report of the WHO Expert Committee on Biological Standardization (*12*). Influenza vaccines should comply with the Requirements for Influenza Vaccine (Inactivated) (Revised 1990), as published in the forty-first report of the WHO Expert Committee on Biological Standardization (*13*). Meningococcal meningitis vaccines should comply with the Requirements for Meningococcal Polysaccharide Vaccine, as published in the report of the WHO Expert Committee on Biological Standardization (*14*) and subsequent Addendum 1980, incorporating Addendum 1976 and Addendum 1977, as published in the thirty-first report of the WHO Expert Committee on Biological Standardization (*15*). Rabies vaccines should comply with the Requirements for Rabies Vaccine for Human Use (Revised 1980), as published in the thirty-first report of the WHO Expert Committee on Biological Standardization (*16*) and subsequent Amendment 1992, as published in the forty-third report of the WHO Expert Committee on Biological Standardization (*17*), or the Requirements for Rabies Vaccine (Inactivated) for Human Use Produced in Continuous Cell Lines (Revised 1986), as published in the thirty-seventh report of the WHO Expert Committee on Biological Standardization (*18*) and subsequent Amendment 1992, as published in the forty-third report of the WHO Expert Committee on Biological Standardization (*19*). Typhoid vaccines should comply with the Requirements for Typhoid Vaccine (Live, Attenuated, Ty 21s, Oral), as published in the report of the WHO Expert Committee on Biological Standardization (*20*) or the Requirements for Vi Polysaccharide Typhoid Vaccine, as published in the forty-third report of the WHO Expert Committee on Biological Standardization (*21*). Yellow fever vaccines should comply with Requirements for Yellow Fever Vaccine (Revised 1995), as published in the forty-sixth report of the WHO Expert Committee on Biological Standardization (*22*).

19. Immunologicals (*continued*)

19.3.1 *For universal immunization*

BCG vaccine

diphtheria vaccine

hepatitis B vaccine

measles vaccine

pertussis vaccine

poliomyelitis vaccine

tetanus vaccine

19.3.2 *For specific groups of individuals*

influenza vaccine

meningococcal meningitis vaccine

mumps vaccine

rabies vaccine (inactivated: prepared in cell culture)

rubella vaccine

typhoid vaccine

yellow fever vaccine

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

□ alcuronium[a]	injection, 5 mg (chloride)/ml in 2-ml ampoule
neostigmine	tablet, 15 mg (bromide)
	injection, 500 micrograms in 1-ml ampoule
	2.5 mg (metilsulfate) in 1-ml ampoule
suxamethonium	injection, 50 mg (chloride)/ml in 2-ml ampoule
	powder for injection (chloride), in vial
Complementary list	
pyridostigmine	tablet, 60 mg (bromide)
	injection, 1 mg in 1-ml ampoule

[a] It is likely that alcuronium will be replaced and that similar products, including atracurium and/or pancuronium will be added at the next meeting of the Expert Committee.

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

20. Muscle relaxants (peripherally-acting) and cholinesterase inhibitors (*continued*)

□ *vecuronium*	powder for injection, 10 mg (bromide) in vial

21. Ophthalmological preparations

This section will be reviewed at the next meeting of the Expert Committee.

21.1 *Anti-infective agents*

□ gentamicin[a]	solution (eye drops), 0.3% (sulfate)
□ idoxuridine	solution (eye drops), 0.1%
	eye ointment, 0.2%
□ tetracycline	eye ointment, 1% (hydrochloride)

21.2 *Anti-inflammatory agents*

□ prednisolone	solution (eye drops), 0.5% (sodium phosphate)

21.3 *Local anaesthetics*

□ tetracaine	solution (eye drops), 0.5% (hydrochloride)

21.4 *Miotics and antiglaucoma medicines*

acetazolamide	tablet, 250 mg
□ pilocarpine	solution (eye drops), 2%, 4% (hydrochloride or nitrate)
□ timolol	solution (eye drops), 0.25%, 0.5% (as maleate)

21.5 *Mydriatics*

atropine	solution (eye drops), 0.1%, 0.5%, 1% (sulfate)
Complementary list	
epinephrine (adrenaline)	solution (eye drops), 2% (as hydrochloride)

22. Oxytocics and antioxytocics

22.1 *Oxytocics*

□ ergometrine	injection, 200 micrograms (hydrogen maleate) in 1-ml ampoule
oxytocin	injection, 10 IU in 1-ml ampoule
Complementary list	
misoprostol	vaginal tablet, 25 micrograms

[a] Final selection depends on indication for use.

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

22. Oxytocics and antioxytocics (*continued*)

mifepristone[a] — misoprostol[a]	tablet, 200 mg — tablet, 200 micrograms

Where permitted under national law and where culturally acceptable.

22.2 *Antioxytocics*

nifedipine	immediate release capsule, 10 mg

23. *Peritoneal dialysis solution*

Complementary list

intraperitoneal dialysis solution (of appropriate composition)	parenteral solution

24. Psychotherapeutic medicines

24.1 *Medicines used in psychotic disorders*

□ chlorpromazine	tablet, 100 mg (hydrochloride)
	syrup, 25 mg (hydrochloride)/5 ml
	injection, 25 mg (hydrochloride)/ml in 2-ml ampoule
□ fluphenazine	injection, 25 mg (decanoate or enantate) in 1-ml ampoule
□ haloperidol	tablet, 2 mg, 5 mg
	injection, 5 mg in 1-ml ampoule

24.2 *Medicines used in mood disorders*

24.2.1 *Medicines used in depressive disorders*

□ amitriptyline	tablet, 25 mg (hydrochloride)

24.2.2 *Medicines used in bipolar disorders*

carbamazepine	scored tablet, 100 mg, 200 mg
lithium carbonate	capsule or tablet, 300 mg
valproic acid	enteric coated tablet, 200 mg, 500 mg (sodium salt)

24.3 *Medicines used in generalized anxiety and sleep disorders*

□ diazepam	scored tablet, 2 mg, 5 mg

24.4 *Medicines used for obsessive–compulsive disorders and panic attacks*

clomipramine	capsules, 10 mg, 25 mg (hydrochloride)

[a] Requires close medical supervision.
□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

24. Psychotherapeutic medicines (*continued*)

24.5 *Medicines used in substance dependence programmes*

Complementary list

□ *methadone*[a]	oral solution, 5 mg/5 ml, 10 mg/5 ml
	concentrate for oral solution, 5 mg/ml, 10 mg/ml (hydrochloride)

25. Medicines acting on the respiratory tract

25.1 *Antiasthmatic and medicines for chronic obstructive pulmonary disease*

□ beclometasone	inhalation (aerosol), 50 micrograms per dose (dipropionate)
	250 micrograms (dipropionate) per dose
epinephrine (adrenaline)	injection, 1 mg (as hydrochloride or hydrogen tartrate) in 1-ml ampoule
ipratropium bromide	inhalation (aerosol), 20 micrograms/ metered dose
□ salbutamol	tablet, 2 mg, 4 mg (as sulfate)
	inhalation (aerosol), 100 micrograms (as sulfate) per dose
	syrup, 2 mg (as sulfate)/5 ml
	injection, 50 micrograms (as sulfate)/ml in 5-ml ampoule
	respirator solution for use in nebulizers, 5 mg (as sulfate)/ml

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

26.1 *Oral*

oral rehydration salts (for glucose–electrolyte solution)	For composition see section 17.5.1
potassium chloride	powder for solution

26.2 *Parenteral*

glucose	injectable solution, 5%, 10% isotonic, 50% hypertonic
glucose with sodium chloride	injectable solution, 4% glucose, 0.18% sodium chloride (equivalent to Na^+ 30 mmol/l, Cl^- 30 mmol/l)

[a] The square box is added to include buprenorphine. The medicines should be used only within an established support programme.

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

26. Solutions correcting water, electrolyte and acid-base disturbances (*continued*)	
potassium chloride	solution, 11.2% in 20-ml ampoule (equivalent to K^+ 1.5 mmol/ml, Cl^- 1.5 mmol/ml)
sodium chloride	injectable solution, 0.9% isotonic (equivalent to Na^+ 154 mmol/l, Cl^- 154 mmol/l
sodium hydrogen carbonate	injectable solution, 1.4% isotonic (equivalent to Na^+ 167 mmol/l, HCO_3^- 167 mmol/l)
	solution, 8.4% in 10-ml ampoule (equivalent to Na^+ 1000 mmol/l, HCO_3^- 1000 mmol/l)
□ sodium lactate, solution compound	injectable solution
26.3 *Miscellaneous*	
water for injection	2-ml, 5-ml, 10-ml ampoules
27. Vitamins and minerals	
ascorbic acid	tablet, 50 mg
□ ergocalciferol	capsule or tablet, 1.25 mg (50 000 IU); oral solution, 250 micrograms/ml (10 000 IU/ml)
iodine	iodized oil, 1 ml (480 mg iodine), 0.5 ml (240 mg iodine) in ampoule (oral or injectable)
	0.57 ml (308 mg iodine) in dispenser bottle
	capsule, 200 mg
□ nicotinamide	tablet, 50 mg
pyridoxine	tablet, 25 mg (hydrochloride)
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 (as palmitate)/ml in multidose dispenser
	water-miscible injection, 100 000 IU (as palmitate) (55 mg) in 2-ml ampoule
riboflavin	tablet, 5 mg

□ Recommended example within a pharmaceutical class. See Explanatory notes on page 61.

27. Vitamins and minerals (*continued*)	
sodium fluoride	in any appropriate topical formulation
thiamine	tablet, 50 mg (hydrochloride)
Complementary list	
calcium gluconate	injection, 100 mg/ml in 10-ml ampoule

References

1. *Cancer pain relief with a guide to opioid availability.* 2nd ed. Geneva, World Health Organization, 1996.
2. Requirements for the Collection, Processing and Quality Control of Blood, Blood Components, and Plasma Derivatives (Revised 1992). In: *WHO Expert Committee on Biological Standardization. Forty-third report.* Geneva, World Health Organization, 1994, Annex 2 (WHO Technical Report Series, No. 840).
3. Requirements for Tuberculins (Revised 1985). In: *WHO Expert Committee on Biological Standardization. Thirty-sixth report.* Geneva, World Health Organization, 1987, Annex 1 (WHO Technical Report Series, No. 745).
4. Requirements for Dried BCG Vaccine (Revised 1985). In: *WHO Expert Committee on Biological Standardization. Thirty-sixth report.* Geneva, World Health Organization, 1987, Annex 2 (WHO Technical Report Series, No. 745).
5. Requirements for Dried BCG Vaccine (Amendment 1987). In: *WHO Expert Committee on Biological Standardization. Thirty-eighth report.* Geneva, World Health Organization, 1988, Annex 12 (WHO Technical Report Series, No. 771).
6. Requirements for Diphtheria, Tetanus, Pertussis and Combined Vaccines (Revised 1989). In: *WHO Expert Committee on Biological Standardization. Fortieth report*. Geneva, World Health Organization, 1990, Annex 2 (WHO Technical Report Series, No. 800).
7. Requirements for Hepatitis B Vaccine Prepared from Plasma (Revised 1994). In: *WHO Expert Committee on Biological Standardization. Forty-fifth report*. Geneva, World Health Organization, 1995, Annex 3 (WHO Technical Report Series, No. 858).
8. Requirements for Measles, Mumps and Rubella Vaccines and Combined Vaccine (Live) (Revised 1992). In: *WHO Expert Committee on Biological Standardization. Forty-third report*. Geneva, World Health Organization, 1994, Annex 3 (WHO Technical Report Series, No. 840).
9. Requirements for Measles, Mumps and Rubella Vaccines and Combined Vaccine (Live). In: *WHO Expert Committee on Biological Standardization. Forty-fourth report*. Geneva, World Health Organization, 1994, Note (WHO Technical Report Series, No. 848).
10. Requirements for Poliomyelitis Vaccine (Oral) (Revised 1989). In: *WHO Expert Committee on Biological Standardization. Fortieth report*. Geneva,

World Health Organization, 1990, Annex 1 (WHO Technical Report Series, No. 800).

11. Requirements for Poliomyelitis Vaccine (Inactivated) (Revised 1981). In: *WHO Expert Committee on Biological Standardization. Fortieth report*. Geneva, World Health Organization, 1982, Annex 2 (WHO Technical Report Series, No. 673).
12. Requirements for Poliomyelitis Vaccine (Inactivated) (Addendum 1985). In: *WHO Expert Committee on Biological Standardization Thirty-sixth report.* Geneva, World Health Organization, 1987, Annex 4 (WHO Technical Report Series, No. 745).
13. Requirements for Influenza Vaccine (Inactivated) (Revised 1990). In: *WHO Expert Committee on Biological Standardization. Forty-first report.* Geneva, World Health Organization, 1991, Annex 2 (WHO Technical Report Series, No. 814).
14. Requirements for Meningococcal Polysaccharide Vaccine. In: *WHO Expert Committee on Biological Standardization.* Geneva, World Health Organization, 1976, Annex 2 (WHO Technical Report Series, No. 594).
15. Requirements for Meningococcal Polysaccharide Vaccine (Addendum 1980, incorporating Addendum 1976 and Addendum 1977). In: *WHO Expert Committee on Biological Standardization. Thirty-first report.* Geneva, World Health Organization, 1981, Annex 6 (WHO Technical Report Series, No. 658).
16. Requirements for Rabies Vaccine for Human Use (Revised 1980). In: *WHO Expert Committee on Biological Standardization. Thirty-first report*. Geneva, World Health Organization, 1981, Annex 2 (WHO Technical Report Series, No. 658).
17. Requirements for Rabies Vaccine for Human Use (Amendment 1992). In: *WHO Expert Committee on Biological Standardization. Forty-third report*. Geneva, World Health Organization, 1994, Annex 4 (WHO Technical Report Series, No. 840).
18. Requirements for Rabies Vaccine (Inactivated) for Human Use Produced in Continuous Cell Lines (Revised 1986). In: *WHO Expert Committee on Biological Standardization. Thirty-seventh report*. Geneva, World Health Organization, 1987, Annex 9 (WHO Technical Report Series, No. 760).
19. Requirements for Rabies Vaccine (Inactivated) for Human Use Produced in Continuous Cell Lines (Amendment 1992). In: *WHO Expert Committee on Biological Standardization. Forty-third report*. Geneva, World Health Organization, 1994, Annex 5 (WHO Technical Report Series, No. 840).
20. Requirements for Typhoid Vaccine (Live, Attenuated, Ty 21a, Oral) In: *WHO Expert Committee on Biological Standardization*. Geneva, World Health Organization, 1984, Annex 3 (WHO Technical Report Series, No. 700).
21. Requirements for Vi Polysaccharide Typhoid Vaccine. In: *WHO Expert Committee on Biological Standardization. Forty-third report*. Geneva, World Health Organization, 1994, Annex 1 (WHO Technical Report Series, No. 840).
22. Requirements for Yellow Fever Vaccine (Revised 1995). In: *WHO Expert Committee on Biological Standardization. Forty-sixth report*. Geneva, World Health Organization, 1998, Annex 2 (WHO Technical Report Series, No. 872).

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Annex 2
The Anatomical Therapeutic Chemical (ATC) classification system[1]

The following list provides the corresponding Anatomical Therapeutic Chemical (ATC) classification codes for all items on the 14th WHO Model List of Essential Medicines, sorted by ATC code number.

ATC code	ATC group/medicine or item
A	**ALIMENTARY TRACT AND METABOLISM**
A02	**Drugs for acid related disorders**
A02A	**Antacids**
A02AA	*Magnesium compounds*
A02AA04	magnesium hydroxide
A02AB	*Aluminium compounds*
A02AB01	aluminium hydroxide
A02B	**Drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD)**
A02BA	*H_2-receptor antagonists*
A02BA02	ranitidine
A02BB	*Prostaglandins*
A02BB01	misoprostol
A03	**Drugs for functional gastrointestinal disorders**
A03B	**Belladonna and derivatives, plain**
A03BA	*Belladonna alkaloids, tertiary amines*
A03BA01	atropine
A03F	**Propulsives**
A03FA	*Propulsives*
A03FA01	metoclopramide
A06	**Laxatives**
A06A	**Laxatives**
A06AB	*Contact laxatives*
A06AB06	senna*

[1] Based on the ATC list as of January 2005 and prepared with the assisance of the WHO Collaborating Centre for Drug Statistics Methodology, Oslo, Norway.

ATC code	ATC group/medicine or item
A07	**Antidiarrheals, intestinal antiinflammatory/antiinfective agents**
A07A	**Intestinal antiinfectives**
A07AA	*Antibiotics*
A07AA02	nystatin
A07B	**Intestinal adsorbents**
A07BA	*Charcoal preparations*
A07BA01	charcoal, activated*
A07C	**Electrolytes with carbohydrates**
A07CA	*oral rehydration salts**
A07E	**Intestinal antiinflammatory agents**
A07EA	*Corticosteroids for local use*
A07EA02	hydrocortisone
A07EC	*Aminosalicylic acid and similar agents*
A07EC01	sulfasalazine
A10	**Drugs used in diabetes**
A10A	**Insulins and analogues**
A10AB	*insulin injection (soluble)**
A10AC	*insulin, intermediate-acting**
A10B	**Oral blood glucose lowering drugs**
A10BA	*Biguanides*
A10BA02	metformin
A10BB	*Sulfonamides, urea derivatives*
A10BB01	glibenclamide
A11	**Vitamins**
A11C	**Vitamin A and D, incl. combinations of the two**
A11CA	*Vitamin A, plain*
A11CA01	retinol
A11CC	*Vitamin D and analogues*
A11CC01	ergocalciferol
A11D	**Vitamin B_1, plain and in combination with vitamin B_6 and B_{12}**
A11DA	*Vitamin B_1, plain*
A11DA01	thiamine
A11G	**Ascorbic acid (vitamin C), incl. combinations**
A11GA	*Ascorbic acid (vitamin C), plain*
A11GA01	ascorbic acid
A11H	**Other plain vitamin preparations**
A11HA	*Other plain vitamin preparations*
A11HA01	nicotinamide

ATC code	ATC group/medicine or item
A11HA02	pyridoxine
A11HA04	riboflavin
A12	**Mineral supplements**
A12A	**Calcium**
A12AA	*Calcium*
A12AA03	calcium gluconate
A12C	**Other mineral supplements**
A12CB	*Zinc*
A12CB01	zinc sulfate
A12CD	*Fluoride*
A12CD01	sodium fluoride
A12CX	*Other mineral products*
A12CX	iodine*
B	**BLOOD AND BLOOD FORMING ORGANS**
B01	**Antithrombotic agents**
B01A	**Antithrombotic agents**
B01AA	*Vitamin K antagonists*
B01AA03	warfarin
B01AB	*Heparin group*
B01AB01	heparin sodium*
B01AC	*Platelet aggregation inhibitors excl. heparin*
B01AC06	acetylsalicylic acid
B01AD	*Enzymes*
B01AD01	streptokinase
B02	**Antihemorrhagics**
B02B	**Vitamin K and other hemostatics**
B02BA	*Vitamin K*
B02BA01	phytomenadione
B02BD	*Blood coagulation factors*
B02BD01	factor IX complex (coagulation factors II, VII, IX, X) concentrate*
B02BD02	factor VIII concentrate*
B03	**Antianemic preparations**
B03A	**Iron preparations**
B03A	ferrous salt*
B03AD	*ferrous salt + folic acid**
B03B	**Vitamin B_{12} and folic acid**
B03BA	*Vitamin B_{12} (cyanocobalamin and analogues)*
B03BA03	hydroxocobalamin

ATC code	ATC group/medicine or item
B03BB	*Folic acid and derivatives*
B03BB01	folic acid
B05	**Blood substitutes and perfusion solutions**
B05A	**Blood and related products**
B05AA	*Blood substitutes and plasma protein fractions*
B05AA05	dextran 70*
B05AA06	polygeline*
B05B	**I.v. solutions**
B05BA	*Solutions for parenteral nutrition*
B05BB	*Solutions affecting the electrolyte balance*
B05BB01	sodium lactate, compound solution*
B05BB02	glucose with sodium chloride*
B05BC	*Solutions producing osmotic diuresis*
B05BC01	mannitol
B05D	**Peritoneal dialytics**
B05DA	*intraperitoneal dialysis solution**
B05X	**I.v. solution additives**
B05XA	*Electrolyte solutions*
B05XA01	potassium chloride
B05XA02	sodium hydrogen carbonate*
B05XA03	sodium chloride
B05XA05	magnesium sulfate
C	**CARDIOVASCULAR SYSTEM**
C01	**Cardiac therapy**
C01A	**Cardiac glycosides**
C01AA	*Digitalis glycosides*
C01AA05	digoxin
C01B	**Antiarrhythmics, class I and III**
C01BA	*Antiarrhythmics, class Ia*
C01BA01	quinidine
C01BA02	procainamide
C01BB	*Antiarrhythmics, class Ib*
C01BB01	lidocaine
C01C	**Cardiac stimulants excl. cardiac glycosides**
C01CA	*Adrenergic and dopaminergic agents*
C01CA04	dopamine
C01CA24	epinephrine
C01D	**Vasodilators used in cardiac diseases**
C01DA	*Organic nitrates*
C01DA02	glyceryl trinitrate
C01DA08	isosorbide dinitrate

ATC code	ATC group/medicine or item
C02	**Antihypertensives**
C02A	**Antiadrenergic agents, centrally acting**
C02AB	*Methyldopa*
C02AB01	methyldopa*
C02D	**Arteriolar smooth muscle, agents acting on**
C02DD	*Nitroferricyanide derivatives*
C02DD01	sodium nitroprusside*
C03	**Diuretics**
C03A	**Low-ceiling diuretics, thiazides**
C03AA	*Thiazides, plain*
C03AA03	hydrochlorothiazide
C03C	**High-ceiling diuretics**
C03CA	*Sulfonamides, plain*
C03CA01	furosemide
C03D	**Potassium-sparing agents**
C03DA	*Aldosterone antagonists*
C03DA01	spironolactone
C03DB	*Other potassium-sparing agents*
C03DB01	amiloride
C05	**Vasoprotectives**
C05A	**Antihemorrhoidals for topical use**
C05A	antihemorrhoidal preparation: local anaesthetic, astringent, and anti-inflammatory medicine*
C07	**Beta blocking agents**
C07A	**Beta blocking agents**
C07AA	*Beta blocking agents, non-selective*
C07AA05	propranolol
C07AB	*Beta blocking agents, selective*
C07AB03	atenolol
C08	**Calcium channel blockers**
C08C	**Selective calcium channel blockers with mainly vascular effects**
C08CA	*Dihydropyridine derivatives*
C08CA01	amlodipine
C08CA05	nifedipine
C08D	**Selective calcium channel blockers with direct cardiac effects**
C08DA	*Phenylalkylamine derivatives*
C08DA01	verapamil
C09	**Agents acting on the renin-angiotensin system**
C09A	**ACE inhibitors, plain**
C09AA	*ACE inhibitors, plain*
C09AA02	enalapril

ATC code	ATC group/medicine or item
D	**DERMATOLOGICALS**
D01	**Antifungals for dermatological use**
D01A	**Antifungals for topical use**
D01AA	*Antibiotics*
D01AA01	nystatin
D01AC	*Imidazole and triazole derivatives*
D01AC02	miconazole
D01AE	*Other antifungals for topical use*
D01AE02	methylrosanilinium chloride (gentian violet)*
D01AE12	salicylic acid
D01AE13	selenium sulfide
D01AE20	benzoic acid + salicylic acid*
D01B	**Antifungals for systemic use**
D01BA	*Antifungals for systemic use*
D01BA01	griseofulvin
D02	**Emollients and protectives**
D02A	**Emollients and protectives**
D02AB	*Zinc products*
D02AB	calamine lotion*
D02AE	*Carbamide products*
D02AE01	urea*
D05	**Antipsoriatics**
D05A	**Antipsoriatics for topical use**
D05AA	*coal tar**
D05AC	*Antracen derivatives*
D05AC01	dithranol
D06	**Antibiotics and chemotherapeutics for dermatological use**
D06A	**Antibiotics for topical use**
D06AX	*Other antibiotics for topical use*
D06AX04	neomycin + bacitracin*
D06B	**Chemotherapeutics for topical use**
D06BA	*Sulfonamides*
D06BA01	silver sulfadiazine
D06BB	*Antivirals*
D06BB04	podophyllum resin*
D07	**Corticosteroids, dermatological preparations**
D07A	**Corticosteroids, plain**
D07AA	*Corticosteroids, weak (group I)*
D07AA02	hydrocortisone
D07AC	*Corticosteroids, potent (group III)*
D07AC01	betamethasone

ATC code	ATC group/medicine or item
D08	**Antiseptics and disinfectants**
D08A	**Antiseptics and disinfectants**
D08AC	*Biguanides and amidines*
D08AC02	chlorhexidine
D08AE	*Phenol and derivatives*
D08AE05	chloroxylenol
D08AG	*Iodine products*
D08AG02	polyvidone iodine
D08AX	*Other antiseptics and disinfectants*
D08AX	chlorine base compound*
D08AX06	potassium permanganate
D08AX08	ethanol
D10	**Anti-acne preparations**
D10A	**Anti-acne preparations for topical use**
D10AE	*Peroxides*
D10AE01	benzoyl peroxide
D10AX	*Other anti-acne preparations for topical use*
D10AX05	aluminium diacetate
G	**GENITO URINARY SYSTEM AND SEX HORMONES**
G01	**Gynecological antiinfectives and antiseptics**
G01A	**Antiinfectives and antiseptics, excl. combinations with corticosteroids**
G01AA	*Antibiotics*
G01AA01	nystatin
G01AF	*Imidazole derivatives*
G01AF02	clotrimazole
G02B	**Contraceptives for topical use**
G02BA	*Intrauterine contraceptives*
G02BA02	copper-containing intrauterine device*
G02BB	*Intravaginal contraceptives*
G02BB	diaphragms*
G03	**Sex hormones and modulators of the genital system**
G03A	**Hormonal contraceptives for systemic use**
G03AA	*Progestogens and estrogens, fixed combinations*
G03AA05	ethinylestradiol + norethisterone*
G03AB	*Progestogens and estrogens, sequential preparations*
G03AB03	ethinylestradiol + levonorgestrel*
G03AC	*Progestogens*
G03AC01	norethisterone enantate*
G03AC03	levonorgestrel
G03AC06	medroxyprogesterone acetate*

ATC code	ATC group/medicine or item
G03B	**Androgens**
G03BA	*3-Oxoandrosten (4) derivatives*
G03BA03	testosterone
G03C	**Estrogens**
G03CA	*Natural and semisynthetic estrogens, plain*
G03CA01	ethinylestradiol
G03D	**Progestogens**
G03DC	*Estren derivatives*
G03DC02	norethisterone
G03G	**Gonadotropins and other ovulation stimulants**
G03GB	*Ovulation stimulants, synthetic*
G03GB02	clomifene
G03X	**Other sex hormones and modulators of the genital system**
G03XB	*Antiprogesterons*
G03XB01	mifepristone
H	**SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS**
H01	**Pituitary, hypothalamic hormones and analogues**
H01B	**Posterior pituitary lobe hormones**
H01BB	*Oxytocin and analogues*
H01BB02	oxytocin
H02	**Corticosteroids for systemic use**
H02A	**Corticosteroids for systemic use, plain**
H02AB	*Glucocorticoids*
H02AB02	dexamethasone
H02AB06	prednisolone
H02AB09	hydrocortisone
H03	**Thyroid therapy**
H03A	**Thyroid preparations**
H03AA	*Thyroid hormones*
H03AA01	levothyroxine*
H03B	**Antithyroid preparations**
H03BA	*Thiouracils*
H03BA02	propylthiouracil
H03C	**Iodine therapy**
H03CA	*potassium iodide**
J	**ANTIINFECTIVES FOR SYSTEMIC USE**
J01	**Antibacterials for systemic use**
J01A	**Tetracyclines**
J01AA	*Tetracyclines*
J01AA02	doxycycline

ATC code	ATC group/medicine or item
J01B	**Amphenicols**
J01BA	*Amphenicols*
J01BA01	chloramphenicol
J01C	**Beta-lactam antibacterials, penicillins**
J01CA	*Penicillins with extended spectrum*
J01CA01	ampicillin
J01CA04	amoxicillin
J01CE	*Beta-lactamase sensitive penicillins*
J01CE01	benzylpenicillin
J01CE02	phenoxymethylpenicillin
J01CE08	benzathine benzylpenicillin
J01CE09	procaine benzylpenicillin*
J01CF	*Beta-lactamase resistant penicillins*
J01CF02	cloxacillin
J01CR	*Combinations of penicillins, incl. beta-lactamase inhibitors*
J01CR02	amoxicillin + clavulanic acid*
J01D	**Other beta-lactam antibacterials**
J01DD	*Third-generation cephalosporins*
J01DD02	ceftazidime
J01DD04	ceftriaxone
J01DD08	cefixime
J01DH	*Carbapenems*
J01DH51	imipenem + cilastatin*
J01E	**Sulfonamides and trimethoprim**
J01EA	*Trimethoprim and derivatives*
J01EA01	trimethoprim
J01EC	*Intermediate-acting sulfonamides*
J01EC02	sulfadiazine
J01EE	*Combinations of sulfonamides and trimethoprim, incl. derivatives*
J01EE01	sulfamethoxazole + trimethoprim
J01F	**Macrolides, lincosamides and streptogramins**
J01FA	*Macrolides*
J01FA01	erythromycin
J01FA10	azithromycin
J01FF	*Lincosamides*
J01FF01	clindamycin
J01G	**Aminoglycoside antibacterials**
J01GA	*Streptomycins*
J01GA01	streptomycin

ATC code	ATC group/medicine or item
J01GB	*Other aminoglycosides*
J01GB03	gentamicin
J01GB04	kanamycin
J01GB06	amikacin
J01M	**Quinolone antibacterials**
J01MA	*Fluoroquinolones*
J01MA01	ofloxacin
J01MA02	ciprofloxacin
J01MA12	levofloxacin
J01X	**Other antibacterials**
J01XA	*Glycopeptide antibacterials*
J01XA01	vancomycin
J01XD	*Imidazole derivatives*
J01XD01	metronidazole
J01XE	*Nitrofuran derivatives*
J01XE01	nitrofurantoin
J01XX	*Other antibacterials*
J01XX04	spectinomycin
J02	**Antimycotics for systemic use**
J02A	**Antimycotics for systemic use**
J02AA	*Antibiotics*
J02AA01	amphotericin B
J02AC	*Triazole derivatives*
J02AC01	fluconazole
J02AX	*Other antimycotics for systemic use*
J02AX01	flucytosine
J04	**Antimycobacterials**
J04A	**Drugs for treatment of tuberculosis**
J04AA	*Aminosalicylic acid and derivatives*
J04AA01	*p*-aminosalicylic acid*
J04AB	*Antibiotics*
J04AB01	cycloserine
J04AB02	rifampicin
J04AB30	capreomycin
J04AC	*Hydrazides*
J04AC01	isoniazid
J04AD	*Thiocarbamide derivatives*
J04AD03	ethionamide
J04AK	*Other drugs for treatment of tuberculosis*
J04AK01	pyrazinamide
J04AK02	ethambutol

ATC code	ATC group/medicine or item
J04AM	*Combinations of drugs for treatment of tuberculosis*
J04AM02	rifampicin + isoniazid*
J04AM02	rifampicin + isoniazid + pyrazinamide*
J04AM02	rifampicin + isoniazid + pyrazinamide + ethambutol*
J04AM03	isoniazid + ethambutol*
J04B	**Drugs for treatment of lepra**
J04BA	*Drugs for treatment of lepra*
J04BA01	clofazimine
J04BA02	dapsone
J05	**Antivirals for systemic use**
J05A	**Direct acting antivirals**
J05AB	*Nucleosides and nucleotides excl. reverse transcriptase inhibitors*
J05AB01	aciclovir
J05AE	*Protease inhibitors*
J05AE01	saquinavir (SQV)
J05AE02	indinavir (IDV)
J05AE03	ritonavir (r)
J05AE04	nelfinavir (NFV)
J05AE30	lopinavir + ritonavir (LPV/r)*
J05AF	*Nucleoside reverse transcriptase inhibitors*
J05AF01	zidovudine (ZDV or AZT)
J05AF02	didanosine (ddI)
J05AF04	stavudine (d4T)
J05AF05	lamivudine (3TC)
J05AF06	abacavir (ABC)
J05AG	*Non-nucleoside reverse transcriptase inhibitors*
J05AG01	nevirapine (NVP)
J05AG03	efavirenz (EFV or EFZ)
J06	**Immune sera and immunoglobulins**
J06A	**Immune sera**
J06AA	*Immune sera*
J06AA01	diphtheria antitoxin
J06AA03	antivenom sera*
J06B	**Immunoglobulins**
J06BB	*Specific immunoglobulins*
J06BB01	anti-D immunoglobulin (human)
J06BB02	antitetanus immunoglobulin (human)
J06BB05	rabies immunoglobulin
J07	**Vaccines**
J07A	**Bacterial vaccines**
J07AH	*meningococcal meningitis vaccine**

ATC code	ATC group/medicine or item
J07AJ	*Pertussis vaccines*
J07AJ51	diphtheria-pertussis-tetanus vaccine*
J07AM	*Tetanus vaccines*
J07AM51	diphtheria-tetanus vaccine*
J07AN	*Tuberculosis vaccines*
J07AN01	BCG vaccine*
J07AP	*typhoid vaccine*
J07B	**Viral vaccines**
J07BB	*influenza vaccine*
J07BC	*Hepatitis vaccines*
J07BC01	hepatitis B vaccine
J07BD	*measles vaccine**
J07BD52	measles-mumps-rubella vaccine*
J07BF	*poliomyelitis vaccine*
J07BG	*rabies vaccine*
J07BJ	*rubella vaccine*
J07BL	*yellow fever vaccine*
L	**ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS**
L01	**Antineoplastic agents**
L01A	**Alkylating agents**
L01AA	*Nitrogen mustard analogues*
L01AA01	cyclophosphamide
L01AA02	chlorambucil
L01AA05	chlormethine
L01AX	*Other alkylating agents*
L01AX04	dacarbazine
L01B	**Antimetabolites**
L01BA	*Folic acid analogues*
L01BA01	methotrexate
L01BB	*Purine analogues*
L01BB02	mercaptopurine
L01BC	*Pyrimidine analogues*
L01BC01	cytarabine
L01BC02	fluorouracil
L01C	**Plant alkaloids and other natural products**
L01CA	*Vinca alkaloids and analogues*
L01CA01	vinblastine
L01CA02	vincristine
L01CB	*Podophyllotoxin derivatives*
L01CB01	etoposide

ATC code	ATC group/medicine or item
L01D	**Cytotoxic antibiotics and related substances**
L01DA	*Actinomycines*
L01DA01	dactinomycin
L01DB	*Anthracyclines and related substances*
L01DB01	doxorubicin
L01DB02	daunorubicin
L01DC	*Other cytotoxic antibiotics*
L01DC01	bleomycin
L01X	**Other antineoplastic agents**
L01XA	*Platinum compounds*
L01XA01	cisplatin
L01XB	*Methylhydrazines*
L01XB01	procarbazine
L01XX	*Other antineoplastic agents*
L01XX02	asparaginase
L02	**Endocrine therapy**
L02B	**Hormone antagonists and related agents**
L02BA	*Anti-estrogens*
L02BA01	tamoxifen
L04	**Immunosuppressive agents**
L04A	**Immunosuppressive agents**
L04AA	*Selective immunosuppressive agents*
L04AA01	ciclosporin
L04AX	*Other immunosuppressive agents*
L04AX01	azathioprine
M	**MUSCULO-SKELETAL SYSTEM**
M01	**Antiinflammatory and antirheumatic products**
M01A	**Antiinflammatory and antirheumatic products, non-steroids**
M01AE	*Propionic acid derivatives*
M01AE01	ibuprofen
M01C	**Specific antirheumatic agents**
M01CC	*Penicillamine and similar agents*
M01CC01	penicillamine
M03	**Muscle relaxants**
M03A	**Muscle relaxants, peripherally acting agents**
M03AA	*Curare alkaloids*
M03AA01	alcuronium
M03AB	*Choline derivatives*
M03AB01	suxamethonium
M03AC	*Other quaternary ammonium compounds*
M03AC03	vecuronium

ATC code	ATC group/medicine or item
M04	**Antigout preparations**
M04A	**Antigout preparations**
M04AA	*Preparations inhibiting uric acid production*
M04AA01	allopurinol
N	**NERVOUS SYSTEM**
N01	**Anesthetics**
N01A	**Anesthetics, general**
N01AB	*Halogenated hydrocarbons*
N01AB01	halothane
N01AF	*Barbiturates, plain*
N01AF03	thiopental
N01AX	*Other general anesthetics*
N01AX03	ketamine
N01AX13	nitrous oxide
N01B	**Anesthetics, local**
N01BB	*Amides*
N01BB01	bupivacaine
N01BB02	lidocaine
N01BB52	lidocaine + epinephrine (adrenaline)*
N02	**Analgesics**
N02A	**Opioids**
N02AA	*Natural opium alkaloids*
N02AA01	morphine
N02B	**Other analgesics and antipyretics**
N02BA	*Salicylic acid and derivatives*
N02BA01	acetylsalicylic acid
N02BE	*Anilides*
N02BE01	paracetamol
N03	**Antiepileptics**
N03A	**Antiepileptics**
N03AA	*Barbiturates and derivatives*
N03AA02	phenobarbital
N03AB	*Hydantoin derivatives*
N03AB02	phenytoin
N03AD	*Succinimide derivatives*
N03AD01	ethosuximide
N03AF	*Carboxamide derivatives*
N03AF01	carbamazepine
N03AG	*Fatty acid derivatives*
N03AG01	valproic acid

ATC code	ATC group/medicine or item
N04	**Anti-parkinson drugs**
N04A	**Anticholinergic agents**
N04AA	*Tertiary amines*
N04AA02	biperiden
N04B	**Dopaminergic agents**
N04BA	*Dopa and dopa derivatives*
N04BA02	levodopa + carbidopa*
N05	**Psycholeptics**
N05A	**Antipsychotics**
N05AA	*Phenothiazines with aliphatic side-chain*
N05AA01	chlorpromazine
N05AB	*Phenothiazines with piperazine structure*
N05AB02	fluphenazine
N05AD	*Butyrophenone derivatives*
N05AD01	haloperidol
N05AN	*Lithium*
N05AN01	lithium carbonate*
N05B	**Anxiolytics**
N05BA	*Benzodiazepine derivatives*
N05BA01	diazepam
N06	**Psychoanaleptics**
N06A	**Antidepressants**
N06AA	*Non-selective monoamine reuptake inhibitors*
N06AA04	clomipramine
N06AA09	amitriptyline
N07	**Other nervous system drugs**
N07A	**Parasympathomimetics**
N07AA	*Anticholinesterases*
N07AA01	neostigmine
N07AA02	pyridostigmine
N07B	**Drugs used in addictive disorders**
N07BC	*Drugs used in opioid dependence*
N07BC01	buprenorphine
N07BC02	methadone
P	**ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS**
P01	**Antiprotozoals**
P01A	**Agents against amoebiasis and other protozoal diseases**
P01AB	*Nitroimidazole derivatives*
P01AB01	metronidazole

ATC code	ATC group/medicine or item
P01AC	*Dichloroacetamide derivatives*
P01AC01	diloxanide
P01B	**Antimalarials**
P01BA	*Aminoquinolines*
P01BA01	chloroquine
P01BA03	primaquine
P01BA06	amodiaquine
P01BB	*Biguanides*
P01BB01	proguanil
P01BC	*Methanolquinolines*
P01BC01	quinine
P01BC02	mefloquine
P01BD	*Diaminopyrimidines*
P01BD01	pyrimethamine
P01BD51	sulfadoxine + pyrimethamine*
P01BE	*Artemisinin and derivatives*
P01BE02	artemether
P01BE03	artesunate
P01BE52	artemether + lumefantrine*
P01C	**Agents against leishmaniasis and trypanosomiasis**
P01CA	*Nitroimidazole derivatives*
P01CA02	benznidazole
P01CB	*Antimony compounds*
P01CB01	meglumine antimoniate
P01CC	*Nitrofuran derivatives*
P01CC01	nifurtimox
P01CD	*Arsenic compounds*
P01CD01	melarsoprol
P01CX	*Other agents against leishmaniasis and trypanosomiasis*
P01CX01	pentamidine*
P01CX02	suramin sodium
P01CX03	eflornithine
P02	**Anthelmintics**
P02B	**Antitrematodals**
P02BA	*Quinoline derivatives and related substances*
P02BA01	praziquantel
P02BA02	oxamniquine
P02BX	*Other antitrematodal agents*
P02BX04[a]	triclabendazole

[a] Provisional code pending formal approval by the WHO International Working Group for Drug Statistics Methodology, Oslo, Norway.

ATC code	ATC group/medicine or item
P02C	**Antinematodal agents**
P02CA	*Benzimidazole derivatives*
P02CA01	mebendazole
P02CA03	albendazole
P02CB	*Piperazine and derivatives*
P02CB02	diethylcarbamazine
P02CC	*Tetrahydropyrimidine derivatives*
P02CC01	pyrantel
P02CE	*Imidazothiazole derivatives*
P02CE01	levamisole
P02CF	*Avermectines*
P02CF01	ivermectin
P02D	**Anticestodals**
P02DA	*Salicylic acid derivatives*
P02DA01	niclosamide
P03	**Ectoparasiticides, incl. scabicides, insecticides and repellents**
P03A	**Ectoparasiticides, incl. scabicides**
P03AC	*Pyrethrines, incl. synthetic compounds*
P03AC04	permethrin
P03AX	*Other ectoparasiticides, incl. scabicides*
P03AX01	benzyl benzoate
R	**RESPIRATORY SYSTEM**
R03	**Drugs for obstructive airway diseases**
R03A	**Adrenergics, inhalants**
R03AC	*Selective beta-2-adrenoreceptor agonists*
R03AC02	salbutamol
R03B	**Other drugs for obstructive airway diseases, inhalants**
R03BA	*Glucocorticoids*
R03BA01	beclometasone
R03BB	*Anticholinergics*
R03BB01	ipratropium bromide
R03C	**Adrenergics for systemic use**
R03CA	*Alpha- and beta-adrenoreceptor agonists*
R03CA02	ephedrine
R03CC	*Selective beta-2-adrenoreceptor agonists*
R03CC02	salbutamol
R05	**Cough and cold preparations**
R05D	**Cough suppressants, excl. combinations with expectorants**
R05DA	*Opium alkaloids and derivatives*
R05DA04	codeine

ATC code	ATC group/medicine or item
R06	**Antihistamines for systemic use**
R06A	**Antihistamines for systemic use**
R06AB	*Substituted alkylamines*
R06AB04	chlorphenamine
R06AD	*Phenothiazine derivatives*
R06AD02	promethazine
S	**SENSORY ORGANS**
S01	**Ophthalmologicals**
S01A	**Antiinfectives**
S01AA	*Antibiotics*
S01AA09	tetracycline
S01AA11	gentamicin
S01AD	*Antivirals*
S01AD01	idoxuridine
S01B	**Antiinflammatory agents**
S01BA	*Corticosteroids, plain*
S01BA04	prednisolone
S01E	**Antiglaucoma preparations and miotics**
S01EA	*Sympathomimetics in glaucoma therapy*
S01EA01	epinephrine
S01EB	*Parasympathomimetics*
S01EB01	pilocarpine
S01EC	*Carbonic anhydrase inhibitors*
S01EC01	acetazolamide
S01ED	*Beta blocking agents*
S01ED01	timolol
S01F	**Mydriatics and cycloplegics**
S01FA	*Anticholinergics*
S01FA01	atropine
S01FA06	tropicamide
S01H	**Local anesthetics**
S01HA	*Local anesthetics*
S01HA03	tetracaine
S01J	**Diagnostic agents**
S01JA	*Colouring agents*
S01JA01	fluorescein
V	**VARIOUS**
V03	**All other therapeutic products**
V03A	**All other therapeutic products**
V03AB	*Antidotes*
V03AB03	sodium calcium edetate*

ATC code	ATC group/medicine or item
V03AB06	sodium thiosulfate*
V03AB08	sodium nitrite
V03AB09	dimercaprol
V03AB14	protamine sulfate*
V03AB15	naloxone
V03AB17	methylthioninium chloride (methylene blue)
V03AB23	acetylcysteine
V03AB26	DL-methionine*
V03AB31	potassium ferric hexacyanoferrate (II).2H_2O (Prussian blue)
V03AC	*Iron chelating agents*
V03AC01	deferoxamine
V03AF	*Detoxifying agents for antineoplastic treatment*
V03AF03	calcium folinate
V03AN	*Medical gases*
V03AN	oxygen
V04	**Diagnostic agents**
V04C	**Other diagnostic agents**
V04CF	*Tuberculosis diagnostics*
V04CF01	tuberculin, purified protein derivative (PPD)*
V07	**All other non-therapeutic products**
V07A	**All other non-therapeutic products**
V07AB	*Solvents and diluting agents, incl. irrigating solutions*
V07AB	water for injection*
V07AV	Technical disinfectants
V07AV	glutaral
V08	**Contrast media**
V08A	**X-ray contrast media, iodinated**
V08AA	*Watersoluble, nephrotropic, high osmolar X-ray contrast media*
V08AA01	amidotrizoate*
V08AB	*Watersoluble, nephrotropic, low osmolar X-ray contrast media*
V08AB02	iohexol
V08AC	*Watersoluble, hepatotropic X-ray contrast media*
V08AC02	meglumine iotroxate*
V08AC06	iopanoic acid
V08AD	*Non-watersoluble X-ray contrast media*
V08AD03	propyliodone
V08B	**X-ray contrast media, non-iodinated**
V08BA	*Barium sulfate containing X-ray contrast media*
V08BA01	barium sulfate*

* Medicine or item name differs slightly from the name used in the ATC classification system.

Alphabetical list of essential medicines (with ATC classification code numbers)

Medicine or item	ATC code	Section
abacavir (ABC)	J05AF06	6.4.2a
acetazolamide	S01EC01	21.4
acetylcysteine	V03AB23	4.2
acetylsalicylic acid	B01AC06	12.5
acetylsalicylic acid	N02BA01	22.1; 7.1
aciclovir	J05AB01	6.4.1
albendazole	P02CA03	6.1.1
alcuronium	M03AA01	20
allopurinol	M04AA01	2.3
aluminium diacetate	D11AA	13.4
aluminium hydroxide	A02AB01	17.1
amidotrizoate*	V08AA01	14.2
amikacin	J01GB06	6.2.4
amiloride	C03DB01	16
p-aminosalicylic acid*	J04AA01	6.2.4
amitriptyline	N06AA09	24.2.1
amlodipine	C08CA01	
amodiaquine	P01BA06	6.5.3a
amoxicillin	J01CA04	6.2.1
amoxicillin + clavulanic acid*	J01CR02	6.2.1
amphotericin B	J02AA01	6.3; 6.5.2
ampicillin	J01CA01	6.2.1
anti-D immunoglobulin (human)	J06BB01	19.2
antihaemorrhoidal preparation: local anaesthetic, astringent, and anti-inflammatory drug*	C05A	17.3
antitetanus immunoglobulin (human)*	J06BB02	19.2
antivenom sera*	J06AA03	19.2
artemether	P01BE02	6.5.3a
artemether + lumefantrine*	P01BE52	6.5.3a
artesunate	P01BE03	6.5.3a
ascorbic acid	A11GA01	27
asparaginase	L01XX02	8.2
atenolol	C07AB03	12.1; 12.2; 12.3
atropine	A03BA01	1.3; 4.2
atropine	S01FA01	21.5
azathioprine	L04AX01	2.4; 8.1
azithromycin	J01FA10	6.2.2
barium sulfate*	V08BA01	14.2
BCG vaccine*	J07AN01	19.3.1
beclometasone	R03BA01	25.1
benzathine benzylpenicillin	J01CE08	6.2.1
benznidazole	P01CA02	6.5.5b
benzoic acid + salicylic acid*	D01AE20	13.1

Medicine or item	ATC code	Section
benzoyl peroxide	D10AE01	13.5
benzyl benzoate	P03AX01	13.6
benzylpenicillin	J01CE01	6.2.1
betamethasone	D07AC01	13.3
biperiden	N04AA02	9
bleomycin	L01DC01	8.2
bupivacaine	N01BB01	1.2
buprenorphine	N07BC01	
calamine lotion*	D02AB	13.3
calcium folinate	V03AF03	8.2
calcium gluconate	A12AA03	4.2; 27
capreomycin	J04AB30	6.2.4
carbamazepine	N03AF01	5; 24.2.2
cefixime	J01DD08	
ceftazidime	J01DA11	6.2.1
ceftriaxone	J01DA13	6.2.1
charcoal, activated*	A07BA01	4.1
chlorambucil	L01AA02	8.2
chloramphenicol	J01BA01	6.2.2
chlorhexidine	D08AC02	15.1
chlorine base compound*	D08AX	15.2
chlormethine	L01AA05	8.2
chloroquine	P01BA01	2.4; 6.5.3a; 6.5.3.b
chloroxylenol	D08AE05	15.2
chlorphenamine	R06AB04	3
chlorpromazine	N05AA01	24.1
ciclosporin	L04AA01	8.1
ciprofloxacin	J01MA02	6.2.2; 6.2.4
cisplatin	L01XA01	8.2
clindamycin	J01FF01	6.2.2
clofazimine	J04BA01	6.2.3
clomifene	G03GB02	18.6
clomipramine	N06AA04	24.4
clotrimazole	G01AF02	
coal tar*	D05AA	13.5
codeine	R05DA04	2.2; 17.7.2
condoms		18.3.3
copper-containing intrauterine device*	G02BA02	18.3.2
cyclophosphamide	L01AA01	8.2
cycloserine	J04AB01	6.2.4
cytarabine	L01BC01	8.2
dacarbazine	L01AX04	8.2
dactinomycin	L01DA01	8.2
dapsone	J04BA02	6.2.3
daunorubicin	L01DB02	8.2
deferoxamine	V03AC01	4.2

Medicine or item	ATC code	Section
dexamethasone	H02AB02	3; 8.3
dextran 70*	B05AA05	11.1
diaphragms	G02BB	18.3.3
diazepam	N05BA01	1.3; 5; 24.3
dicloxacillin	J01CF01	6.2.1
didanosine (ddI)	J05AF02	6.4.2a
diethylcarbamazine	P02CB02	6.1.2
digoxin	C01AA05	12.2; 12.4
diloxanide	P01AC01	6.5.1
dimercaprol	V03AB09	4.2
diphtheria-pertussis-tetanus vaccine*	J07AJ51	19.3.1
diphtheria antitoxin	J06AA01	19.2
diphtheria-tetanus vaccine*	J07AM51	19.3.1
dithranol	D05AC01	13.5
dopamine	C01CA04	12.4
doxorubicin	L01DB01	8.2
doxycycline	J01AA02	6.2.2; 6.5.3b; 6.5.3a
efavirenz (EFV or EFZ)	J05AG03	6.4.2b
eflornithine	P01CX03	6.5.5a
enalapril	C09AA02	12.3
ephedrine	R03CA02	1.2
epinephrine (adrenaline)	C01CA24	3; 25.1; 12.2
epinephrine (adrenaline)	S01EA01	21.5
ergocalciferol	A11CC01	27
erythromycin	J01FA01	6.2.2
ethambutol	J04AK02	6.2.4
ethanol	D08AX08	15.1
ethinylestradiol	G03CA01	18.4
ethinylestradiol + levonorgestrel*	G03AB03	18.3.1
ethinylestradiol + norethisterone*	G03AA05	18.3.1
ethionamide	J04AD03	6.2.4
ethosuximide	N03AD01	5
etoposide	L01CB01	8.2
factor IX complex (coagulation factors II, VII, IX,X) concentrate*	B02BD01	11.2
factor VIII concentrate*	B02BD02	11.2
ferrous salt*	B03A	10.1
ferrous salt + folic acid*	B03AD	10.1
fluconazole	J02AC01	6.3
flucytosine	J02AX01	6.3
fluorescein	S01JA01	14.1
fluorouracil	L01BC02	13.5; 8.2
fluphenazine	N05AB02	24.1
folic acid	B03BB01	10.1
furosemide	C03CA01	16

Medicine or item	ATC code	Section
gentamicin	J01GB03	6.2.2
gentamicin	S01AA11	21.1
glibenclamide	A10BB01	18.5
glucose*	B05BA03	26.2
glucose with sodium chloride*	B05BB02	26.2
glutaral	V07AV	15.2
glyceryl trinitrate	C01DA02	12.1
griseofulvin	D01BA01	6.3
haloperidol	N05AD01	24.1
halothane	N01AB01	1.1
heparin sodium*	B01AB01	10.2
hepatitis B vaccine	J07BC01	19.3.1
hydralazine	C02DB02	12.3
hydrochlorothiazide	C03AA03	12.3; 12.4; 16
hydrocortisone	A07EA02	17.4
hydrocortisone	D07AA02	13.3
hydrocortisone	H02AB09	3; 8.3
hydroxocobalamin	B03BA03	10.1
ibuprofen	M01AE01	2.1
idoxuridine	S01AD01	21.1
imipenem + cilastatin*	J01DH51	6.2.1
indinavir (IDV)	J05AE02	6.4.2c
influenza vaccine	J07BB	19.3.2
insulin injection (soluble)*	A10AB	18.5
insulin, intermediate-acting*	A10AC	18.5
intraperitoneal dialysis solution*	B05DA	23
iodine*	A12CX	27
iohexol	V08AB02	14.2
iopanoic acid	V08AC06	14.2
ipratropium bromide	R03BB01	25.1
isoniazid	J04AC01	6.2.4
isoniazid + ethambutol*	J04AM03	6.2.4
isosorbide dinitrate	C01DA08	12.1
ivermectin	P02CF01	6.1.2
kanamycin	J01GB04	6.2.4
ketamine	N01AX03	1.1
lamivudine (3TC)	J05AF05	6.4.2a
levamisole	P02CE01	6.1.1; 8.2
levodopa + carbidopa*	N04BA02	9
levofloxacin	J01MA12	6.2.4
levonorgestrel	G03AC03	18.3.1
levothyroxine*	H03AA01	18.8
lidocaine	C01BB01	12.2
lidocaine	N01BB02	1.2
lidocaine + epinephrine (adrenaline)*	N01BB52	1.2

Medicine or item	ATC code	Section
lithium carbonate*	N05AN01	24.2.2
lopinavir + ritonavir (LPV/r)*	J05AE30	6.4.2c
magnesium hydroxide	A02AA04	17.1
magnesium sulfate	B05XA05	5
mannitol	B05BC01	16
measles-mumps-rubella vaccine*	J07BD52	19.3
mebendazole	P02CA01	6.1.1
medroxyprogesterone acetate*	G03AC06	18.3.1; 18.7
mefloquine	P01BC02	6.5.3a
meglumine antimoniate	P01CB01	6.5.2
meglumine iotroxate*	V08AC02	14.2
melarsoprol	P01CD01	6.5.5
meningococcal meningitis vaccine*	J07AH	19.3.2
mercaptopurine	L01BB02	8.2
metformin	A10BA02	18.5
methadone	N07BC02	
DL-methionine*	V03AB26	4.2
methotrexate	L01BA01	2.4; 8.2
methyldopa*	C02AB01	12.3
methylrosanilinium chloride (gentian violet)*	D01AE02	13.2
methylthioninium chloride (methylene blue)	V03AB17	4.2
metoclopramide	A03FA01	17.2
metronidazole	J01XD01	6.2.2
metronidazole	P01AB01	6.5.1
miconazole	D01AC02	13.1
mifepristone	G03XB01	
misoprostol	A02BB01	
morphine	N02AA01	1.3; 2.2
naloxone	V03AB15	4.2
nelfinavir (NFV)	J05AE04	6.4.2c
neomycin + bacitracin*	D06AX30	13.2
neostigmine	N07AA01	20
nevirapine (NVP)	J05AG01	6.4.2b
niclosamide	P02DA01	6.1.1
nicotinamide	A11HA01	27
nifedipine	C08CA05	12.3
nifurtimox	P01CC01	6.5.5b
nitrofurantoin	J01XE01	6.2.2
nitrous oxide	N01AX13	1.1
norethisterone	G03DC02	18.7
norethisterone enantate*	G03AC01	18.3.1
nystatin	A07AA02	6.3
nystatin	D01AA01	6.3
nystatin	G01AA01	6.3
ofloxacin	J01MA01	6.2.4
oral rehydration salts (for glucose–electrolyte solution)*	A07CA	17.7.1; 26.1

Medicine or item	ATC code	Section
oxamniquine	P02BA02	6.1.3
oxygen	V03AN	1.1
oxytocin	H01BB02	22.1
paracetamol	N02BE01	2.1; 7.1
penicillamine	M01CC01	2.2; 4.2
pentamidne*	P01CX01	6.5.1; 6.5.4; 6.5.5a
permethrin	P03AC04	13.6
phenobarbital	N03AA02	5
phenoxymethylpenicillin	J01CE02	6.2.1
phenytoin	N03AB02	5
phytomenadione	B02BA01	10.2
pilocarpine	S01EB01	21.4
podophyllum resin*	D06BB04	13.5
poliomyelitis vaccine	J07BF	19.3.1
polyvidone iodine*	D08AG02	15.1
potassium chloride	B05XA01	26.1; 26.2
potassium ferric hexacyanoferrate (II).2H_2O (Prussian blue)	V03AB31	4.2
potassium iodide*	H03CA	18.8; 6.3
potassium permanganate	D08AX06	13.2
praziquantel	P02BA01	6.1.1; 6.1.3
prednisolone	H02AB06	3; 8.3
prednisolone	S01BA04	21.2
primaquine	P01BA03	6.5.3[a]
procainamide	C01BA02	12.2
procaine benzylpenicillin*	J01CE09	6.2.1
procarbazine	L01XB01	8.2
proguanil	P01BB01	6.5.3b
promethazine	R06AD02	1.3; 17.2
propranolol	C07AA05	7.2
propyliodone	V08AD03	14.2
propylthiouracil	H03BA02	18.8
protamine sulfate*	V03AB14	10.2
pyrantel	P02CC01	6.1.1
pyrazinamide	J04AK01	6.2.4
pyridostigmine	N07AA02	20
pyridoxine	A11HA02	27
pyrimethamine	P01BD01	6.5.4
quinidine	C01BA01	12.2
quinine	P01BC01	6.5.3a
rabies immunoglobulin	J06BB05	19.2
rabies vaccine	J07BG	19.3.2
ranitidine	A02BA02	17.1
retinol	A11CA01	27
riboflavin	A11HA04	27

Medicine or item	ATC code	Section
rifampicin	J04AB02	6.2.3; 6.2.4
rifampicin + isoniazid*	J04AM02	6.2.4
rifampicin + isoniazid + pyrazinamide*	J04AM02	6.2.4
rifampicin + isoniazid + pyrazinamide + ethambutol*	J04AM02	6.2.4
ritonavir (r)	J05AE03	6.4.2c
rubella vaccine	J07BJ	19.3.2
salbutamol	R03AC02	25.1
salbutamol	R03CC02	25.1
salicylic acid	D01AE12	13.5
saquinavir (SQV)	J05AE01	6.4.2c
selenium sulfide	D01AE13	13.1
senna*	A06AB06	17.6
silver sulfadiazine	D06BA01	13.2
sodium calcium edetate*	V03AB03	4.2
sodium chloride	B05XA03	26.2
sodium fluoride	A12CD01	27
sodium hydrogen carbonate*	B05XA02	26.2
sodium lactate, compound solution*	B05BB01	26.2
sodium nitrite	V03AB08	4.2
sodium nitroprusside*	C02DD01	12.3
sodium thiosulfate*	V03AB06	4.2; 13.1
spectinomycin	J01XX04	6.2.2
spironolactone	C03DA01	16
stavudine (d4T)	J05AF04	6.4.3a
streptokinase	B01AD01	12.5
streptomycin	J01GA01	6.2.4
sulfadiazine	J01EC02	6.2.2
sulfadoxine + pyrimethamine*	P01BD51	6.5.3a
sulfamethoxazole + trimethoprim	J01EE01	6.2.2; 6.5.4
sulfasalazine	A07EC01	2.4; 17.4
suramin sodium	P01CX02	6.5.5a; 6.1.2
suxamethonium	M03AB01	20
tamoxifen	L02BA01	8.3
testosterone	G03BA03	18.2
tetracaine	S01HA03	21.3
tetracycline	S01AA09	21.1
thiamine	A11DA01	27
thiopental	N01AF03	1.1
timolol	S01ED01	21.4
triclabendazole	P02BX04[a]	6.1.3
trimethoprim	J01EA01	6.2.2
tropicamide	S01FA06	14.1
tuberculin, purified protein derivative (PPD)*	V04CF01	19.1
typhoid vaccine	J07AP	19.3.2
urea*	D02AE01	13.5

Medicine or item	ATC code	Section
valproic acid	N03AG01	5; 24.2.2
vancomycin	J01XA01	6.2.2
vecuronium	M03AC03	20
verapamil	C08DA01	12.1; 12.2
vinblastine	L01CA01	8.2
vincristine	L01CA02	8.2
warfarin	B01AA03	10.2
water for injection*	V07AB	26.3
yellow fever vaccine	J07BL	19.3.2
zidovudine (ZDV or AZT)	J05AF01	6.4.2a
zinc sulfate	A12CB01	

* Medicine or item name differs slightly from the name used in the ATC classification system.

[a] Provisional code pending formal approval by the WHO International Working Group for Drug Statistics Methodology.