WHO/EDM/PAR/2004.8

HOW TO DEVELOP A NATIONAL FORMULARY BASED ON THE *WHO MODEL FORMULARY*

A PRACTICAL GUIDE

World Health Organization

2004

Authors

Richard Laing[1] (Editor)

Klara Tisocki[2]

With contributions from: Douglas E. Ball[2], Joe Collier[3], Dinesh K. Mehta[4], Rachel S. M. Ryan[4], Andrea Tarr[3],

The text was reviewed by: Jude Nwokike[5], Rachel Ryan[4], Khalid H.M. Said[6], Wong Wai See[7], Robert S. Summers[8], Monika Zweygarth[8]

[1] Department of Essential Drugs and Medicines Policy, World Health Organization, Geneva Switzerland

[2]Faculty of Pharmacy, Kuwait University, Kuwait City, Kuwait

[3]Editorial Committee, British National Formulary, Royal Pharmaceutical Society of Great Britain, London, United Kingdom

[4]Drug and Therapeutics Bulletin, London, United Kingdom

[5]Centre for Pharmaceutical Management, Management Sciences for Health, Inc (MSH), Windhoek, Namibia

[6]Directorate General of Pharmacy, Federal Ministry of Health, Khartoum, Sudan

[7]Department of Pharmaceutical Services, Ministry of Health, Bandar Seri Begawan, Brunei

[8]MEDUNSA School of Pharmacy, Pretoria, South Africa

HOW TO DEVELOP A NATIONAL FORMULARY BASED ON THE *WHO MODEL FORMULARY*

A practical guide

Contents

Abbreviations iii

1 INTRODUCTION 1
Objectives 1
The need for formularies 1
What is a formulary? 1
The essential medicines concept 1
The WHO model list of essential medicines and the WHO model formulary 2

2 OVERVIEW OF THE NATIONAL FORMULARY PROCESS 3
Organization of the national formulary committee 3
The editorial team 3
The advisory group 3
Agreement on purpose, content, structure and format 3
Financing 4
Selection of medicines to be included in the national formulary 4
Development of the draft 4
Reviewing and finalizing content 5
Production, dissemination and implementation 5
Evaluation and review 5

3 DEVELOPING THE PRELIMINARY INFORMATION SECTION 7
Developing locally relevant introductory information 7
General entries at the front of a national formulary 7
Acknowledgements 7
Introduction or preface 7
Table of contents 7
Abbreviations 8
Units of measurement 8
Additional information at the front of the national formulary 8
Instructions on how to use the formulary 8
Glossary 8
Policies and procedures of the national formulary and national formulary committee 8
National policies and regulations 8
List of changes 9
Adapting the "General advice to prescribers" section of the WHO model formulary 9

4 DEVELOPMENT OF THERAPEUTIC INFORMATION AND MONOGRAPHS USING THE *WHO MODEL FORMULARY* 10
Adapting the therapeutic classification system of the WHO model formulary 11
Options for adapting information from the WHO model formulary in the national formulary 11
Addition of locally important, specific information to the WHO model formulary text 14
Introductory text of therapeutic sections 14
Monographs 14
Brand name(s) 14
Price 15
Writing new material for the national formulary 15
Language, style and presentation 16
Technical copy-editing 16

5 ADDITIONAL SOURCES OF INFORMATION 18
The evidence-based approach in formulary development 18
Information retrieval 18
Types of source 18
Primary information sources 19
Secondary information sources 19
Tertiary information sources 19
Manufacturer's literature 19
Searching for the best evidence 20
Using tertiary sources 20
Using secondary sources: evidence-based reviews and guidelines 20
Searching the primary literature 21
Accessibility 21
Printed sources 21
Electronic sources 22
Critical appraisal 22

6 DEVELOPING SPECIFIC INFORMATION SECTIONS 24
Creating locally important appendices 24
Adopting appendices from the WHO model formulary 25
Additions 25
Deletions 25
Working with a master document in Microsoft Word® to create a table of contents and index 26
Creating the table of contents 27
Creating the index 27

7 PRODUCTION, DISTRIBUTION AND IMPLEMENTATION 29
Production of the paper-based formulary 29
Final editing and layout of manuscript 29
Utilizing the electronic version of the WHO model formulary 29
Editing of final text 29
Printing 30
Distribution 31
Electronic publishing and distribution of the national formulary 31
Implementation to gain acceptance and credibility for the national formulary 31

8 EVALUATION 33
Evaluation of the NF within the framework of existing monitoring and evaluation activities 33
How to design the evaluation 33
What to evaluate 34
Policy, legal framework and management support 34
Selection 35
Procurement 35
Distribution of formulary 35
Rational use 36

9 REVIEW AND UPDATE 37
Planning for review 37
How frequently does the national formulary need to be reviewed? 37
Review process 38
Identification of areas in need of change 38
Drafting of updated texts for areas where change is necessary 38
Updating texts based on the WHO model formulary 38
Updating texts containing locally added information 39
Approval by the national formulary committee and expert advisers 39

REFERENCES 40

Abbreviations

EML	Essential medicines list
EDP	Essential drug programme
NF	National formulary
NFC	National formulary committee
rINN	Recommended International Non-proprietary Name
SI unit	Système Internationale unit
VEN	Vital, Essential, Necessary
WMLEM	WHO model list of essential medicines
WMF	*WHO model formulary*
WHO	World Health Organization

1 INTRODUCTION

Objectives

The overall aim of this manual is to provide information and tools for the development of national formularies (NF) based on and using the World Health Organization (WHO) *model formulary* (WMF). The purpose of such formularies is to provide objective unbiased information to health workers in a country and to promote the safe, effective and rational use of medicines.[1] Although the drug information included would be based mainly on the WMF, we suggest that a national or institutional formulary should also contain locally useful information.

The main purpose of this manual is to show how the WMF can best be utilized as a core resource for the production of a NF. The manual is aimed at health professionals and production staff who are involved in the development and maintenance of their NF.

The need for formularies

Medicines play a crucial role in the prevention and treatment of diseases. When used correctly, they can offer simple and cost-effective solutions to many health problems. Today many people have little or no access to safe and effective drug therapies and may be at risk of serious health problems due to treatment with ineffective, poor quality products, or incorrect and irrational use of medicines.

Formularies can be useful tools in solving some of these problems of drug therapy as they can:

- provide impartial drug information to counteract biased promotional activities or fill the gap where access to accurate, and up-to-date information is limited;
- promote the appropriate use of safe, effective and good quality medicines;
- help in the elimination of unsafe, ineffective or poor quality medicinal products by identifying effective and safe medications; and
- support cost-effective utilization of drug budgets and improve access to essential medicines.

What is a formulary?

A formulary is a manual containing clinically oriented summaries of pharmacological information about selected drugs. The manual may also include administrative and regulatory information pertaining to the prescribing and dispensing of drugs (*1*).

A national formulary generally concentrates on available and affordable medicines that are relevant to the treatment of diseases in a particular country. Formularies are also frequently created for different levels of health care, different sectors and for individual hospitals.

The essential medicines concept

The essential medicines concept (*2*) states that a limited number of carefully selected essential medicines,[2] with proven efficacy, safety and quality, leads to better health care, better management of medicines and lower health care costs for the majority of the population with common diseases.

---

[1] The terms “drug” and “medicine” are used interchangeably in this manual.

[2] Comprehensive information on the current essential medicine concept and the *Model list of essential medicines* can be found at http://www.who.int/medicines/

The WHO model list of essential medicines and the WHO model formulary

The *WHO model list of essential medicines* (WMLEM) (3) identifies over 300 medicinal agents and devices for the prevention or treatment of priority diseases. In 2002, WHO released the first edition of the *WHO model formulary*. The second revised edition based on the thirteenth *Model list of essential medicines* was published in 2004. This formulary contains detailed information about the indications, dosage, adverse effects, contra-indications and warnings for medicines included in the WMLEM**,** together with summaries of recommendations on their appropriate use.

The WMF is intended to be a starting point for national governments and institutions to develop their own formularies, as well as an information source for individual prescribers. A NF or institutional formulary will be different from the WMF because of the addition of locally useful information on treatment of prevalent diseases, prices, distribution rules and other locally relevant details (see Box 1.1). Country-specific information will be discussed in Chapters 2, 3 and 6.

The WMF is freely available on the Internet.[3] It is also available on CD-ROM in different file formats that can be used for electronic editing of NFs. The WMF will be updated every two years and will continue to be available in electronic formats to support the review and update of NFs.

Box 1.1. Difference between content of the *WHO model formulary* and a national formulary

Content	*WHO model formulary*	National formulary
General advice to prescribers	✓	✓
Individual drug information	✓	✓
Therapeutic information, recommendations	✓	✓
Medicine prices	–	✓
Brand names	–	✓
Availability at health facilities	–	✓
National policies on prescribing/dispensing	–	✓
Reference to, or brief summary of, local guidelines	–	✓
Specific information on drug interactions, prescribing in pregnancy, breastfeeding, hepatic and renal impairment	✓	✓
Forms for reporting of adverse drug reactions and product quality problems	–	✓
Nomograms, dose calculators or other tools	–	✓

[3] The WMF is available on the Internet at: http://mednet3.who.int/eml/modelFormulary.asp

2 OVERVIEW OF THE NATIONAL FORMULARY PROCESS

The development and maintenance of a NF is a dynamic process and requires careful planning and coordination. Widespread support of relevant government, professional and possibly health insurance organizations is vital. The major stages of the development and maintenance processes are illustrated in Figure 2.1.

Organization of the national formulary committee

The national formulary committee (NFC) makes final decisions on the purpose, structure, content and format of the NF. This group should be limited in size to enable effective functioning and should act with the endorsement of national policy-making bodies. If there is an established essential drug programme (EDP) in the country, then the existing multidisciplinary committee or a subcommittee of it can serve as the NFC.

If there is no EDP committee or any other national medicine or therapeutic committee then a NFC should be formed. This committee should include practising physicians, clinical pharmacists, pharmacologists and medical specialists. Asking professional bodies (national medical and pharmaceutical associations) to nominate representatives can lead to better acceptance of NF through widespread ownership. Care should also be taken to ensure that the group is balanced geographically, with representatives from all areas of the country.

The editorial team

The editorial team includes the editors and possibly technical assistants. They will be responsible for drafting and producing the NF as a formal publication as well as for conducting reviews and updating subsequent editions. Ideally the editorial team should be able to design the final layout of the NF. Therefore, they should have sufficient computer skills to be able to generate the electronic master file and the final camera-ready copy. Although, these technical aspects of the production can be passed to a commercial publishing company this can be very expensive and time-consuming.

The advisory group

Expert advisers should be invited to review and comment on the draft text of the NF. Representatives of the intended audience (i.e. doctors, nurses, pharmacists and other health care workers) should be invited to comment on the relevance and applicability of information to local practice. In addition, they can comment or advise on the local best practices when there is no reliable experimental evidence available. The greater the participation of the practising health professionals, the more chance there is that the formulary will respond to local information needs and therefore become a truly useful resource for all health care workers.

Agreement on purpose, content, structure and format

The WMF could serve as a model for the structure, content and depth of information provided in a NF. However, depending on the intended audience and purpose of the NF, substantial differences will still exist between countries with regard to inclusion of local drug policies, synopses of national guidelines and locally collected information on medicines. Therefore, the NFC and the editors should clearly define these attributes of the formulary and identify the procedures necessary to achieve them.

Important structural and formatting decisions regarding classification, indexing, number of sections, technicality of language, etc. will need to be made early in the drafting process.
The development of a NF can be greatly facilitated by the extensive adoption of WMF structures and content. Clearly the intended purpose of a NF will strongly influence whether the NF will be a slim, compact drug handbook or a more substantial and comprehensive drug reference book. However, a balance will have to be struck between including all possible information and producing a manageable volume for everyday use. It is useful to look at other published formularies at this planning stage to obtain helpful ideas.

Developing a small "pilot" draft section of the formulary based on the WMF and discussing content and format issues again before the entire draft is developed can be a useful way to save editorial time and make production of the draft consistent.

Financing

Securing an adequate amount of initial and recurring funding may prove difficult, but to maintain the integrity and independent status of the NF, it is best that funding is mainly sought from national or international professional bodies and donors. Pharmaceutical industry support may influence procedures or the content of the NF and can affect its independent status and authority.

Selection of medicines to be included in the national formulary

One of the most important decisions to be made by the NFC is what medicines to include in the NF, or what is on the formulary list. The starting point for the formulary list should be the existing essential medicines list (EML). The NFC may consider the addition of selected medicines to this list based on clear criteria that reflect the main purpose of the NF.

In countries without any EML or other approved national medicine list, it will be necessary to gain some insight on drug needs and use for the compilation of the formulary list based on:

- national morbidity data to determine patterns of prevalent diseases;
- recommendations of appropriate national, regional or international clinical guidelines to link selection of medicines to evidence-based treatment guidelines;
- original research and review papers, particularly local research;
- the list of pharmaceuticals registered by the national drug regulatory authority and currently marketed in the country (to assess availability and cost); and
- available financial, human and health facility resources, and demographic, genetic and environmental factors.

Development of the draft

The editorial group should create and present the draft texts to the NFC and the expert advisers in a predetermined standard style. A formulary is typically presented in three parts and for all three parts the WMF text can be extensively utilized. The three parts are:

- preliminary information;
- drug and therapeutic information; and
- appendices.

National information relevant to all three parts should be integrated with the WMF data. If information for the NF is simply copied from the WMF without the inclusion of information that is locally relevant and important, the NF may have only a minor influence on local prescribing habits.

Reviewing and finalizing content

The review and finalization of the content of the NFC takes into account the input of various expert advisers and their consolidated comments, before agreement is reached on the final draft. The credibility and authority of the NF depend heavily on this consultation process, which will affect the acceptance and potential impact of the NF. Reaching consensus on the final text can be a lengthy process and it is important to use the most effective means of communication, follow-up meetings or workshops to avoid delays.

Production, dissemination and implementation

Production of the final manuscript for a formulary calls for meticulous and intensive editorial work that requires adequate human and technical resources (for example a full-time editor and appropriate computer hardware and software).

Planning for widespread dissemination and active introduction of the NF is very important; research has shown that without active implementation, printed drug information may have a negligible effect on prescribing (*4*).

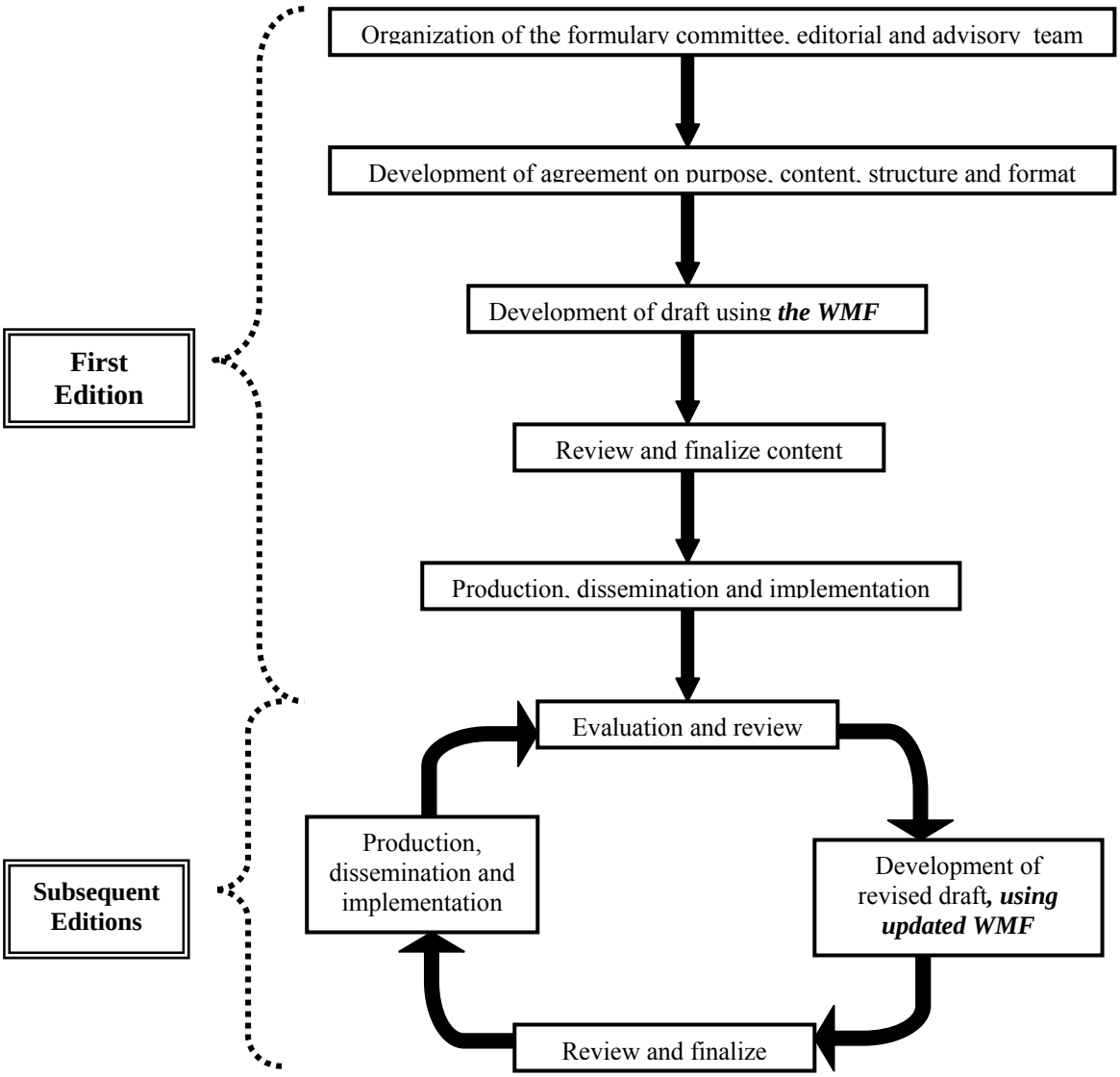
Evaluation and review

Evaluation of the availability, use and impact of the NF is best integrated with existing, regular monitoring and evaluation activities. In addition, specific surveys and/or interviews can also be conducted and the results of these, together with the written and verbal comments received from users, should be carefully considered in the review process.

The most recent edition of the WMF should be used in the scheduled revision of the NF and information from the updated WMF texts should be carefully transferred into subsequent editions of the NF.

During the review process, clear procedures will need to be established to cover deletion, addition and modification of entries in the revised NF as well as possible changes in scope and presentation.

Figure 2.1. Overview of the development and maintenance of a national formulary



WMF, *WHO model formulary*.

3 DEVELOPING THE PRELIMINARY INFORMATION SECTION

Developing locally relevant introductory information

The intended purpose, audience and ease of use should be kept in focus when compiling information for the preliminary section of the NF. Overloading the front of the NF with numerous copies of local documents may increase the volume and the production costs of the NF, without offering much helpful and practical information to the user.

The preliminary section of a formulary usually contains the following sections and can include additional information, as listed below. Please note that the ordering of this list does not necessarily reflect the ideal order of entries in a NF.

General entries at the front of a national formulary

Acknowledgements

The acknowledgements should include the names of those who contributed to the development of the NF, i.e. the members of the NFC, the editorial group, members of the advisory group, any technical support personnel and other institutions, professional organizations and donor agencies who provided either technical or financial support.

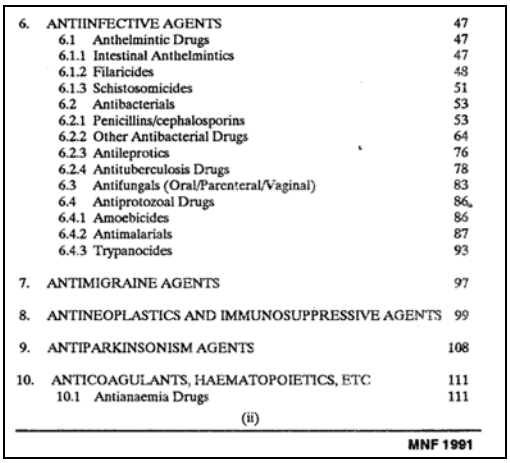
Introduction or preface

This section is usually a brief description of the purpose of the formulary, the intended audience, the "ownership" of the NF or the official publisher, the range and types of medicines included and the methodology of development. It commonly contains a correspondence address to which comments can be sent by post, fax or email.

Table of contents

Together with the index at the back, the table of contents is often the most frequently consulted section in a formulary, so care must be taken to design the structure and layout to achieve the greatest clarity and ease of use. The table of contents at the front of the NF can be very brief, giving only the titles and page numbers of the main sections, whereas detailed tables of contents are presented at the beginning of subsections; as in the WMF. Alternatively the table of contents at the front can be more detailed listing the main headings and subheadings for all subsections as in the Malawi National Formulary (see Box 3.1).

Box. 3.1. Example of a detailed table of contents, Malawi National Formulary, 1991



6. ANTIINFECTIVE AGENTS 47
6.1 Anthelmintic Drugs 47
6.1.1 Intestinal Anthelmintics 47
6.1.2 Filaricides 48
6.1.3 Schistosomicides 51
6.2 Antibacterials 53
6.2.1 Penicillins/cephalosporins 53
6.2.2 Other Antibacterial Drugs 64
6.2.3 Antileprotics 76
6.2.4 Antituberculosis Drugs 78
6.3 Antifungals (Oral/Parenteral/Vaginal) 83
6.4 Antiprotozoal Drugs 86
6.4.1 Amoebicides 86
6.4.2 Antimalarials 87
6.4.3 Trypanocides 93

7. ANTIMIGRAINE AGENTS 97

8. ANTINEOPLASTICS AND IMMUNOSUPPRESSIVE AGENTS 99

9. ANTIPARKINSONISM AGENTS 108

10. ANTICOAGULANTS, HAEMATOPOIETICS, ETC 111
10.1 Antianaemia Drugs 111

Abbreviations

Internationally accepted units and symbols should be used wherever possible. The use of abbreviations in the NF should be kept to a minimum to avoid any potential misinterpretation or confusion. In the WMF, great care has been taken to avoid the use of any abbreviations (Latin or English) regarding the route and frequency of administration of medicines because of the risk of misinterpretation and also because their conventional use may vary greatly from country to country: it is therefore advisable to follow this principle in a NF. For example misinterpretation or careless reading of:

qd = *quoque die* = once a day, or qid = *quater in die* = four times a day,

can have life-threatening consequences to the patient. Always use unambiguous instructions, e.g. 4 times daily, *by mouth,* as in the WMF.

Units of measurement

The WMF employs units and prefixes conforming with the Système Internationale (SI units). Including a short table of the acceptable units of measure at the front of the NF can encourage safe prescription-writing practices. Also remember to maintain the same safe practices when adding text to the NF, e.g. write microgram in full instead of µg or mcg, which may be misinterpreted as mg. In those countries where imperial measures are still widely used, it can be useful to include a conversion table for SI units.

Additional information at the front of the national formulary

Instructions on how to use the formulary

This section can give a very brief description of what to expect in the different parts of the book (e.g. monographs) and provide explanations on use of local symbols and codes for distribution and prescription categories; information on origin and interpretation of prices can also be included.

Glossary

A list of some of the medical terms commonly used in the NF, together with short definitions in one or two pages, can be useful if the users' educational backgrounds are likely to differ, but the compilers should avoid writing a whole medical dictionary.

Policies and procedures of the national formulary and national formulary committee

The text on policies and procedures of the NF and NFC can briefly outline the role and responsibilities of the NFC and any other organizations, such as the Ministry of Health, involved in producing the NF. Information presented here can verify the authority of a NF and promote its widespread acceptance. If the NF is implemented within a national or regional formulary system or linked to any reimbursement scheme, this can also be specified here.

National policies and regulations

The following items can be included as separate sections, or some of them may be adapted from the "General advice to prescribers" section of the WMF:

— guidelines for prescribers on national requirements on prescription writing, prescribing dangerous or controlled preparations, principles of rational drug use, prescribing for patients with special needs (children, the elderly, pregnant and lactating women, those with renal and hepatic disease, and those requiring intensive and palliative care);

— guidelines on good dispensing practices including checking prescriptions, accuracy of dispensing, labelling, packaging and patient counselling;
— reporting of adverse drug reactions; and
— reporting of defective medicines or counterfeit products.

List of changes

Lists of changes can alert the reader to changes in revised editions of the NF. They should be presented in a clear way, with a brief explanation or reference when necessary. Potential changes that may be listed are:

— significant changes in therapeutic information;
— deletion or addition of drugs;
— discontinuation or addition of individual preparations; and
— changes in dose or classification of existing entries.

Adapting the "General advice to prescribers" section of the WHO model formulary

This section of the WMF aims to point prescribers towards good prescribing practices and important factors that can influence the outcome of drug therapy.

It could be useful to include the whole of the WMF text for this section in the NF and to supplement it with relevant national information as mentioned above.

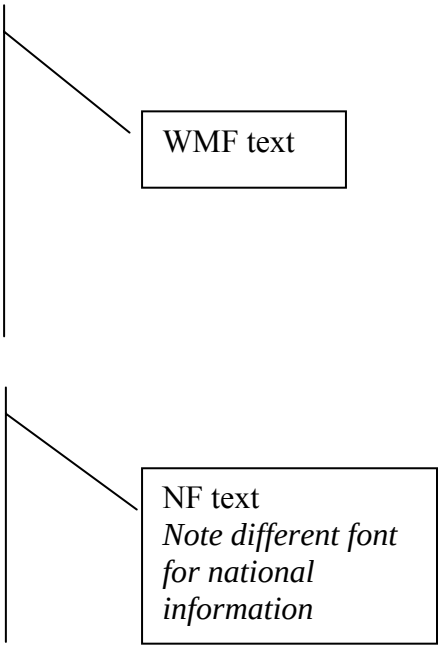
The local information inserted can be presented using a different text style so that the user can access it quickly in cases when local recommendations are not in agreement with WMF recommendations or editors wish to add emphasis to local text (see example in Box 3.2). However this may be confusing to readers, and a uniform style and agreement by the expert advisers on what to include in the final text is possibly a better solution.

Box 3.2. Addition of local information in "Prescription writing" section

Narcotics and controlled substances

The prescribing of a medicinal product that is liable to abuse requires special attention and may be subject to specific statutory requirements. Practitioners may need to be authorized to prescribe controlled substances; in such cases it might be necessary to indicate details of the authority on the prescription. In particular, the strength, directions and the quantity of the controlled substance to be dispensed should be stated clearly, with all quantities written in words as well as in figures to prevent alteration. Other details such as patient particulars and date should also be filled in carefully to avoid alteration.

In Zimbabwe all prescriptions for narcotics must be hand written with the quantity of prescribed drug written in full words as well as with numbers and the prescription may be repeated on not more than two occasions. All other requirements for prescriptions also apply and must be filled completely. The pharmacist must keep a record of all dispensed narcotics and prescriptions and make it available for inspection by the Medicine Control Authority of Zimbabwe. *Dangerous Drugs Regulations (S.I. 111/75) and Dangerous Drugs Act [Chapter 15:02]*



4 DEVELOPMENT OF THERAPEUTIC INFORMATION AND MONOGRAPHS USING THE *WHO MODEL FORMULARY*

Guidance in this section mainly applies to the initial development of the NF; those who wish to use the WMF for reviews and updates of their existing NF should consult Chapter 9.
The scope and depth of drug information included in the NF should be appropriate for its intended audience. The WMF can be extensively utilized for the presentation of basic and supplementary information (see Box 4.1) on each drug and therapeutic class. However, there are likely to be cases when new information has to be added. Before new information is inserted, a comprehensive review of available and appropriate drug and therapeutic information should be conducted (more details are given in Chapter 5).

The editorial team will need to draft new text, or suitably qualified professionals can be asked to produce these drafts. To achieve uniform standards of writing and reviewing, and to maintain quality of additional information it is useful to introduce standard requirements for style, content, structure and format; standard operating procedures are useful especially when several people are involved in the writing of the additional material for the NF. For example, the *British National Formulary* editorial group apply more than 30 written standard operating procedures to direct the different information construction, review and editorial tasks needed for the repeated review process. The use of such quality assurance tools can help to maintain high standards and will also serve as a guide during future revisions of the NF.

Box 4.1. Information to be presented for individual drugs in a formulary

Basic information	**Supplementary information**
Generic name ✔	Common brand name(s)
Dosage form and strength ✔	Price
Main indication ✔	Level of use or distribution code
Pharmacology/pharmacokinetics ✔	Prescription category
Contraindications ✔	Patient information ✔
Precautions ✔	Labelling information
Dosage schedule ✔	Storage instructions and stability
Adverse effects ✔	Essential drug list number
Drug and food interactions ✔	Main supplier catalogue number
Instructions, warnings ✔	Procurement priority code (VEN)
	Re-imbursement scheme code

✔, present in the WMF
VEN, Vital, Essential, Necessary
WMF, *WHO model formulary*.

Adapting the therapeutic classification system of the *WHO model formulary*

To date, the WMF has mainly kept the therapeutic classification system used in the WMEML with only minor modifications. This system is widely used by countries with existing EMLs as well as local and international suppliers such as the United Nations Children's Fund (UNICEF) or the International Dispensary Association. It is strongly recommended that the same classification system be maintained in the NF, as this can help the NFC and the editors to:

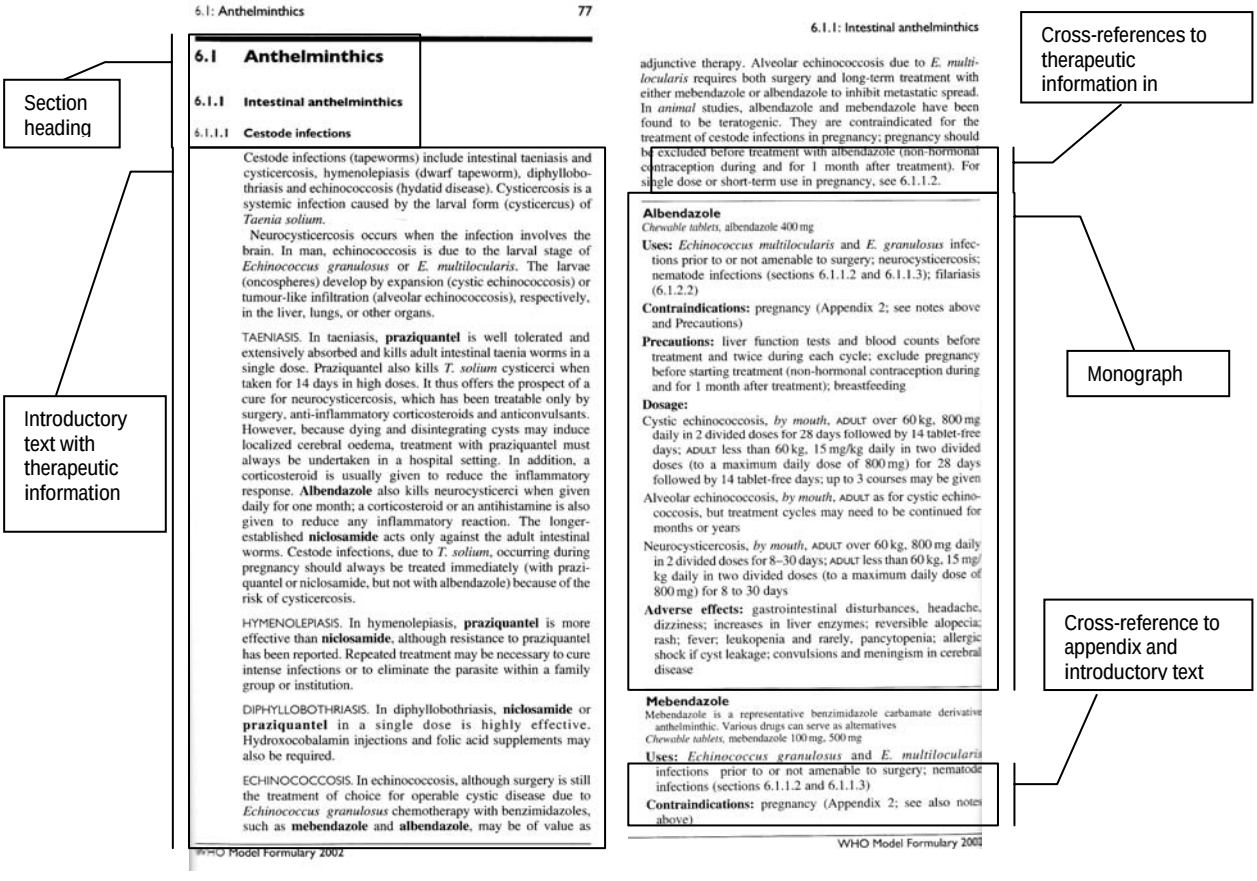
— incorporate a list of essential and/or other selected medicines into a well-known therapeutic classification system;
— adopt all introductory texts of the WMF and maintain their integrity as much as possible, thus reducing the risk of lost or potentially invalid information;
— save time and effort on word-processing of the NF, by using the complete electronic text of the WMF on all 27 categories, instead of importing WMF sections in fragments into a different classification system; and
— take advantage of the existing table of contents and indexing field codes present in the WMF Word® files for generation of contents lists and indexes, thus decreasing the time necessary for production.

However, if there is already a widely used national classification system for essential medicines, this should be matched in the NF, rather than using the WMF structure.

Options for adapting information from the WHO model formulary in the national formulary

In the WMF, individual drug monographs are closely associated with the introductory information for each section and the information in the appendices (Figure 4.1).

Figure 4.1. Interconnected structure of the *WHO model formulary*



This structure means that certain facts about an individual drug do not always appear in the relevant monograph: instead cross-reference is made to the introductory text of the section or other sections, and to the appendices.

This can make transferring single monographs or chapters into the NF complicated. Because of this existing structure, there are two main ways in which passages from the WMF may be adapted for inclusion in a NF:

Option 1. Keep the full text of the WMF and make additions by inserting the text of national recommendations and drug information in the relevant places and use limited deletions in "blocks" to remove irrelevant WMF information.

Option 2. Very thoroughly edit (cut and paste, delete and modify) all types of entries, including the appendices.

Option 1.

If the first option is used, the full text of the WMF is reproduced without alteration or with minimal changes. National recommendations and important information on local medicines are inserted in a consistent manner in the appropriate places into the copy of the WMF text. This can best be achieved by using a uniform formatting style, i.e. a different font and type-size to distinguish the additional NF information from the WMF content and to alert the reader to the national information. Other formatting techniques, i.e. the use of bold text, underlining and italics should be avoided except in the contexts in which they are used in the WMF. An example of the insertion of national information is shown in Figure 4.2.

Deletions should be made very cautiously, preferably in "blocks", i.e. if it is not intended to keep the section on Leprosy, then the complete subsection of "6.2.3. Antileprosy drugs" may be deleted, or monographs on irrelevant drugs deleted in full. Care should be taken to ensure that the remaining sections do not contain cross-references to the one that has been deleted.

If the NF list is very comprehensive, extensive additions to the monograph sections may be necessary. Since many of these additions will be "me-too" medicines (i.e. belonging to the same pharmacological class and having similar efficacy and safety), the introductory text of the WMF could remain relevant and can promote rational choices. For the writing of new monographs it is essential to use authoritative drug information resources (see Chapter 5) and very careful editing (see notes on copy-editing below).

The use of this first option can be relatively straightforward for those countries where either there is no national EML and treatment guidelines, or there is a good overlap between the WMLEM and the national EML and it is possible to maintain the same or a very similar classification.

Figure 4.2. Example of addition of national information to *WHO model formulary* text

INTRODUCTORY TEXT

Various regimens have been used to specifically prevent the transmission of HIV from mother to the neonate at term. More information is available in *New Data on the Prevention of Mother-to-Child Transmission of HIV and their Policy Implications: Conclusions and Recommendations* (WHO/ RHR/01.28), which reflects an inter-agency consultation held on 11-13 October 2000.

In Zimbabwe the risk of mother to child transmission of HIV is high. Based on seroprevalence data collected in 2001 and the estimated 15-45% transmission rate, approximately 50 000 infants get infected annually. The simple nevirapine regimen is recommended for prevention as outlined in *the Prevention of Mother to Child transmission of HIV (PMTCT) – National site protocols for Ministry of Health & Child Welfare, Edition 1 February 2003.* It is important to integrate the administration of nevirapine in a comprehensive care package including essential interventions such as counselling and voluntary testing of pregnant women, safe obstetrical practices and infant feeding education. Nevirapine is freely available at public health care facilities enrolled in PMTCT programmes (more than 160 sites with 120 rural health centres included as of July 2003). For more details contact the National AIDS & TB Unit in MOH&CW.

MONOGRAPH TEXT

Nevirapine
NVP
Tablets, nevirapine 200 mg
Oral suspension, nevirapine 50 mg/5 ml
Uses: HIV infection, in combination with at least two other antiretroviral drugs; prevention of mother-to-child transmission in HIV-infected patients (but see notes above under Pregnancy)
Precautions:
hepatic impairment (see below and Appendix 5); renal impairment; pregnancy (see notes above); breastfeeding (see notes above);
interactions: Appendix 1

HEPATIC DISEASE. Potentially life-threatening hepatotoxicity including fatal fulminant hepatitis reported usually occurring in first 8 weeks; monitor liver function before long-term treatment then every 2 weeks for 2 months then after 1 month and then every 3-6 months; discontinue permanently if abnormalities in liver function tests accompanied by hypersensitivity reaction (rash, fever, arthralgia, myalgia, lymphadenopathy, hepatitis, renal impairment, eosinophilia, granulocytopenia); suspend if severe abnormalities in liver function tests but no hypersensitivity reaction; discontinue permanently if significant liver function abnormalities recur; monitor patient closely if mild to moderate abnormalities in liver function tests with no hypersensitivity reaction

RASH. Rash, usually in first 8 weeks, is most common adverse effect; incidence reduced if introduced at low dose and dose increased gradually; discontinue permanently if severe rash or if rash accompanied by blistering, oral lesions, conjunctivitis, swelling, general malaise or hypersensitivity reactions; if rash mild or moderate may continue without interruption but dose should not be increased until rash resolves

Patient Advice. Patients should be told how to recognize hypersensitivity reactions and advised to seek immediate medical attention if symptoms develop

Dosage:
HIV infection (in combination with other antiretroviral drugs), *by mouth* , **ADULT** 200 mg once daily for first 14 days then (if no rash present) 200 mg twice daily; **INFANT** 15-30 days old, 5 mg/kg once daily for 14 days, then (if no rash present) 120 mg/m^2 twice daily for 14 days, then 200 mg/m^2 twice daily; **CHILD** 1 month-13 years, 120 mg/m^2 twice daily for first 14 days, then (if no rash present) 200 mg/m^2 twice daily

Prevention of mother-to-child transmission of HIV (see also notes above under Pregnancy), *by mouth* , **ADULT** 200 mg as a single dose at onset of labour; **NEONATE** 2 mg/kg as a single dose within 72 hours of birth

NOTE. If treatment interrupted for more than 7 days reintroduce with 200 mg daily (**INFANT** 15-30 days old, 5 mg/kg; **CHILD** over 1 month, 120 mg/m^2) and increase dose cautiously

NEVIRAPINE for PMTCT in Zimbabwe:

- One 200 mg dose *by mouth* to HIV positive mother at onset of labour (aim for early administration so mother delivers 24-48 hours after taking the nevirapine)
- SOME HIV exposed babies will receive a 0.6 ml or 6 mg dose of nevirapine suspension *by mouth* immediately after delivery (under special circumstances e.g. speedy delivery, mother did not take NVP prior to delivery)
- ALL HIV exposed babies will receive one 0.6 ml or 6 mg dose of suspension 48-72 hours after delivery (this includes babies who have already been given a dose immediately after birth).

Note: For information on procedures to be followed for women in labour with unknown HIV status and other details, see the national protocol mentioned above.

Adverse effects:
rash including Stevens-Johnson syndrome and rarely, toxic epidermal necrolysis (see also Precautions above); hepatitis or jaundice reported (see also Precautions above); nausea, vomiting, abdominal pain, diarrhoea, headache, drowsiness, fatigue, fever; hypersensitivity reactions (may involve hepatic reactions and rash, see Precautions above); anaphylaxis, angioedema, urticaria also reported
Brand names: Viramune 200mg tablets and 50 mg/ 5ml suspension (*Ingelheim Pharmaceuticals*), Nevimune 200mg tablets (*CIPLA Pvt. Ltd.*) Nevipane 200 mg tablets (Ranbaxy Pvt Ltd),

Price : Viramune 200mg 60 tabl. Z$ IIIIII, 50mg.5ml 240ml suspension ; Nevimune 200mg 60 tablets Z$ CCCC, Nevipane 200 mg 60 tablets, Z$ RRRR

Option 2.

The second option might be necessary when the NF list (the classification system used and medicines included) and the national recommendations are different from those in the WMF. The rearrangement of sections and re-editing of clinical information to match recommendations to local protocols will be unavoidable in those countries where an EML and national standard treatment guidelines already exist and are widely used. Although the monographs themselves may need little change, extensive work will be required to correct the cross-references.

Extensive changes to the WMF will require highly skilled editorial input, complex rearrangements and the addition of substantial amounts of new text. As such extensive re-editing can easily introduce new errors and unwanted artefacts, it will be crucial to validate the draft text, using up-to-date and suitable drug information resources (see Chapter 5). The adoption of the second option will require considerably more time and resources than the first option.

Addition of locally important, specific information to the *WHO model formulary* text

As outlined under Option 1 above, the insertion of local information into the full WMF text can facilitate the production of a NF. Details on the addition of information on local therapeutic practice and on individual drugs are discussed below.

Introductory text of therapeutic sections

General statements about national clinical guidelines, policies and warnings can be added to the introductory text using the uniform text style mentioned above. For example, a summary of the national tuberculosis treatment schedules can be given a prominent place, with a clear title at the beginning of Section 6.2.4 "Antituberculosis drugs", whereas contact details for treatment centres for multi-drug resistant tuberculosis in the country can be inserted near to the relevant WMF text.

The *Producing drug and therapeutic information — the Malawi approach to developing standard treatment guidelines*[4] manual gives useful information and practical tips for those who may be simultaneously developing or revising national standard treatment guidelines while working on the NF.

Monographs

If there is any need to alter the basic information about individual drugs (e.g. dosage schedule) (see box 4.1) this should be done using the same uniform text style to show that this is a national recommendation or national information. In this case, the original WMF text should be deleted in order to avoid any confusion. The locally specific, supplementary information for individual drugs can be inserted at the end of each monograph (see box 4.1.) or can be summarized in tables as described below.

Brand name(s)

Brand names of locally marketed original products (produced by the innovator) and/or brand names of multi-source products (branded generics) can be included under this heading.

[4]Available on the Internet at: http://www.who.int/medicines/library/dap/who-dap-94-14/who-dap-94-14.doc

Listing the names of nationally registered, quality products (with established bioequivalence in the case of generics) can help to decrease the use of substandard or counterfeit products.

Price

In certain countries it may not be possible to include prices for all products because of inflation and frequent changes in suppliers, or if the time taken to produce the formulary would result in outdated price information.

In such cases symbols or codes can be used to alert users to high-cost products or to show the relative costs of products, for example on a scale of cheapest = $ to most expensive = $$$$$, the following could be used: *Salbutamol inhaler, price: $; Beclomethasone inhaler, price: $$$.* However, this type of price banding system may not always be accurate and the following should be borne in mind:

- Careful monitoring is needed to ensure that price has not moved from one band to another.
- It may be difficult to judge the price in the top band if it is too broad, i.e. if prices vary by a factor of 10 or more.

In other countries the NFC may choose to publish actual prices (as in the *British national formulary*).

Instead of showing individual unit cost of products, therapy cost comparison charts can be useful and informative for specific therapies. They can show the cost of a full course, or the daily and monthly cost of therapy with a number of alternatives being compared on the same graph (Figure 4.3 shows an example). The inclusion of such price comparison charts is advisable when wide ranges of alternatives are available for the treatment of common conditions such as infectious diseases and cardiovascular conditions or for pain control.

Scheduling status and availability codes

Scheduling status and availability codes can be indicated by the use of codes or abbreviations. For example:

- **Distribution code (*Malawi national formulary*, 1991):**
  C = central hospitals only;
  D = district and central hospitals only;
  H = health centres and all other levels of health institution.
- **Prescribing category code (*British national formulary*, 47th ed., 2004)**
  PoM = prescription only medicine.

Codes for procurement, such as catalogue numbers necessary for ordering from the central medical store, priority codes as defined in a VEN system (Vital, Essential, Necessary priority), or symbols indicating eligibility for re-imbursement can also be useful.

Writing new material for the national formulary

Once information has been collected and summarized for the purpose of insertion into the NF (see Chapter 5), it is crucial that development of the draft text follows a rigorous process including:

- **Writing** the draft text in a clear, accurate style that is tailored to the purpose of the NF with sufficient detail in both introductory texts and in the monographs. The writing style used for additional text in the NF should be in harmony with the adapted WMF writing style.

- **Structuring** the draft text to make the information easily accessible. Subheadings should follow existing structures. If the additional medicine will be used for different conditions, the relevant cross-references should be carefully included and monographs should reflect all recommended indications, dosage schedules, warnings, etc. for the different uses.
- **Reviewing** the draft text at several levels:
  - peer-review by members of the editorial team;
  - content review by members of the advisory group to check readability and relevance to the intended audience; and
  - technical copy-editing and proofreading to check accuracy and validity, as already described.
- **Formatting** the draft text using a clearly distinguishable style that indicates additions to WMF text as discussed earlier.
- **Positioning** of the draft text within the adapted text of the WMF. When inserting additional text in the introductory section, try to maintain the clarity of the WMF text while giving the necessary prominence to the additional local information. New monographs should be placed within the relevant therapeutic/pharmacological section. In the case of multiple indications, a decision needs to be made on where to place the main monograph and how to provide clear cross-references in other chapters where the medicine is mentioned.
- **Creating** additional information to be included in specific sections such as that on drug interactions, other appendices, table of contents and indexing field codes.

Language, style and presentation

The language and style used for writing local additions or modifications should be clear and provide immediate access to information. The local information inserted should remain concise and relevant to the purpose of the NF. The editorial group should agree on the writing style for the inserted and modified texts (wording of indications, contraindications, adverse effects, dosage statements, etc.); it is desirable to use a writing style similar to that of the WMF to maintain clarity and consistency.

Presentation of local facts in tables or visually appealing figures is useful when making comparisons, whereas for more extensive information text is more suitable. Tabulated information can offer the advantage of quick browsing and location of information by the user and simplified editing and verification of local facts for the editor. In addition, an eye-catching layout with clear titles can help to direct the reader to important local additions in the NF.

Technical copy-editing

Copy-editing is the process whereby editors check the draft text to ensure correct spelling, grammar and conformity with the pre-agreed style requirements and to correct any inconsistencies or inaccuracies. General aspects of copy-editing are discussed in Chapter 7, but it is important to pay attention to those technical copy-editing tasks necessary to ensure validity of drug and therapeutic information. Inserted text should be checked for:

- the consistent use of drug names (recommended International Non-proprietary Names (rINN)), and disease names;
- conformity of all units of measurement with the SI units applied in the WMF text;
- accuracy of local units of measure and provision of explicit and accurate conversions to SI units;
- definitions of any local abbreviations added;

— compatibility between new local text in the introduction and in the newly added monographs; and
— accurate cross-references and potential connections to existing cross-references.

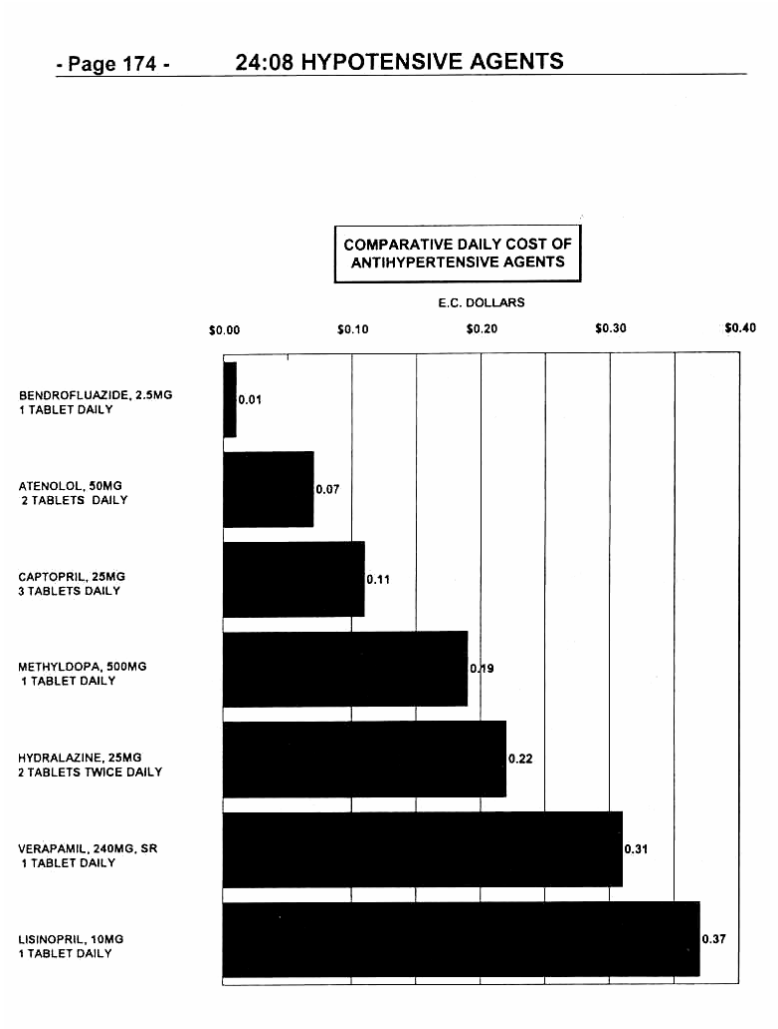
Special attention must also be paid to the careful validation of the new text using current references (i.e. Martindale drug reference guide and other drug information textbooks, selected clinical guidelines, drug reviews and manufacturer's literature) .

Finally, meticulous proofreading of the last draft to check for accuracy of content and consistency of style will ensure a high-quality publication (see further details in Chapter 7).

The writing and editing of special information sections is discussed in Chapter 6.

Figure 4.3. Cost comparison of antihypertensive agents

(*Regional formulary and therapeutic manual*, 6th ed., 2002, Organisation of Eastern Caribbean States and Pharmaceutical Procurement Services)



SR = Slow release

5 ADDITIONAL SOURCES OF INFORMATION

When the NF editorial team has completed its adaptation of the WMF material it may be necessary to include additional materials on medicines which are on the national EML, but not on the WHO list. Creating this new text requires a process of gathering and evaluating available information and then summarizing it for the NF in a way that is compatible with the adapted WMF material. Very thorough editing procedures will need to be followed to produce accurate, relevant and good quality information.

The evidence-based approach in formulary development

Any new information included in the NF should promote the rational and evidence-based use of medicines. Evidence-based drug therapy means integrating the best, currently available clinical evidence from scientific research with the individual clinical expertise of the prescriber to improve patient care. Informing prescribers about current evidence-based practices and national guidelines can help close the gap between research findings and their implementation in routine practice. Therefore a NF presenting such up-to-date information can be a valuable educational tool in the promotion of evidence-based drug therapy.

When trying to fill gaps in the drug and therapeutics information included in the NF, there are three important questions that need to be answered.

- Where do we find the information?
- Is this the most up-to-date and valid information?
- How relevant and applicable is this information to our local conditions?

Answering these questions requires good information retrieval and critical appraisal skills. The editors and the NFC can be assisted with both of these tasks by experienced health information specialists, such as medical librarians or personnel from national drug information centres and independent drug bulletins. The Society of Hospital Pharmacists of Australia[5] (SHPA) has an international register of drug information services on its web site and the International Society of Drug Bulletins[6] (ISDB) also lists contact addresses for independent drug information bulletins around the world.

Information retrieval

A vast amount of information is available about medicines and can be accessed in a number of ways, i.e. through journals, books, electronic sources and the Internet. Often, it is difficult to separate the "wheat from the chaff", i.e. to find relevant and useful information. All efforts should be made to locate high-quality local evidence, if it exists, as this will reduce any uncertainty about transferring recommendations to local patient populations.

Types of source

Published information can be divided into primary, secondary and tertiary sources; manufacturer's literature can fall into any of these three categories but will be discussed separately here. For examples of selected sources that are useful in the development of formulary information see Table 5.1.

[5] SHPA http://www.shpa.org.au/frame.htm

[6] ISDB http://www.isdbweb.org

Primary information sources

Primary literature is defined as publications containing original research on drug therapy. It can include published reports of randomized controlled trials, cohort studies, case reports, pharmacological research, toxicological research and other types of evaluation. Journals that publish such information about drug therapies are often available both as printed and electronic publications.

Secondary information sources

Secondary sources either review the primary literature or direct a researcher to it, as described below:

1. *Reviews* are presented as systematic reviews, secondary journal publications (critical appraisal comments added to the abstract of a primary article), clinical practice guidelines, health technology assessments or drug information bulletins. They all review the original evidence and may draw additional conclusions about it. They can be fairly up-to-date, and if the review process has followed a rigorous method such as that used by the *Cochrane Collaboration*, they can provide quick access to valid, summarized research evidence, including some unpublished "grey literature".[7]
2. *"Indexing type"* bibliographical databases can be used to locate both primary and secondary published literature. The indexing system usually provides bibliographical information indexed by topic and allows the user to view citation details and the abstract of the published manuscript. They are normally searched as electronic databases.

Tertiary information sources

Tertiary information sources generally present a summary of well-established and documented drug and therapeutic information and include textbooks, formularies, drug compendia and electronic drug databases. Several of these basic references are available electronically, but they are most commonly available as printed books. They may contain outdated information because of the delays in producing and publishing such texts.

Manufacturer's literature

There are two main types of manufacturer's literature.

1. *Promotional materials* including advertisements on handouts, posters, articles in scientific journals (sometimes paid for as an advertisement), books, videos and web site promotions. They frequently tend to exaggerate the benefits of the medicines being promoted while playing down their potential harmful effects; such materials should never be used as a basic source of NF information (*7, 8*).
2. *Documentation approved by drug regulatory authorities* include the Summary of product characteristics or Product information file, package inserts and labelling information. Clinical information in these documents can sometimes be limited and outdated on indications, contraindications, dosages, adverse effects and drug interactions, especially in countries with weak drug regulatory authorities. In some countries due to financial disincentives or lack of enforcement by the regulatory authority, manufacturers may not apply for renewed approval for new indications

[7] The "grey" or unpublished literature can provide useful information because it often shows lack of superiority of newer medicines or other negative findings. Systematic reviews will seek out *all* scientifically sound studies and include "grey literature" to obtain a comprehensive evaluation.

and/or the updating of labelling and package inserts. Therefore these materials may not reflect the current, evidence-based use of the product.

However, this type of document may be a suitable source of specialized pharmaceutical information for NF monographs on aspects such as instructions for administration and reconstitution, and cautions on handling and storage.

The quality of information generated directly by the manufacturer can vary greatly from country to country and if these sources are used in the development of the NF, the information extracted from them should *always* be confirmed by comparing it to other independent sources.

Searching for the best evidence

The sequence of searching for drug and therapeutic information frequently follows the pattern of first searching tertiary, then secondary, then primary sources.

Using tertiary sources

The easiest and quickest way to find drug information is to consult major, comprehensive reference texts such as *Martindale: The Complete Drug Reference*, *British national formulary or American Hospital Formulary Service (AHFS) Drug Information*.

However, some of the disadvantages of textbooks should be borne in mind when retrieving drug or therapeutic information for the NF, i.e.

- Even in the latest reference books, some of the information (frequently that on management of diseases) can be 1–2 years out of date by the time the book is available to the reader. In the case of therapies where our knowledge is rapidly evolving, e.g. antiretroviral therapy, information from tertiary sources may prove to be inadequate. Frequently published manuals, such as the *British national formulary***,** are an exception, as they are updated much more quickly than standard textbooks.
- Some reference texts such as the *Physician's desk reference or monthly index of medical specialties (MIMS)* basically contain manufacturers' literature with potentially limited information (*9, 10*). It is important to bear in mind that manufacturers pay for the inclusion of their product information in these publications and often generic products are under-represented, whereas the latest expensive branded products dominate. Any information extracted from these sources must be carefully validated against other independent texts.

Using secondary sources: evidence-based reviews and guidelines

For more current therapeutic information, systematic reviews and evidence-based clinical guidelines can be a good source of therapeutic information for the NF when local treatment guidelines do not exist or are in need of review.

Of several databases containing reviews about the effectiveness of health care interventions the *Cochrane database of systematic reviews* available within the Cochrane Library[8] is one of the best sources of rigorously conducted systematic reviews.

Current evidence-based clinical practice guidelines are often published in primary journals or can be accessed in guideline databases using the Internet. The web site of the Guidelines

[8] http://www.update-software.com/cochrane/

International Network (GIN)[9] provides a portal to selected links to international guideline databases[10] and organizations producing guidelines. WHO treatment guidelines are available in the WHO Essential Medicines Library.[11]

Searching the primary literature

When using the primary and secondary literature, it is important to develop good systematic literature search skills to avoid unnecessarily wasting time on irrelevant information. This involves:

1. Defining the type of *questions* to be asked about medicines (e.g. efficacy, adverse effects, economy and effect on quality of life).
2. Selecting the best type of *research evidence* or *study* to provide answers (e.g. randomized controlled trials, cohort studies, cost–benefit analysis or qualitative research).
3. Selecting the best type of *information resource* that would provide access to such research evidence (e.g. original publications in journals, systematic reviews, textbooks and bibliographical databases).
4. Designing the *search strategy*, i.e. narrowing the search sufficiently to find the relevant information while using criteria that are suitably inclusive so as not to miss important items. In the case of bibliographical databases this means using the right combinations of keywords, with Boolean operators and methodological filters.

Medline

There are several bibliographical databases that can be used to locate important primary or secondary literature (see examples in Table 5.1). Medline is the largest biomedical bibliographical database that can be accessed at no cost via PubMed[12] on the Internet. PubMed has several features that can support systematic searches, one example is the Clinical Queries[13] service that can help retrieve sound clinical studies or systematic reviews on etiology, prognosis, diagnosis, prevention or treatment of diseases by applying research methodology filters. You can find further instructions on how to search Medline in the Pubmed Tutorial.[14]

Accessibility

Today many of the resources mentioned above are accessible in both print and electronic formats.

Printed sources

For development of the NF there are some comprehensive core references that can provide the greater part of the information necessary for writing new entries. Some of the latest editions of the basic reference books listed under the tertiary sources in Table 5.1 are essential requisites for the editorial team, particularly in places where access to the Internet is difficult.

[9] http://www.g-i-n.net/
[10] http://www.leitlinien.de/leitlinienanbieter/fremdsprachig_en/view
[11] http://mednet3.who.int/mf/

[12] http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed
[13] http://www.ncbi.nlm.nih.gov/entrez/query/static/clinical.html
[14] http://www.nlm.nih.gov/bsd/pubmed_tutorial/m1001.html

Electronic sources

Electronic products allow access to scientific articles, books and databases on hand-held computers, desktop computers, via institutional Intranets (local area networks) or via the Internet. It is easy to be overwhelmed with the large volume of information available about medicines on the Internet and it is not always easy to establish the validity and accuracy of this information especially about pharmaceuticals. For guidance on how to identify reliable sites see WHO's guidelines (*11*) **.** Focusing searches through the web sites of major national and international professional organizations and major biomedical gateways (directories of web sites) can help to identify sites of reliable information. Some examples of major gateways leading to medical and pharmaceutical sites include:

- HealthWeb[15]
- Martindale's The "Virtual" - Pharmacy Center[16]
- OMNI[17] (Organising Medical Networked Information).

Critical appraisal

Critical appraisal provides a *systematic way* of assessing the *validity*, *results* and *usefulness* of published literature. During critical appraisal we seek to answer the following questions:

1. Is this clinical trial (systematic review or guideline, etc.) valid?
   Several questions about methodology can be contained within this main query. Obviously, if the answers reveal significant flaws in the design of a clinical trial or consensus process of a clinical guideline that may lead to biased conclusions or recommendations, then this source should not be considered as a basis for making choices for drug therapies.

2. What are the valid results and are they important?
   If the evidence seems to be scientifically sound then we need to find out about the potential clinical benefits and adverse effects. To evaluate the clinical significance of the effects of a particular drug therapy we need to ask questions about the size of the effect and its relevance to clinical outcomes and the precision of the estimate. A statistically significant result may not actually bring clinically important benefits.

3. Will these results help locally?
   Questions should be asked about the transferability of the intervention, i.e. what are the differences between the study population and our patients, the potential benefits, adverse effects, cost-effectiveness and other possible outcomes in our local settings?

Sound evaluation of the primary and secondary literature about drug therapies requires good critical appraisal skills and sufficient time. For further information on how to develop appraisal skills and where to find appraisal tools for different types of study see the Critical Appraisal section of the major evidence-based practice gateway: Netting the Evidence.[18]

[15] http://www.healthweb.org/
[16] http://www.martindalecenter.com/Pharmacy_6_HuD.html#DF
[17] http://omni.ac.uk/
[18] http://www.shef.ac.uk/~scharr/ir/netting/

Table 5.1. Examples of the different types of sources and their accessibility in print or Online

TYPE OF SOURCE	ACCESSIBILITY		
	Print	Electronic products	Access to full text online
PRIMARY SOURCES			
Annals of Internal Medicine	✓	Internet version: http://www.annals.org	via HINARI
British Medical Journal (BMJ)	✓	Internet version: http://bmj.com	Free for all
BioMed Central International Health and Human Rights	—	Internet version: http://www.biomedcentral.com/bmcinthealthhumrights	Free for all
New England Journal of Medicine	✓	Internet version: http://content.nejm.org	via HINARI
The Lancet	✓	Internet version: http://thelancet.com	via HINARI, certain articles free for all
SECONDARY SOURCES			
Review type			
ACP Journal Club	✓	Internet version: http://www.acpjc.org/?hp	Subscription only
Evidence Based Medicine EBM	✓	Internet version: http://www.evidence-basedmedicine.com/	Via HINARI
Clinical Evidence	✓	Internet version: http://www.clinicalevidence.com	Free for developing countries, see web site
The Cochrane Library	—	Desktop CD-ROM and Internet version: http://www.cochranelibrary.net/cochrane/provisions.htm	Several options for free access, see web site
Database of Reviews of Effectiveness	—	Internet version: http://nhscrd.york.ac.uk/darehp.htm	Free for all
Indexing type			
Medline	—	Different platforms exist. Free Internet version: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi/	Free for all
CANCERLIT		Internet version: http://www.cancer.gov/search/pubmed/	Free for all
WHOLIS (WHO library database)	—	Internet version: http://www.who.int/library/database/index.en.shtml	Some free but not always full-text
African Journals online	—	Internet version: http://www.inasp.info/ajol/index.html	Free for all, abstracts only
TERTIARY SOURCES			
American Hospital Formulary Service (AHFS)	✓	Hand-held, desktop CD-ROM and Internet version: http://www.ashp.org/ahfs/	Single purchase for each edition
British national formulary (BNF)	✓	Hand-held, desktop, Intranet and Internet version: http://www.bnf.org/bnf/index.html	Internet version free for all
Drug information handbook Ed. Lacy CF, Lexi-Comp, Hudson,US	✓	—	Single purchase for each edition
Martindale: The complete drug reference	✓	Desktop CD-ROM http://www.micromedex.com/products/martindale/	Single purchase for each edition
WHO model formulary	✓	Internet version: http://www.who.int/medicines/organization/par/formulary.shtml	Internet version free for all
USP Drug information for the health care professional, Volume 1.	✓	Desktop CD-ROM http://micromedex.com/products/uspdi/v1/	Single purchase for each edition
The Merck manual of diagnosis and therapy	✓	Hand-held, desktop CD-ROM and Internet version: http://www.merck.com/pubs/	free Internet version

Via HINARI (Health InterNetwork Access to Research Initiative) provides free online access to more than 2200 high-quality biomedical journals and other sources for 69 low-income countries or access at a reduced rate of US$ 1000/annum for 43 middle-income countries. For more details on how to access these and to check your country's eligibility see: http://www.healthinternetwork.org/src/eligibility.php

6 DEVELOPING SPECIFIC INFORMATION SECTIONS

The appendices usually contain additional therapeutic, safety, pharmaceutical and administrative information (see Table 6.1) to supplement the monographs and general introductory texts. The information in this part of the formulary is frequently presented in a tabulated or summarized form and can also be illustrated with specific examples of local requirements.

Creating locally important appendices

When planning the topics and the content of individual appendices, the purpose and the intended audience of the NF should be borne in mind. It is likely a number of additional appendices will need to be developed for each country (see Table 6.1). The main focus of the individual appendices should be agreed upon by the NFC in the initial planning stage. The members of the advisory group should also comment at an early stage on the planned appendices; useful suggestions on inclusion of locally important information often come from these potential users.

Table 6.1. Examples of different types of information presented in appendices of a NF

Main category	Examples
Therapeutic and safety information	1. Interactions,[a] e.g. medicine–medicine, medicine–food/herb, medicine–diagnostic test 2. Medicine use and prescribing[a] in special patient populations i.e. during pregnancy,[a] breastfeeding,[a] renal[a] and hepatic impairment[a] 3. Pharmacokinetic data, dosing guidelines for medicines with narrow therapeutic index (e.g. digoxin, aminoglycosides) and therapeutic drug monitoring information[b] 4. Dose calculators, nomograms (e.g. for paediatric dose and emergency medicine dose calculations, dilutions)[b] 5. Protocols for emergency treatment of common poisonings
Pharmaceutical information	1. Pharmaceutical incompatibilities, guidance on intravenous additives, instructions for specific intravenous infusions 2. Standard parenteral nutrition formulas 3. Electrolyte content of large-volume parenterals 4. List of sugar-free products
Administrative information	1. List of miscellaneous items i.e. food supplements, surgical dressings etc. 2. Lists of medicines restricted to special prescribing practices, e.g. narcotics, anticancer medicines, intravenous antibiotics etc. and examples of special prescription forms and instructions for completing them; definitions of who is authorized to prescribe them 3. Model texts for labelling of medicines, and other dispensary information, i.e. cautionary and advisory labels 4. Instructions for reporting of adverse drug reactions (ADRs), reporting form and list of medicines for which all ADRs are to be reported 5. Form for submission of recommendation for addition/deletions/corrections to the formulary 6. Reference list of national clinical treatment guidelines 7. Contact details of national drug information and poison control centres 8. Contact details of essential medicine suppliers and procurement agencies

[a]This type of information is presented in the WMF in Appendices I–V.

[b]A limited amount of this type of information is given in the WMF.

Adopting appendices from the WHO model formulary

There are five appendices in the WMF which complement the information on medicines presented in the main sections. These are as follows:

Appendix 1. Interactions
Appendix 2. Pregnancy
Appendix 3. Breastfeeding
Appendix 4. Renal impairment
Appendix 5. Hepatic impairment

Each appendix has a general introductory text and a detailed medicine-specific information section.

There are two important steps to be taken during the adoption of appendices:

Step 1. Adoption of the general introductory text of an appendix

It is advisable to copy and maintain the full introductory texts from the WMF for each appendix because they contain universally valid information and instructions on how to use each specific appendix. If it is necessary to add locally important information to the introductory text, this should be distinguished from the rest of the text by using a different text style, as discussed in Chapter 4 for the main sections.

Step 2. Adoption of specific information for individual medicines

In most cases, it is likely that both additions and deletions will be necessary.

Additions

When a new monograph is developed for the NF, where the specific information is to be included in the appendices, this material should also be written at the time of development. In the case of interactions, the new entry would be inserted under the medicine being characterized in the new monograph as well as under the interacting medicines (reversals) (see the example of epoetin in Box 6.1). In the other appendices, additional information would be inserted into the existing alphabetical lists as appropriate.

Deletions

If a decision is made not to include certain WMF monographs in the NF, then all associated information from the appendices should also be removed. In the interaction appendix, a careful search should be made (using the ***Find*** command under the ***Edit*** menu of the word processor) for the name of the active ingredient and this should be followed by careful deletion of all interactions and reversals for the deleted medicine. As most of the interactions and reversals in the WMF are presented with individual medicine names (except for antacids, oral contraceptives and vaccines) this could be a straightforward task, but care must be taken to avoid the accidental deletion of any other information.

Box 6.1. Examples of modifications in Appendix 1. Interactions

-	~~Efavirenz~~	~~Contraceptives, Oral~~	~~Efficacy of oral contraceptives possibly reduced~~
-	~~Efavirenz~~	~~Grapefruit Juice~~	~~Plasma concentration of efavirenz may be affected~~
-	~~Efavirenz~~	~~Indinavir~~	~~Efavirenz reduces plasma concentration of indinavir (increase indinavir dose)~~
-	~~Efavirenz~~	~~Lopinavir~~	~~Plasma concentration of lopinavir reduced~~
-	~~Efavirenz~~	~~Rifampicin~~	~~Reduced plasma concentration of efavirenz (increase efavirenz dose)~~
-	~~Efavirenz~~	~~Ritonavir~~	~~Increased risk of toxicity (monitor liver function)~~
-	~~Efavirenz~~	~~Saquinavir~~	~~Efavirenz significantly reduces plasma concentration of saquinavir~~
	Ephedrine	Chlorpromazine	Antagonism of pressor action
	Ephedrine	Dexamethasone	Metabolism of dexamethasone accelerated
	Ephedrine	Fluphenazine	Antagonism of pressor action
	Ephedrine	Haloperidol	Antagonism of pressor action
	Ephedrine	Oxytocin	Hypertension due to enhanced vasopressor effect of ephedrine
*	Epinephrine	Amitriptyline	Hypertension and arrhythmias (but local anaesthetics with epinephrine appear to be safe)
*	Epinephrine	Atenolol	Severe hypertension
	Epinephrine	Chlorpromazine	Antagonism of pressor action
*	Epinephrine	Clomipramine	Hypertension and arrhythmias (but local anaesthetics with epinephrine appear to be safe)
*	Epinephrine	Ether, Anaesthetic	Risk of arrhythmias
	Epinephrine	Fluphenazine	Antagonism of pressor action
	Epinephrine	Haloperidol	Antagonism of pressor action
*	Epinephrine	Halothane	Risk of arrhythmias
	Epinephrine	Oxytocin	Hypertension due to enhanced vasopressor effect of epinephrine
*	Epinephrine	Propranolol	Severe hypertension
*	Epinephrine	Timolol	Severe hypertension
	Epoetin	Captopril	antagonism of hypotensive effect; increased risk of hyperkalaemia
	Epoetin	Enalapril	antagonism of hypotensive effect; increased risk of hyperkalaemia

Deletion
Delete all main efavirenz entry rows and all 7 reversals for efavirenz under contraceptives, grape-fruit juice, indinavir, lopinavir, rifampicin, ritonavir and saquinavir.

Addition
New information for Epoetin included in NF is added. The same text should also be inserted under the main Captopril entry. Note the different font style used for the addition.

Working with a master document in Microsoft Word® to create a table of contents and index

Generation of both the table of contents and the index is a final editing task that should be carried out once all the chapters have been finalized and corrected. These tasks can be performed in one step within a master document. A master document contains links to a set of related subdocuments, i.e. the individual chapters of the NF, and allows the creation of the table of contents, index, cross-references, and headers and footers for all of the subdocuments. Box 6.2 outlines the important steps in the creation of a master document from the individual files using Microsoft Word®.

The person creating the master document should also check the instruction given in ***Word® Help*** for that particular version, as slight differences exist between different versions.

Working with a master document and subdocuments can be cumbersome and other solutions may work just as well.

- A final document may be created as a single document, in which the final page numbers, the table of contents and the index can be generated.
- If the document is too large to work with as a single document, it is possible to follow the example of the School of Pharmacy at the Medical University of Southern Africa (MEDUNSA). When creating a *Formulary for primary health care* based on the WMF they retained separate sections in different documents and indexed them separately. The partial indexes were pasted into a new ("text only") document, combined and sorted alphabetically.

Box. 6.2. How to create a master document using Microsoft Word®

Step 1	Finalize all individual chapters, appendices etc. Make sure that the files have no header, footer or page numbers and that all main headings and subheadings have been created consistently using matching styles. Files should have the same page setup information, i.e. the margins, page size and layout of information should be the same.
Step 2	Make sure that you copy all the finalized chapters together into one directory.
Step 3	Open a new document and insert several blank paragraphs by pressing the enter key and position the cursor on the middle line.
Step 4	Switch to ***Outline View*** and on the ***Outline View*** toolbar find the ***Insert Subdocument*** button and insert all chapters in the correct order, one after the other, and save the file once all chapters have been inserted.
Step 5	Switch back to N***ormal view***. Now your master document works as one large file. You can insert page numbers for the whole document file, headers and footers for the whole file and/or within individual sections by turning on or off the ***Same as Previous*** toggle switch in the ***View Header and Footer*** toolbar.
Step 6	Use ***Print Preview*** for checking layout.
Trouble shooting	If the master document is not working well, rather than trying to sort out errors, discard it and create a new master document. If files need to be moved e.g. for printing, all subdocuments and master documents should be copied into the same named directory, otherwise the master document cannot locate them. Check the ***Help*** for solutions both under ***About Master Documents*** and **Troubleshoot Master documents** and **subdocuments** of your word processor.

Creating the table of contents

The Word® files of the WMF provided by WHO already contain the information necessary for the generation of a table of contents. The most important thing is to ensure that in all sections the titles and subtitles to be included in the table of contents have styles that have been consistently applied, e.g. Heading 1 style for main section title, Heading 2 style for subsection title etc. The same styles should be applied carefully for all additional local chapters, sections and monographs. Once chapters are combined in a master file, these chapters will take on definitions from the master document and can be made uniform, as long as they were created with the same style name. See Box 6.3 and 6.4. for step-by-step instructions on creating a table of contents.

Creating the index

To ensure easy access for users, it is advisable that a single index, combining both medicine and disease names, be created. An index of brands and corresponding generic names is sometimes presented as a separate table in formularies. If brand names are inserted into all monographs, then it is best to insert the index field at the time of editing to maintain one uniform index. Index entries should be chosen on the basis of relevance and usefulness to the reader, rather than simply being a list of occurrences of the term throughout the text. Sub-entries can be used to guide readers to the relevant section when a medicine is used for multiple indications, or an entry occurs in different parts of the text.

Step-by-step instructions for inserting an index field code and for creating the final index are given in Boxes 6.3 and 6.4.

Technical assistance from professionals experienced in desk-top publishing can be helpful for creating an accurate table of contents, compiling indexes and doing the final layout work. Where access to such professional services is limited, it is important that at least one member of the editorial team gains some expertise in these tasks. Reading through the help files or tutorials of the software package used is a useful starting point.

Box 6.3. How to add an index field code to the words you want to appear in the index

Step 1	Highlight the word that you want to appear in the index.
Step 2	Under the ***Insert*** menu select ***Reference*** then ***Index and Tables***.
Step 3	When the ***Index and Tables*** box appears activate the ***Index*** page and click on ***Mark entry.***
Step 4	In the ***Mark entry*** box click appropriate options and fill in the subentry and cross-reference cells if needed, then click on ***Mark.*** Now the index entry has been created, but will not be visible in the usual view options as it is inserted as a hidden text. To make these hidden texts visible you can use the ¶ icon.
Important warning	When editing Word® files of the WMF it will be important to switch on the hidden text feature in the word processor software to visualize the field codes inserted for generation of the index. If WMF text is deleted or moved around, these field codes may be accidentally deleted resulting in the loss of index entries. To display hidden entries in Microsoft Word® simply switch on the ¶ icon. If the field codes e.g. {XE "name of drug" } do not appear, go to the ***Tools*** menu, ***Options, View*** and make sure the box for ***Hidden text*** is clicked on in ***Formatting marks*** (or "***Nonprinting characters***" in some versions)

WMF, *WHO model formulary*.

Box. 6.4. How to create a final index and table of contents in a master document using Word®

Step 1	Open the master document and expand the subdocuments by clicking on  button on the ***Outlining Toolbar*** before you insert the index.
Step 2	Position the cursor where you want to insert the final index.
Step 3	To make sure that the document is paginated correctly, you need to hide field codes and hidden text. If the XE (***Index Entry***) fields are visible, click off the ¶ icon.
Step 4	On the ***Insert*** menu, point to ***Reference***, click ***Index and Tables***, and then click ***Index***.
Step 5	Choose a design from templates from the ***Formats*** box, then click on OK.
Note	To update the index, click to the left of the field and press F9.
Trouble shooting	If you add, delete, move, or edit index entries or other text in a document after the index has been created, you should manually update the index. For example, if you edit an index entry and move it to a different page, you need to make sure that the index reflects the revised entry and page number. To update the index, click to the left of the field and press F9. Check for further information under ***Help*** under ***Troubleshoot Indexes.***

7 PRODUCTION, DISTRIBUTION AND IMPLEMENTATION

Production of the paper-based formulary

This chapter describes some of the essential tasks involved in production of the final copy of the NF, printing issues and important considerations for its distribution and successful implementation.

Final editing and layout of manuscript

The final editing and layout of the NF may be done by a professional publisher, but if the editorial team is responsible for production of the final manuscript it is important that they are familiar with the features of an easy to use word-processing or desk-top publishing program. Appropriate use of macros and style-sheets can help the capable editor and reduce editing time and effort.

Utilizing the electronic version of the WHO model formulary

The text of the WMF is available as Word® files on the CD-ROM. Editing the WMF Word® files will generally be possible with current versions of widely used word-processing and desktop publishing programs.

IMPORTANT WARNING

When editing the Word® files of the WMF it will be important to switch on the hidden text feature in the word-processor software to visualize the field codes inserted for the generation of the index. If WMF text is deleted or moved around, these field codes may be accidentally deleted, resulting in loss of index entries.

To show hidden entries in Microsoft Word® simply switch on the ¶ icon. If the field codes e.g. {XE "name of drug" } do not appear go to the ***Tools*** menu, ***Options, View*** and make sure the box for ***Hidden text*** is clicked on in ***Formatting marks*** (or "***Nonprinting characters***" in some versions).

Editing of final text

Editors will need to check for correct and consistent writing style, grammatical accuracy and application of agreed styles to produce a uniform layout. These copy-editing tasks are somewhat different from the final proofreading as outlined in Box 7.1. Ideally a different person should do the proofreading, but this may not always be feasible.

Box 7.1. Important tasks during copy-editing and proofreading

Copy-editing tasks	Proofreading tasks
Check for clarity of message. All new text or modified WMF texts must express a clear and unmistakable meaning.	Check for accuracy of typing; remember computer spellcheckers will not pick up typing errors such as "for times" instead of "four times".
Check for consistency of application of the local style developed for insertion of local information.	Check for correct appearance and internal consistency of headings, subheadings, tables, index and any other material included.
Remove all unnecessary duplications.	Check for correct labelling/ numbering of chapters, sections, subsections, tables and illustrations.
Check the hierarchy of headings for sections and subsections.	Check for correct appearance of style of text i.e. font, bold, italic and type-size.
Check accuracy of indexing and table of contents.	Check final printed page numbers against table of contents and index.

WMF, *WHO model formulary*.

Printing

Good-quality printing and binding can prevent premature "falling apart" of the NF and can ensure the desired "life" of the publication. Looking at examples of published manuals designed for everyday use can help with decisions on printing design. The following should be considered when planning for a NF:

- **The size of the formulary**. Pocket-sized books that fit easily in the hand and into the pocket of white coats are preferred for ease of use and carrying around in various settings. Inappropriate size and weight of a NF can be a major barrier to its everyday use.
- **Paper quality.** The paper quality should be chosen to ensure ease of use and durability while not making the book too heavy or too thick to carry around.
- **Covers.** The covers should be durable and attractive. They should also show the publishing organization or government department logo.
- **Colour or monochrome printing**. Although colour printing can give the NF an attractive appearance, its cost is often prohibitive in developing countries. Using two colours as in the *British national formulary* can help quick navigation. When using monochrome printing, selecting different coloured papers for certain chapters (e.g. for the appendices) can make the NF more "appealing" and can assist the user to find specific sections quickly.
- **The number of copies to be printed.** The number of targeted users should be estimated in advance and the final print run should take into account the need for additional copies to meet unforeseen demand or to replace copies lost as a result of wear and tear. The planned frequency of revisions, the additional number of professionals likely to enter into service during that period and the number of students in training should be considered in making the estimates.
- **Copyright issues.** Copyright laws and registration of copyright can vary from country to country and it will be necessary to check national legislation. The publisher of the NF may grant permission for its partial or full reproduction. Information regarding reproduction and how to apply for permission to do so should be included in the copyright statement.

Distribution

Timely and targeted distribution will be a key factor for successful application and use of the NF, and the following issues should be considered:

- **The method of distribution chosen** should ensure that copies of the NF are delivered promptly to the targeted audience and do not remain in boxes in hospital or library storerooms. Posters, circulars, letters to heads of medical and nursing units can be sent to inform users on when and where to collect their copies. Existing medicine distribution systems may be utilized for rapid delivery to individual health facilities throughout the country.
- If **mailing** is used for distribution of the NF to individuals or institutions, it is essential that the mailing list is checked for accuracy of names and addresses. It should list only those who should be receiving the NF to reduce waste of resources on mailing costs and lost and unused copies.
- **Price.** NFs are frequently provided free of charge to targeted health professionals in the public health sector of the country to ensure equal access. Additional copies may be provided either free, or at a cost, to other users such as private health care providers and students in private institutions who request copies of the NF.

Electronic publishing and distribution of the national formulary

As access to information technology increases, it will become feasible to produce the NF in electronic formats in some countries. For example, the NF may be made available on the Internet for browsing, provided as downloadable files (PDF) or CD-ROMs for individual or Intranet installations or as an application to be used with hand-held devices. The technical issues involved in such electronic publishing are beyond the scope of this manual. Some useful information about electronic publishing in developing countries can be found on the following web sites:

- Electronic Publishing Trust For Development[19] (EPT);
- International Network for the Availability of Scientific Publications[20] (INASP); and
- The Association of Learned and Professional Society Publishers[21] (ALPSP).

Implementation to gain acceptance and credibility for the national formulary

The process of implementation will be important for the rapid acceptance and use of information contained in the NF. Unless users are aware of, and know how to access and use the NF, the desired impact on rational use of medicines may not achieved. Several methods may be employed or combined to promote the use of the NF including:

— organization of an official launch supported by respected authorities including the Ministry of Health, professional societies (e.g. medical and pharmaceutical) and coverage by the media;

— placing advertisements, articles and interviews about the NF in national professional journals and the media;

[19] EPT http://www.epublishingtrust.org/

[20] INASP http://www.inasp.info/index.html

[21] ALPSP http://www.alpsp.org/default.htm

— circulars, letters and posters sent out to health institutions and involving opinion leaders in the launching of the NF; and

— integrating dissemination of information about the NF with dissemination of other health policy, clinical guidelines or protocols.

These efforts should not be made only for the initial introduction of the NF, but some of them should be continued to raise wider awareness of the purpose and use of the NF.

The above recommendations are intended to point out basic essential tasks in the final production stage and do not attempt to give advice on professional book publishing. Various organizations provide support and training for publishers in developing countries; a comprehensive list of links to these organizations can be found on the ***Links*** page of the INASP's web site.

8 EVALUATION

Periodic evaluation of the national NF can be an important and valuable activity used to determine:

— whether the objectives of the NF have been met and what impact has been achieved;

— the strengths and weaknesses of the NF; and

— the reasons for success or failure of the NF.

Information gathered from a well-conducted evaluation can be useful for correcting problems and optimizing the performance of the NF.

Evaluation of the NF within the framework of existing monitoring and evaluation activities

Assessment of the NF can be integrated with ongoing monitoring and evaluation of the national pharmaceutical sector and/or with any health facility quality assurance programme.

WHO and other agencies have developed assessment packages to systematically monitor and evaluate pharmaceutical policies and systems and various components at the national level.[22] Indicators relevant to the evaluation of the NF can be developed, and the data collection and analysis can be combined with existing monitoring and evaluation activities. This can save considerable time and resources and reduce duplication of effort when compared with setting up and conducting completely independent evaluations. However, the NFC may also wish to carry out some specifically focused evaluations from time to time.

How to design the evaluation

Evaluation of the NF will require standards and processes similar to those for a research project. These include:

— defining the scope and questions to be answered by the evaluation;

— selecting or developing the appropriate methods and testing data collection instruments;

— collecting and analysing the data; and

— interpreting results and

Depending on the objective of the evaluation, the types of information collected may include:

- *Descriptive information* (specific information obtained from close-ended questions) e.g. Is there a national policy to endorse the regular production and dissemination of the NF, Yes or No):?
- *Quantitative information* (numbers): e.g. What percentage of prescribers in a health facility have a personal copy of the NF?
- *Qualitative information* (statements, opinions): e.g. Why do prescribers use (or not use) the NF regularly?

A valid evaluation requires the collection of the right amount of relevant information. Some practical hints on how to avoid common pitfalls of evaluations are offered in Table 8.1.

[22] Detailed information and links to resources on pharmaceutical system evaluations can be found on the Internet at: http://www.who.int/medicines/strategy/policy/indicators_intro.shtml

Table 8.1. Useful hints for planning and conducting an evaluation

Dos	Don'ts
Make sure to involve important partners in the design of the evaluation.	Do not treat evaluation as a trivial task after production of a NF.
Consider carefully the available resources when deciding on depth and complexity of evaluation.	Do not be overambitious.
Ask important questions that matter for future production and measuring the impact of the NF.	Do not collect data unless they are needed to answer the questions identified.
Make sure that data collection tools and indicators are reliable, i.e. that they measure what they are intended to.	Do not try to gather information that is very difficult to obtain.
Make sure that results of the evaluation are disseminated to all relevant decision-makers to influence future strategies and plans.	Do not lock up results and forget about them.

What to evaluate

Specific questions related to the production, distribution and impact of the formulary can be categorized according to the medicine management cycle of selection, procurement, distribution and rational use, and can be supported by policies, a legal framework and management structures. The following examples of indicators and questions are listed together with these assessment points.

Policy, legal framework and management support

Indicators

1. Are there any policies or legal requirements relevant to the production, distribution and use of the NF at the national or regional or health facility level? Yes/No
2. Is there continuing financial and human resource support from government or sponsors for production and implementation of the NF? Yes/No
3. Is there a fair representation of all professionals on the NFC? For example, does the committee have a minimum of seven members representing the medical, nursing, pharmacy and laboratory health professions. Yes/No
4. Is the coverage of the formulary adequate? Yes/No

   Coverage is calculated as:

   $$= \frac{\text{No. of printed/distributed copies}}{\text{Number of targeted health professionals + those in clinical training}} \times 100$$

   The ideal figure is close to or above 100%; if too few copies have been printed this will limit impact.
5. Are NF activities linked with other programme activities promoting the rational use of medicines, e.g. production of clinical guidelines, basic and continuing education of health professionals, activities of the drug and therapeutics committee? Yes/No

Selection

Indicators

1. Percentage of essential medicines by active ingredient from the national EML included in the NF list

Calculate:

$$\frac{\text{Number of unique essential medicinal products on the national EML}}{\text{Number of unique medicinal products in the NF}} \times 100$$

Unique: Products with the same active ingredient, dosage form, to be administered by the same route listed both in EML and NF. If there are several strengths of the same product available they will be counted as one product (not unique).

2. Percentage of essential medicines from the WMF adopted in the NF

Calculate:

$$\frac{\text{Number of essential medicines included in NF that are also in WMF}}{\text{Number of medicines in WMF (319 medicines in 2004 edition)}} \times 100$$

Procurement

Indicators

1. Is there a policy limiting procurement in public sector facilities to medicines listed in the NF? Yes/No
2. Percentage of medicines included in NF procured in a central hospital.

   It is easier to restrict this indicator to a few therapeutic categories, for example systemic antibacterial medications and antihypertensive medications.

Calculate:

$$\frac{\text{Number of medicines procured within selected therapeutic category in a central hospital per year}}{\text{Number of medicines listed in NF for use within selected therapeutic category}} \times 100$$

Distribution of formulary

Indicators

1. Percentage of health facilities with copies of NF

Calculate:

$$\frac{\text{Number of health facilities with copy of NF}}{\text{Total number of health facilities visited}} \times 100$$

Facilities from all levels of care where the formulary is intended to be used must be included in the sample.

2. Percentage of prescribing and dispensing staff with personal copies of NF

Calculate:

$$\frac{\text{Number of prescribing/dispensing staff with a personal copy of NF}}{\text{Total number of prescribing/dispensing staff interviewed}} \times 100$$

The sample should include facilities from all levels of care.

Rational use

Indicators

1. Percentage of medicines prescribed from NF as per NF instruction for selected indicator diseases: for example, treatment of uncomplicated malaria in adults or treatment of peptic ulcer.

   It is necessary to identify the recommended dosage schedule from the NF and review prescriptions and/or medication charts for the relevant disease. This can be difficult when diagnosis and prescription information are recorded in separate documents.

   Calculate:

   $$\frac{\text{Number of drugs prescribed appropriately according to NF for indicator disease}}{\text{Total number of any prescribed drugs given for the indicator disease}} \times 100$$

2. Is the NF included in the list of recommended textbooks and used for training of health professionals in the country? Yes/No

The results of the evaluation should be summarized in a short report together with any recommendations for improvements. This report should be circulated to members of the NFC and others involved in production and implementation of the NF, preferably before starting the review process for the next edition.

9 REVIEW AND UPDATE

Constant changes in information about medications and in pharmacotherapy practices necessitate the regular review of the NF in every setting. Revision of the NF will be an important, recurring task of the NFC and the editors and it is best planned for at the initial stages of writing the first edition.

Planning for review

The NF will need reviewing and updating in the future due to:

— changes in the list of medicines to be included;
— newly published evidence and changes to treatment guidelines;
— more information becoming known about medicines e.g. side-effects;
— mistakes made in the previous edition of the formulary; and
— changes in government health policy affecting local information.

Some of these changes may be obvious, for example release of a new national EML list. Others are more subtle and may not be immediately obvious, for example, adjustments in prescribing policies leading to changes in the availability of medicines in different types of health facilities.

How frequently does the national formulary need to be reviewed?

The time between updates or new editions of the formulary will depend upon:

— frequency of changes in information and the importance of the new information requiring changes to the NF;
— availability of resources for review tasks, publishing and implementation.

Generally formularies undergo major revisions every 2–3 years. After 5 years it is likely that there will be a substantial amount of information in the formulary that is outdated; therefore it is important to complete reviews at least every 4–5 years. The WMF is scheduled for revision every 2 years (even years, e.g. 2004 and 2006). In countries without an EML or guidelines, the electronic release of subsequent editions of the WMF can start the NF review process, depending on availability of resources and the need for revisions.

In those countries where an EML and national treatment guidelines are regularly reviewed it is best to link the review of the NF to these events and to the release of revised editions of the WMF.

The *British national formulary* has an ongoing review process which results in updated editions being produced every 6 months. This short publication cycle is a based on a very well-structured and clearly defined operational process, supported by the work of the Joint Formulary Committee, the large and well-qualified editorial team and more than 50 expert clinical advisers, as well as substantial financial resources.

In many other countries with fewer resources, the NF review and production process is likely to require a significantly longer time, at least between 8 and 12 months, to publish a revised edition. This means that a biannual review should start approximately 1 year after the release of the first publication. Good planning with adequate resources can help to achieve a reasonably regular publication cycle.

Review process

The main steps of the review process include:

1. identification of areas in need of change;
2. drafting of updated texts for areas where change is necessary;
3. approval by the NFC and expert advisers;
4. editing of final draft; and
5. production and implementation.

The last two steps essentially repeat the process already described in Chapter 7, therefore only the first three are discussed below.

Identification of areas in need of change

It is useful to have a systematic procedure whereby users of the formulary can comment on the content and make suggestions for future editions (see Chapter 3 on front matter and Chapter 6 on appendices). This is important for identifying and collating errors in the NF and also helps the users to feel part of the process of development of the formulary. The number and scope of the errors and suggestions may help to set a timetable for the review and updating process.

Drafting of updated texts for areas where change is necessary

The review process is similar to the development process (see Chapter 2) and will need careful planning and budgeting. A review committee should be set up and each chapter carefully assessed by an expert subcommittee charged with identifying information that needs changing either in the drug monographs, clinical guidance or additional information sections. This will include consideration of any suggestions received from users of the formulary.

Updating texts based on the WHO model formulary

Revised editions of the WMF include a list of all changes to the WMLEM at the front to alert users to these changes. This list of changes should be checked first to assess whether changes will also be required in the NF. The latest edition of a NF should always be carefully compared to the latest edition of the WMF, particularly the text of the general therapeutics sections. This is best done by the members of the editorial team who will follow through the whole review process of a particular section or chapter.

The acceptance of new changes made to the WMF in the NF should involve careful appraisal of new information in the context of local guidelines and practices. Detailed discussion by the NFC and expert advisers is always necessary before making significant changes to recommendations about the management of diseases. If a different text style was used for texts copied from the WMF this can greatly facilitate the process of comparing new text from the WMF with that of the NF.

Existing word-processing software packages may also have the capacity to compare different versions of the same document, i.e. the revised file of the WMF may be compared to the same file from the previous edition, thus quickly pinpointing places where changes were effected. Although such electronic editing tools can speed up the comparison process, it will still be necessary to carefully read, compare and comprehend relevant texts before deciding on the appropriate actions.

Updating texts containing locally added information

Well-structured communication and follow-up with all the parties involved (e.g. policy-makers and professional associations) will be essential to collect any new local information likely to lead to changes in the NF on local policies, clinical guidelines or other text. It is good practice to maintain a file of relevant local information (e.g. circulars and policy documents) collected between editions of the NF, which can be used in the revision process.

Approval by the national formulary committee and expert advisers

Any new alterations, additions or deletions should be carefully documented, the revised text proofread and assessed by the editorial committee and approved by the NFC. Depending on the extent of the changes, circulation of certain revised chapters to expert advisers may be necessary to check clarity and comprehensibility.

In addition to the cost of production, regular meetings, good communication and adequate funding to support these and related activities will be essential for timely review.

The final editing and production issues will be similar to those already discussed above.

It is important to remember that careful planning, a skilled editorial team, involvement of local experts, adequate resources and sufficient time will all be necessary for the successful production of the formulary.

REFERENCES

1. Chapter 10. Treatment guidelines and formulary manuals. In: Quick JD et al., eds. *Managing drug supply.* 2nd ed. New York, Kumarian Press, 1997.

2. *The rationale of essential medicines.* Geneva, World Health Organization (http://www.who.int/medicines/rationale.shtml).

3. *The thirteenth WHO model list of essential medicines.* Geneva, World Health Organization, 2003 (http://www.who.int/medicines/organization/par/edl/eml.shtml)

4. Grimshaw JM, et al. Changing provider behavior: an overview of systematic reviews of interventions. *Medical Care*, 2001, 39(8 Suppl 2):II2–45.

5. *How to develop and implement a national drug policy*, 2nd ed. Geneva, World Health Organization, 2001 (http://www.who.int/medicines/library/par/ndpeng.pdf).

6. *The selection and use of essential medicines. Report of a WHO Expert Committee, 2002 (including the 12th Model list of essential medicines).* Geneva, World Health Organization, 2003 (WHO Technical Report Series, No. 914) (http://www.who.int/medicines/organization/par/edl/trs/trs914_001to126.pdf).

7. Anonymous. *Prescribing information in 26 countries*. Geneva, World Health Organization, 2003 (WHO Drug Information Vol. 17, No. 3).

8. Osifo NG. Overpromotion of drugs in international product package inserts. *Tropical Doctor* 1983, 13:5–8.

9. Mullen WH et al. Incorrect overdose management advice in the Physicians' Desk Reference. *Annals of Emergency Medicine*, 1997, 29:255–261.

10. Cohen JS. Dose discrepancies between the Physicians' Desk Reference and the medical literature, and their possible role in the high incidence of dose-related adverse drug events. *Archives of Internal Medicine*, 2001, 161:957–964.

11. *Medical products and the Internet — a guide to finding reliable information*. Geneva, World Health Organization, 1999 (WHO/EDM/QSM/99.4) (http://www.who.int/medicines/library/qsm/who-edm-qsm-99-4/medicines-on-internet-guide.html).