

Guidelines for Implementation of Pharmaceutical and Therapeutics Committees in Gauteng Province

First edition



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ABBREVIATIONS AND ACRONYMS

ADR	adverse drug reaction
CEO	chief executive officer
CV	curriculum vitae
EML	essential medicines list
MCC	Medicines Control Council
MSD	Medical Supply Depot
MUE	medicine use evaluation
NEMLC	National Essential Medicines List Committee
PFMA	Public Finance Management Act
PTC	Pharmaceutical and Therapeutics Committee
RMU	rational medicines use
SOP	standard operating procedure
STG	standard treatment guideline
TORs	terms of reference
USAID	US Agency for International Development
WHO	World Health Organization

FOREWORD

It is my pleasure to introduce the first edition of the *Guidelines for Implementation of Pharmaceutical and Therapeutics Committees (PTCs) in Gauteng Province*.

The Gauteng Provincial PTC developed these guidelines to support an integrative PTC network, where PTCs at all levels will strive to optimise available resources and the rational use of medicines. The establishment of governance systems that guard against conflicts of interest and perversities in the prevailing environment shall be a primary concern for PTCs.

The guidelines aim to provide practical tools to hospitals and district PTCs to assist them in fulfilling their role to ensure the quality of therapeutic care with respect to good governance principles.

To gain the most benefit from the guidelines, local PTCs are encouraged to adapt the tools to suit their own settings.



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Chairperson of the Gauteng Provincial Pharmaceutical and Therapeutics Committee

Date: 23 May 2013

ACKNOWLEDGMENTS

So many persons and organisations participated in the development of the *Guidelines for Implementation of Pharmaceutical and Therapeutics Committees in Gauteng Province* that to attempt to list them all would risk leaving out some of the contributors. Suffice it to say that the guidelines were developed following a recommendation of the Gauteng Provincial Pharmaceutical and Therapeutics Committee (PTC). The Gauteng Provincial PTC was revitalised by the Head of the Gauteng Health Department, Dr. N. Xundu, in March 2012.

The contributions of all those who participated in the process are acknowledged with sincere thanks, among them are Ndoda Biyela, Head of Gauteng Health Department for his continuous support; the Gauteng Provincial PTC and its subcommittees; the selection panel for Gauteng Provincial PTC members (Mr. G. Steel, Prof. C. Szabo, Prof. R. Masekela, Prof. S. Banoo, Dr. N. Mazamisa, Ms. N. Mbabama, Ms. L. Deysel, and Dr. S. Berrada); the National Department of Health Pharmaceutical Services for technical support; and the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) for technical support and printing. Special thanks go to Dr. Stephanie Berrada from SIAPS for tirelessly facilitating and ensuring the successful development of these guidelines.

PREFACE

I. Process

The *Guidelines for Implementation of Pharmaceutical and Therapeutics Committees in Gauteng Province* presented in this document are a culmination of a number of steps. The first step was the development of new terms of reference (TORs) for the Gauteng Provincial PTC and the establishment of four subcommittees (Formulary, Rational Medicine Utilization, Safety and Quality, and Procurement). The second step was the stringent selection process to ensure that all types of expertise needed in the Provincial PTC are represented and that selection is fair and transparent.

The newly appointed Gauteng Provincial PTC met for the first time in March 2012.

The establishment of governance systems, the promotion of rational medicine use (RMU), and access to quality, safe, and cost-effective medicines are some of the core functions of the Gauteng Provincial PTC. Each subcommittee has developed the necessary and relevant procedures, forms, recommendations, and tools in their area of expertise.

The provincial *Circular Letters*, procedures, forms, and tools were then compiled into one single document and presented to the Gauteng Provincial PTC for comments.

II. Use of the Guidelines for Implementation of PTCs

The guidelines will serve the health care needs of Gauteng Province by:

- Offering a clear description of the approach by which PTCs should function.
- Offering direction to relevant stakeholders on how they can contribute to strengthening PTCs in the province.
- Providing a clear and logical system for improving governance systems through transparency and evidence-based decision making.
- Facilitating the design and implementation of appropriate interventions to promote safe and rational use of medicines.

III. Implementation of the Guidelines

The Gauteng Pharmaceutical Services will coordinate and supervise the implementation of the Guidelines. The Pharmaceutical Services will support institutional and district activities and strategies, together with the complimentary roles of the different parties and stakeholders.

The Pharmaceutical Services together with the Gauteng Provincial PTC will have responsibility for monitoring and evaluation (M&E) of the implementation of the PTCs.

INTRODUCTION

The establishment of Pharmaceutical and Therapeutics Committees (PTCs) has been advocated by the World Health Organization (WHO) as one of the 12 key interventions¹ to promote rational medicine use (RMU). PTCs are committees designated to ensure the safe and effective use of medicines in health facilities. Their functions include establishing standards, conducting regular assessments, investigating reported problems, and correcting the identified problems to achieve the established standards.

The 1985 Conference of Experts on the Rational Use of Drugs, convened by WHO in Nairobi, defined RMU as follows: “the rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own clinical requirements for an adequate period of time, and at the lowest cost to them and their community.” RMU integrates two major principles:

- Use of medicines according to scientific information on efficacy, safety, and adherence
- Cost-effective use of medicines within the constraints of a health system

Inappropriate use of medicines has far-reaching consequences, both from a health system perspective with a waste of resources and from a public health perspective with an increase in antimicrobial resistance and poor patient-outcomes caused by increased adverse drug reactions (ADRs).

As multidisciplinary committees, PTCs have the expertise to target the various threats to RMU.

¹WHO, Medicines, The Pursuit of Responsible Use of Medicines: Sharing and Learning from Country Experiences, http://www.who.int/medicines/areas/rational_use/en/ (accessed July 17, 2012).

TERMS OF REFERENCE

The TORs describe the purpose and structure of a committee. They are essential at all levels because they provide a documented basis for making future decisions and developing a common understanding of the objectives among members and stakeholders.

The TORs describe the role of the Chair, the secretariat, and various categories of members so that all members are clear about each one's responsibilities.

Subcommittees or task teams are recommended in the PTCs at all levels because they promote effectiveness. This structure can assist in tackling different areas of interventions simultaneously. The expertise of PTC members is used in an optimum way. Each subcommittee develops its own action plan, which contributes to the overall PTC operational plan, thereby re-enforcing the responsibility and accountability of each member toward the common goal. Furthermore, the frequent meetings of the subcommittee encourage active involvement from the members.

The TORs should provide a list of areas of expertise needed for the PTC to perform its functions in an efficient and effective manner.

The draft TORs should be sent to the chief director of the region (district PTC) or chief executive officer (institutional PTC; CEO) for approval.

Generic TORs are provided in annexes A (provincial), B (district), and C (institutional).

SELECTION OF PTC MEMBERS

I. Governance Principles

To protect the integrity of decision-making processes through disclosure and transparency, the Gauteng Provincial PTC issued a *Declaration of Interest Guidance* document.

PTC members at all levels will be asked to complete a declaration form with details of relevant financial relationships with any entity and also sign a confidentiality declaration form, acknowledging the code of conduct. The goal is to protect important deliberations and key decisions by the PTCs from any untoward influence by commercial interests.

II. Governance Tools

- *Declaration of Interests Guidance* document (annex D)
- *Confidentiality Guidance* document (annex E)
- Declaration of Interests form (annex F)
- Confidentiality Declaration form (annex G)

III. Committee Membership Selection Process

The purpose of the selection process is to:

- Ensure that all types of expertise needed by the Provincial PTC are represented
- Ensure a transparent and fair selection process
- Avoid conflicts of interest at all times

The process is identical for all levels of PTCs. The process starts once the draft TORs have been approved by the chief director for the region (district PTC) or CEO (institutional PTC).

- 1) Advertise a call for nominations (annex H, nomination form)
- 2) Keep advert open for one month
- 3) Review nominations and contact nominees to confirm acceptance of nomination
- 4) Send relevant documents to nominees:
 - Curriculum vitae (CV) template (annex I, standardised)
 - *Declaration of Interests Guidance* document (annex D)
 - *Confidentiality Guidance* document (annex E)
 - TORs

- 5) Appoint a selection task team (uneven number of members, no nominees as part of the task team)
- 6) Send nominees' CVs to selection task team for review
- 7) Allow two to four weeks for review and comments
- 8) Call a selection meeting with task team members and ex-officio members as secretariat for the meeting; during the meeting, each CV is discussed among the task team members and the expertise of the nominees are marked according to a pre-designed grid

The nominees with the highest scores in their areas of expertise are selected. The total number of members selected per area of expertise is determined by the TORs.

- 9) The list of nominees with the justification for their selection is submitted to the chief director for the region (district PTC) or CEO (institutional PTC).
- 10) The chief director for the region (district PTC) or CEO (institutional PTC) signs appointment letters for the new PTC members
- 11) At the first meeting of the revitalised PTC, the TORs are adopted by the new PTC members
- 12) The adopted TORs are signed by the chief director for the region (district PTC) or CEO (institutional PTC).

If a member resigns, the CVs previously received for the specific area of expertise will be reviewed. If no suitable candidate is found, there would be another call for nominations to find someone with that specific area of knowledge.

REPORTING ON PTC ACTIVITIES

I. Reporting Strategy

The Gauteng Provincial PTC has developed a reporting template (annex J) to monitor the functionality of local PTCs.

Local PTCs will report to the Safety and Quality Subcommittee of the Gauteng Provincial PTC on a monthly basis by using the reporting template.

A comprehensive report on the functionality of institutional and district PTCs shall be compiled by the Safety and Quality Subcommittee on a quarterly basis; this report shall be disseminated to the local PTCs with recommendations for improvement.

II. Action Plan

A two-year operational plan shall be developed by the PTC members. To ensure cohesion and synergy of action in the province, the local PTCs' operational plans should be aligned with the Gauteng Provincial PTC operational plan. The two-year operational plan of the Gauteng Provincial PTC shall be communicated to local PTCs by a circular letter.

Progress on the plan should be monitored and reported on a quarterly basis to the district chief director for the district PTC and to the hospital CEO for the hospital PTC. A yearly report on the progress of the local PTC shall be submitted to the Provincial PTC.

A list of process, output, and outcome indicators for institutional and district PTCs is provided in annex K.

The action plan template in annex L provides an outline for the local PTCs to follow.

The action plan should include M&E indicators and targets.

FORMULARY MANAGEMENT

I. Criteria for Selection of Formulary Medicines²

- 1) The formulary must be consistent with any national or regional lists or approved standard treatment guidelines (STGs). Any medicine included must meet the needs of the majority of the patient population.
- 2) The formulary must have a limited number of medicines (only those that are necessary to provide for the needs of the hospital or district). Duplicate or alternative medicines that have therapeutic equivalence should not be accommodated on the list.
- 3) The formulary must be ethically correct and must demonstrate no influence or pressure from pharmaceutical manufacturers or suppliers, regarding any product that is considered for addition to or deletion from the formulary on the basis of proven scientific data regarding effectiveness and the need of the institution.
- 4) Sufficient proven scientific data regarding effectiveness and cost-effectiveness must be available. Ideally, medicines that appear on the formulary are well known, have been on the market for years, and have clinical experience to support their pharmacological profiles.
- 5) Any medicine included should have a substantial safety and risk/benefit ratio.
- 6) All products must be of an acceptable quality and must be registered with the Medicines Control Council (MCC).
- 7) The aim, as a rule, is to include only products containing single pharmacologically active ingredients. Combination medicines, as an exception, may be included where patient compliance becomes an important factor.
- 8) Products will be listed in accordance with their generic names only.
- 9) If multiple medicines are clinically equally effective, the medicines shall be compared on the following criteria:
 - Best cost advantage
 - Best researched
 - Best pharmacokinetic properties
 - Best patient compliance
 - Most reliable local manufacturer

²Gauteng Province, Department of Health, Directorate Clinical Support Services, Sub-Directorate Pharmaceutical Services; 2007; Circular Letter 43 of 2007

- 10) A request to include a medicine on the formulary must be supported by scientific data and appropriate independent references on its advantages and benefits over existing products.
- 11) It must be noted that as many as 70 per cent of all medicines on the market are either duplicative or similar in action.
- 12) The institutional or district formulary must be aligned with the budget. This shall be achieved through proper demand planning and budget management.

II. Addition/Deletion of Formulary Items

Principles

The principle of equity among all South Africans for use of medications governs the functioning of the Gauteng Provincial PTC.

The process followed by local institutions to request access to new medications is designed to ensure respect of this principle at all times by providing all local institutions with access to the same level of expertise during the selection process.

The stratified process will strengthen governance principles and assist in avoiding the influence of pharmaceutical companies in the final decision.

The Gauteng provincial motivation form for the inclusion of a new medication on the National Essential Medicines List (annex M) shall be used for the submission. The form should be filled out according to the directions provided in annex N.

Completing a Motivation to Amend the Provincial Formulary/NEML and STGs³

Motivations for inclusion in the list will only be considered if:

- The prescribed form (annex M) has been fully completed
- The motivators' contact details are complete
- The medicine name has been stated
- The submission has been evaluated and approved by the Provincial PTC
- The indication has been clearly stated
- All relevant, comparator medicines have been listed
- There is sufficient evidence to support the proposed amendment

Motivations may address major or minor amendments.

Major amendments include:

- New indications
- New therapeutic entities
- New therapeutic classes

³Gauteng Province, Department of Health, Directorate Clinical Support Services, Sub-Directorate Pharmaceutical Services; 2007; Circular Letter 43 of 2007

All major amendments must be supported by evidence reflecting safety, efficacy, and cost of the medicine compared to an already listed medicine for the same indication.

A major amendment may also include motivations for medicines not listed and for conditions not addressed in the essential medicines list (EML). In such cases, submissions must be supported by demographic data.

Minor amendments include:

- New formulations
- Combination therapies of existing essential medicines

For minor amendments, the supporting evidence should be relevant to the nature of the amendment.

Motivations are screened by the Provincial PTC to ensure that:

- The submission has been approved by the local PTC
- The motivator's contact details are included
- The medicine can be identified by the INN
- An indication has been included
- Relevant comparator medicines have been identified and their corresponding dosing regimens and cost have been completed by the local pharmacist in charge
- The local vetting committee has verified the costing and made funds available
- Supporting references are available to substantiate the request

Figure 1 illustrates the process to follow to access a non-EML medicine.

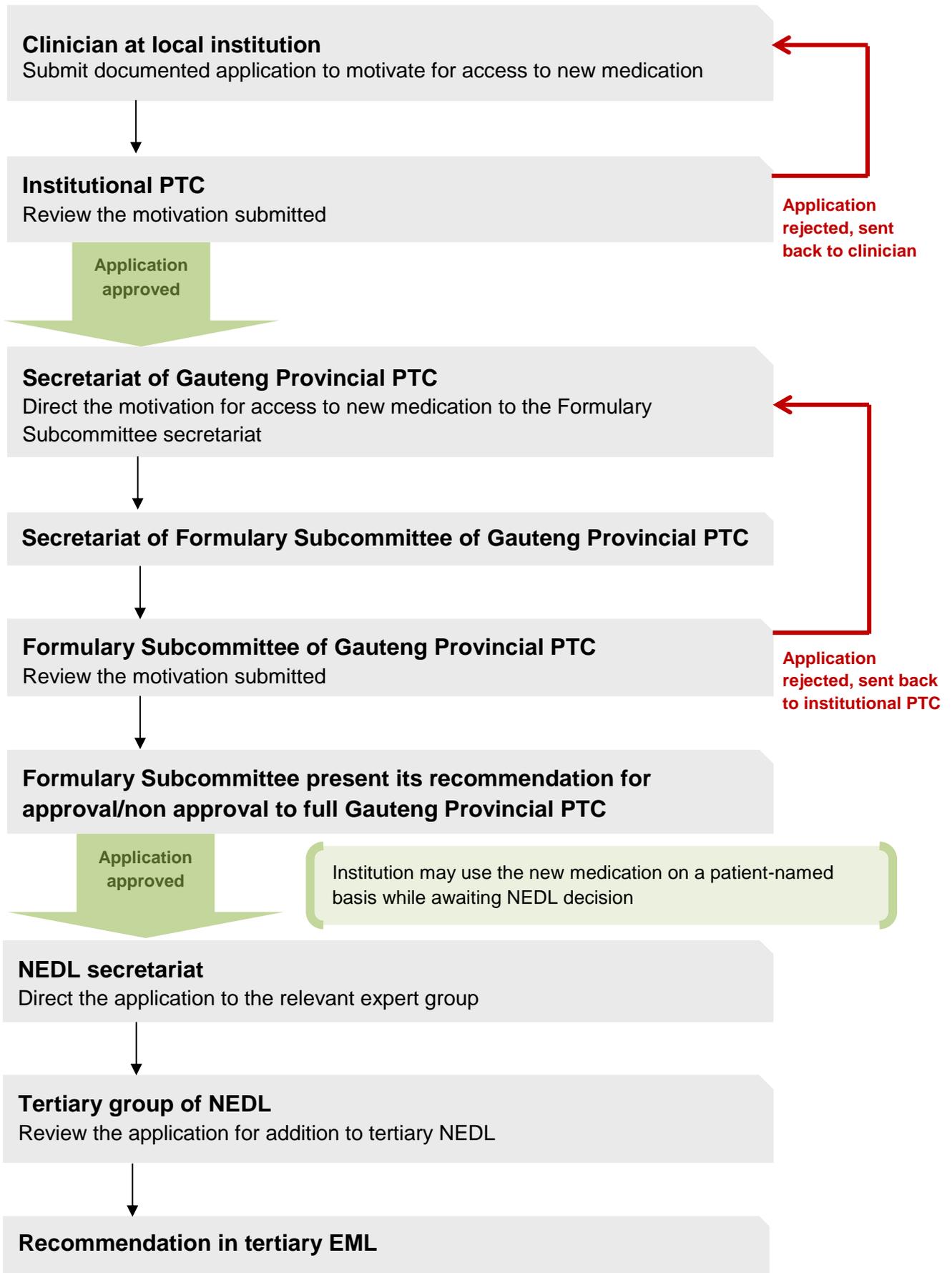


Figure 1. Process for application to access a non-EML medicine

Evidence-Based Decisions

Evidence is a vital component of the submission and review process.

Evidence does not constitute a medicine decision and merely informs the strength of the argument. It forms the basis upon which the decision is made and allows for transparent scrutiny of the decision and facilitates the review.

It is important to note that evidence needs to be relevant to the South African context. Multinational or foreign studies must be supported by the relevance of both the outcome measure as well as socio-economic facets to the South African context.

The inclusion of at least one relevant reference is mandatory. A copy of the full journal article should be included to expedite the review process.

The checklist for guiding formulary decision-making (annex O) “can facilitate a more standardized and critical scrutiny of the evidence and therapeutic alternatives”.⁴

⁴Schiff, G. D., Galanter, W. L., Duhig, J., Koronkowski, M. J., Lodolce, A. E., et al. 2012. A Prescription for Improving Drug Formulary Decision Making. *PLoS Med* 9(5):e1001220; doi:10.1371/journal.pmed.1001220

PROCUREMENT

I. Section 21

Section 21 of the Medicines Related Substances Control Act 101 of 1965 allows the MCC to authorize the sale of unregistered medicines for certain purposes.

It is crucial to stress that access to Section 21 medicine is on a named-patient basis and that relevant MCC procedures need to be followed.

The Section 21 application form is provided in annex P.

II. Procurement of Medically Related Items⁵

All institutions must ensure that the procurement of medically related items from the Medical Supplies Depot (MSD) is aligned with the provincial contract.

All contract items:

- Stored at MSD must be procured using the Z83 green card
- Classified as direct deliveries must be procured using the Z83 pink card

Items not on the provincial contracts will not be procured unless institutions comply with the following requirements with each order.

- Submission of a completed and signed RLSO1.
- The RLSO1 must clearly state the ICN number of the items where available.
- Submission of a detailed motivation by the clinician/user as to why the contract item cannot be used. Clearly detailing product specifications and features alone is unacceptable. The motivation must reflect the additional cost implication due to procuring a buy-out item.
- Submission of a product quality complaint form (available from MSD).
- Submission of three recent quotations based on generic specifications for the product required for consideration by the Local Acquisition Committee at MSD. All quotations reaching the MSD must still be valid for at least three weeks to facilitate placing the order. The MSD reserves the right to obtain other quotes with the generic specifications provided, if necessary.

All incomplete documentation, incomplete descriptions of why the items on contract are unacceptable, and invalid quotes will be returned to the institution for completion.

⁵Gauteng Province, Department of Health, Chief Directorate Clinical Support Services, Directorate Medical Supplies Depot; 2012; Circular Letter 24 of 2012

III. Policy Guideline on Donations⁶ and Samples for Medicine or Similar Products

This also includes blood products and blood monitoring devices.

Although many donations from companies are well intended, others are merely a way of by-passing procedures to make their products available at institutions and thus create an artificial demand for them. Often these products are not on the national EML or the provincial formulary.

PTC guidelines were developed in line with MCC's guidelines to ensure that all donations and samples are accepted in a transparent manner by all persons working for the Department of Health.

All medicine, samples of any kind, and similar products, including blood product donations, should be based on the healthcare needs and disease patterns in the province.

Four core principles interlay the guidelines:

- A medicine donation should benefit the recipient to the maximum extent possible.
- A donation should be given with full respect for the wishes and authority of the recipient and are supportive of existing government policies and administrative arrangements.
- There should be no double standards in quality; if the quality of an item is unacceptable in the donor country, it is also unacceptable as a donation.
- There should be effective communication between the donor and the recipient; donations should be based on an expressed need and should not be sent unannounced.

It is the responsibility of all health professionals to ensure that all products used on their patients are of the highest standards.

To this end, any (proposed) donated product must:

- Appear on the EML and the formulary of the institution
- Be registered with the MCC
- Be discussed with the pharmacist in charge of the MSD
- Undergo the normal laboratory testing at MSD

⁶Gauteng Province, Department of Health, Directorate Clinical Support Services, Sub-Directorate Pharmaceutical Services; 2007; Circular Letter 36 of 2007

- Must be disposed of in accordance with the normal disposal policy and reflected as expired stock on the monthly reports
- Have a shelf life of at least 12 months
- Be approved in accordance with Treasury Regulations chapter 21.2.1 and Circular Minute 83 of 2003 and Addendum 1 after authorisation by the Provincial PTC
- Be disclosed in a note in the annual financial statements of the institution per the Public Finance Management Act (PFMA)
- Be stored, distributed, and issued as per Good Pharmacy Practice and the PFMA.

The Medicines and Related Substances Control Act 101 of 1965 and regulations govern the manufacture, distribution, sale, and marketing of medicines. Section 18B of this Act prohibits the sampling of medicine.

Section 18B. Sampling of medicines

- (1) No person shall sample any medicine.
- (2) For the purposes of this section, “sample” means the free supply of medicines by a manufacturer or wholesaler or its agent to a pharmacist, medical practitioner, dentist, veterinarian, practitioner, nurse, or other person registered under the Health Professions Act of 1974, but does not include the free supply of medicines for the purposes of clinical trials, donations of medicines to the State, tendering to the State, and quality control by inspectors.
- (3) The use of medicines or scheduled substances for exhibition purposes shall be prescribed. (S. 18B inserted by s 12 of Act No. 90 of 1997.)

No medicine or similar products, including blood products, may be accepted by any institution unless prior approval is obtained from the Provincial PTC and in accordance with:

- Policy guidelines
- Circular Minute 83 of 2003 and Addendum 1 Delegation of Authority
- Treasury regulations chapter 21.2.1

Donated medicine or similar products, including blood products and blood monitoring devices, should be treated as if they were procured and should be entered into the inventory and distributed through existing distribution channels.

Estimates of quantities for medicines for the next year must take medicine donations into consideration.

A quarterly report on donated medicine or similar products, including blood products and blood monitoring devices, should be sent to the Directorate of Clinical Support Services.

IV. Visits of Company Representatives to an Institution⁷

The institutional PTC should be ultimately responsible for implementing, monitoring, and enforcing the policy on visits of company representatives to the institution. The Provincial Standard Operating Procedure (SOP) minimises the impact of company representatives on the PTC's efforts to promote cost effectiveness and RMU in accordance with national and provincial policies and guidelines.

The above mentioned policy should include the following points:

- 1) All hospital and district staff, including heads of clinical departments, senior medical staff, and the responsible pharmacist should only be seen by appointment.
- 2) It is recommended that all representatives must first report to the CEO's, clinical executive's, or facility manager's office to sign the visitation book prior to proceeding to another appointment in the hospital. The visitation book should contain the following information:
 - Date and time of arrival
 - Name of representative and contact details
 - Company name
 - Reason for visit
 - Product(s) that will be promoted to the health care professional
 - Department or doctor to be visited
- 3) All medical company representatives visiting the hospital should also make themselves known to the responsible pharmacist.
- 4) Patient care areas may not be used for interviews between company representatives and hospital or district staff.
- 5) Non-patient care areas in the wards or staff facilities may be used for interviews, provided that prior arrangements have been made with the relevant hospital staff.
- 6) Clinicians should not be paged by company representatives unless that method of communication has been specifically requested by the doctor.
- 7) No item that does not appear on the EML, provincial formulary, or institutional formulary should be promoted to any health care workers without prior permission of the institutional PTC.

⁷Gauteng Department of Health: Pharmaceutical Services. January 2013. SOP 32: Visits of Company Representatives to an Institution

- 8) New medicines and pharmaceutical products detailed by company representatives may be considered under certain circumstances.
- New products may be presented for information and continuous professional development purposes only. Products may not be accepted by any health care professional for use on patients within the institution unless approved by the PTC.
 - The institutional PTC must have procedures for clinicians to submit applications if they wish to motivate for new products or medicines to be considered for use in the institution.
 - Provincial guidelines should be followed for the submission of application for new products to be used within the province.
- 9) Medicine samples or starter packs are considered donations.
- The general rule is that samples may not be accepted at the institutional level as this is regarded as a donation, and all donations must be approved and declared by the CEO to the head of health.
 - The use of donations, samples, or starter packs at the institution will only be considered after a formal written submission has been made to the institutional PTC and approved by the CEO, after having taken the financial impact of such practices under consideration.
 - The pharmacy department has the responsibility for the distribution of all medicines to patients within the hospital, and if a donation is accepted, the distribution of such donations must also be made via the pharmacy department.
 - Clear records must be maintained of all donations accepted, received, and used within the institution.
- 10) Educational sessions may be presented under certain conditions.
- Education sessions for the medical, nursing, and pharmacy staff should be organized through the head of the department of the respective unit.
 - Company representatives should not discuss their products with individual members of staff without prior arrangement. Clinical staff should be encouraged to attend group education sessions rather than individual discussion sessions. One-on-one sessions with company representatives should be discouraged.
 - The main purpose of education sessions is to enable company representatives to familiarize medical and other clinical staff with the therapeutic uses of their products. These should be limited to medicines on the EML and STGs.

- Staff members should understand that interactions with company representatives are likely to have promotional intent and are intended to have a direct influence on their subsequent practices. They should therefore also familiarize themselves with other objective information sources to ensure a balanced view of the topic under discussion.
- Product information and consumer medicine information may be issued to staff at such sessions.
- No samples may be issued at such sessions.
- Educational sessions must include an opportunity for open discussion, where members of staff may express independent views relating to the topic.

PHARMACOVIGILANCE

Pharmacovigilance is defined as the science and activities concerned with the detection, assessment, understanding, and prevention of adverse reactions to medicines. The ultimate goal of pharmacovigilance is to improve safety and RMU, thereby improving patient care and public health⁸.

I. Product Complaints⁹

All health care professionals are responsible for reporting product quality problems. The responsible pharmacists at hospital and district pharmacies will be accountable for forwarding the form received to relevant stakeholders for investigation. The responsible pharmacist will also be responsible for maintaining the documents and reports and for feedback.

What Product Quality Problems Should Be Reported?

- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging or labelling
- Therapeutic failures
- Expired batches

If any of these quality problems are found, then the procedure outlined below should be followed to report and return poor-quality products to the supplier.

Process for Reporting Product Quality Problems

- 1) Determine the nature of the product complaint and request that the complainant complete the departmental product complaint form (annex R) and the ADR and product complaint form from the MCC (annex Q).
- 2) All of the affected batches must be identified and isolated until the investigation has been finalised.
- 3) Both the departmental product complaint form and the MCC ADR and product complaint form must be sent to either the hospital or district pharmacy for further management.
 - The district and hospital pharmacy manager will escalate the product complaint together with samples from the affected batches to the MSD for investigation. The supplier will be contacted by MSD to assist with the

⁸Guideline for Reporting Adverse Drug Reactions and Product Quality Problems, GPPTC Safety and Quality Subcommittee; annex T this report

⁹Gauteng Department of Health: Pharmaceutical Services. January 2013. SOP 29: Procedure for the Handling of Product Complaints

investigation and to recall the batch if necessary. The product complaint form will also be forwarded to the contract management office at the health directorate as information for future contracts and awards.

- The product complaint forms must be sent to the procurement office at the MSD (011 628 9000).
- The district and hospital pharmacy managers will also escalate the product complaint to the institution's PTC and to the Gauteng PTC for information. Contact the Secretariat of the Safety and Quality Subcommittee (currently Magalane.Ntlhane@gauteng.gov.za).
- The Safety and Quality Subcommittee may report the product complaint to the MCC, if deemed necessary.
- A file with copies of all the product complaint forms must be kept at the complaining institution and the following must be kept in the product complaint file:
 - Copies of the product complaint forms clearly detailing the nature of the problem
 - Batches involved
 - Dates and times of all complaints escalated
 - Results of the internal investigation
 - Actions taken after the investigation
 - Any other relevant information, e.g., feedback from MSD and Gauteng PTC
- The results of the MSD and Gauteng PTC investigations must be communicated to the district and hospital pharmacists and the complainant.

II. Adverse Drug Reactions^{10,11}

An ADR is defined as a response to a medicine that is harmful or unintended, including lack of effectiveness that occurs at any dosage, and that can also result from an overdose, misuse, or abuse of a medicine.

The purpose of ADR reporting is to reduce the risks associated with drug prescribing and administration and to improve patient care and safety.

¹⁰Gauteng Department of Health: Pharmaceutical Services. January 2013. SOP 30: Procedure for the Reporting and Handling of Adverse Drug Reactions (ADR)

¹¹Guideline for Reporting Adverse Drug Reactions and Product Quality Problems, GPPTC Safety and Quality Subcommittee; annex T this report

What ADRs Should Be Reported?

The following types of adverse reactions should be reported:

- Life-threatening reactions
- Those that require patients to be hospitalized or that prolong hospitalization
- Reactions that are persistent or cause significant disability or incapacity
- Those that cause congenital anomalies or birth defects
- ADRs not included in the package insert and others
- Death

All health care workers, including doctors, dentists, pharmacists, nurses, and other health professionals, should report all suspected adverse reactions to medicines (including vaccines, X-ray contrast media, and traditional and herbal remedies).

Process for Reporting ADRs

All ADRs should be reported on the ADR/product quality form from the MCC (annex Q) available at all pharmacies and primary health care facilities. The form should be completed in as much detail as possible.

Particular attention should be paid to the following when completing the reporting form:

- Patient details, including name initials or reference number), gender, age, date of birth, weight, and height
- Date and time of onset of reaction
- Description of the reaction or problem, providing relevant history, allergies, previous exposure, and clinical and laboratory data
- Medication history, including all concomitant and over-the-counter medicines
- Outcome of the reaction
- Product quality reports: trade name, batch number, registration number, dosage form and strength, expiry date, and size/type of container
- Details of reporter: name, qualifications, contact details, and institution

The completed ADR and product quality complaint form should be sent to the hospital or district pharmacy, who will forward the form to the following:

- National adverse events monitoring centre (contact details can be found on the MCC form)

- Institutions or district PTCs for discussion and action where necessary
- Procurement office at MSD (011 628 9000), which will then inform the responsible company to assist the province with the investigation and for action where required, e.g., to implement educational initiatives, update package inserts, etc.
- Secretariat of the Safety and Quality Subcommittee (currently Magalane.Ntlhane@gauteng.gov.za)

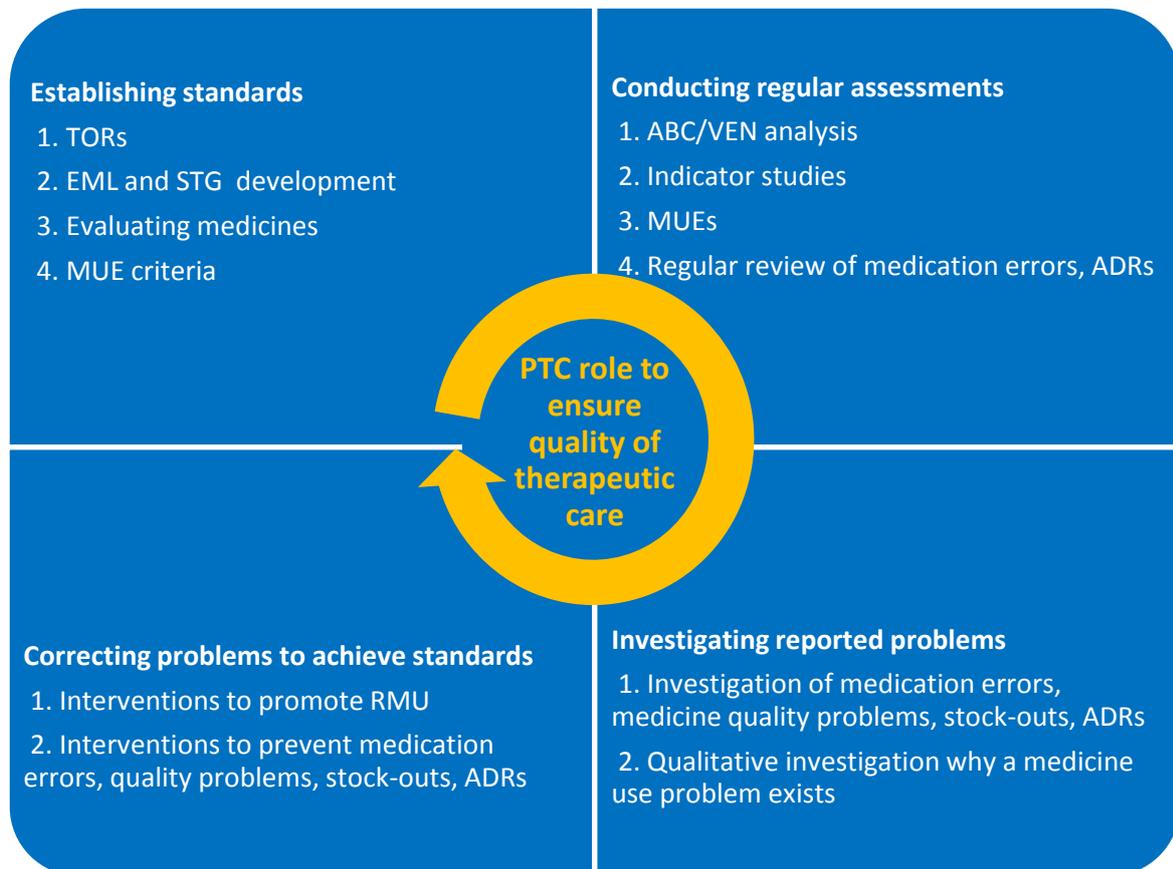
Copies of the ADR and product quality complaint form, together with the reports on the investigation, the results, any actions taken, and any final outcome must be kept at the institution.

The health care professional who submitted the adverse drug reaction or product quality complaint form must be kept informed, by the pharmacist on all progress made and final outcomes.

RATIONAL MEDICINE USE

Unnecessary and irrational use of medicines is a serious problem affecting treatment costs and public health¹².

Figure 2 highlights the role of PTCs in ensuring quality of therapeutic care.



Adapted from Terry Green, John Chalker, Kathleen Holloway, and RPM Plus-WHO. Promoting Drug and Therapeutics Committees in the Developing World, oral presentation at the 2nd International Conference on Use of Medicines, Chiang Mai, Thailand, March 2004.

Figure 2. Responsibilities of a PTC

I. Standard Treatment Guidelines and Essential Medicines List

The cost¹³, time, and effort expended in producing STGs and EML books will be in vain if the concepts of evidence-based selection of medicines and cost-effective treatment protocols are not implemented at the hospital level. To ensure an adequate and reliable supply of safe, quality medicines for all citizens of South

¹²Strengthening Pharmaceutical Systems South Africa. 2012. *Promoting the Rational Use of Medicines through Pharmaceutical and Therapeutics Committees in South Africa: Results, Challenges, and Way Forward*. Submitted to the US Agency for International Development by the Strengthening Pharmaceutical Systems Program. Arlington, VA: Management Sciences for Health.

¹³Gauteng Province, Department of Health. 2007. Circular Letter 37 of 2007

Africa, it is the responsibility of every health professional to advocate the implementation and use of the STGs and EML.

PTCs at all levels should play a pivotal role to ensure that the latest editions of the STGs and EML books are implemented by training healthcare professionals in the institution on the major changes in the STGs and EML. This process shall be driven by the Provincial PTC.

II. Assessments of Medicines Use

1) Identify the medicines that may need further investigation.

ABC analysis is a useful tool to identify potential inappropriate use of medicines. The first step should then be to perform an ABC analysis to scrutinise the use of pharmaceuticals items over a set period of time and identify the class A items. This list should then be compared with one from the previous period.

2) Investigate the use of medicines

The American Society of Health-System Pharmacists¹⁴ defines a medicine use evaluation (MUE) as a performance method that focuses on evaluating and improving medicine use for optimal patient outcomes.

MUE is a proactive, criteria-based process that should be designed and managed by a multidisciplinary team and carried out in a systematic manner. The value and usefulness of the MUE rests on the relevance of the criteria and thresholds. The consultation of prescribers in setting the thresholds is essential.

The steps of an MUE¹⁵ are:

- Establish responsibility
- Develop the scope of activities and define the objectives
- Establish criteria for review of the medicine
- Data collection
- Data analysis
- Feedback to the prescribers and making a plan of action
- Follow up

An example of a data collection tool template is provided in annex S.

Note: MUEs are operational research that local PTCs are encouraged to submit for publication and/or presentation at conferences.

¹⁴American Society of Health-System Pharmacists. 1996. Guidelines on Medicine-Use Evaluation, *Formulary Management—Guidelines*, 127–129; http://www.ashp.org/s_ashp/docs/files/BP07/Form_Gdl_MedUseEval.pdf

¹⁵WHO (2003) *Drug and Therapeutics Committees: A Practical Guide*. World Health Organization, Geneva. WHO/EDM/PAR/2004.1; <http://apps.who.int/medicinedocs/en/d/Js4882e/>

ADMINISTRATIVE CONSIDERATIONS

I. Drawing Up an Agenda for a PTC Meeting

The secretariat of the PTC is responsible for drawing up the agenda of the meetings and circulating it to all PTC members at least one week prior to the meeting so that members of the committee have a chance to prepare for the meeting. The agenda details the matters to be discussed at the meeting. The standing items to be on the agenda are defined by the TORs.

II. Ensuring Respect of Governance Principles

The secretariat shall review the declaration of interests and confidentiality forms for signatures prior to the start of the meeting. Any concerns shall be raised immediately with the Chair prior to the start of the meeting.

The secretariat is responsible for checking the presence of the required quorum.

The secretariat shall keep a record of the CVs of each PTC member and raise any concerns about conflicts of interest related to specific agenda items with the Chair prior to the meeting.

III. Taking Minutes of the PTC Meeting

The secretariat is responsible for writing the minutes at each PTC meeting.

Minutes are written as an accurate record of a group's meetings and a record of the decisions taken. Minutes can also inform people who were not at the meeting about what took place, so the context needs to be carefully set for each topic.

Accurate minutes guarantee the transparency of the decisions taken by the PTC.

The minutes should be written immediately after the meeting; the sooner they are done, the more accurate they are. Writing good meeting minutes takes time; the writing can take as long as the actual meeting.

The minutes should be short and to the point. To record every word and supplement the written minutes, a tape recording might be considered. It is useful to report the ideas, rather than every sentence.

The same template should be used every time and should include the following:

- 1) Time, date, and place of meeting
- 2) List of people attending
- 3) List of absent members of the group
- 4) Approval of the previous meeting's minutes and any matters arising from those minutes

- 5) For each item in the agenda, include:
 - a) Principal points discussed
 - b) Decision taken
 - c) Information
 - d) Action taken with one person responsible and a due date
- 6) Time, date, and place of next meeting
- 7) Name of person taking the minutes

IV. Communication

The secretariat plays a pivotal role in communication and ensures that all members of the PTC receive the same information at the same time and helps to avoid any discussions that may be personal in nature.

All communication or information related to the PTC shall be transmitted through the secretariat.

If a member of the PTC wishes to disseminate information to the other members of the PTC, he/she shall do so through the secretariat.

V. Dissemination and Implementation of PTC Decisions

The minutes are signed by the head of the Health Department or chief of operations in the case of the Provincial PTC; the chief director of the region in the case of the regional/district PTC; and the CEO in the case of the institutional PTC.

The decisions and actions for implementation are disseminated through circular letters or internal memos from the Provincial PTC to the institutions, from the district PTCs to the institutions in the district, and from the hospital PTC to the hospital's departments.

In the case of the regional/district PTC or institutional PTC, the minutes are forwarded to the Provincial PTC, who may revise or amend the decisions if they are not in line with current practices or policies of the national essential medicines concepts.

Any applicant may appeal¹⁶ any decision of the committee to the PTC. The appeal must be in writing and supported by scientific evidence. In the event of an impasse, the PTC will refer the application together with its comments to the head of health, chief of operations, chief director of the region, or the CEO.

¹⁶Gauteng Province, Department of Health, Directorate Clinical Support Services, Sub-Directorate Pharmaceutical Services; 2007; Circular Letter 43 of 2007

CONCLUDING REMARKS

The *Guidelines for Implementation of Pharmaceutical and Therapeutics Committees* cover the wide range of activities that contribute to the PTC effectively fulfilling their role to ensure the quality of therapeutic care. Commitment by all role players and stakeholders and active participation in the process of strengthening PTCs will go a long way toward ensuring that people of Gauteng have access to quality, safe, and cost-effective medicines.

ANNEX A. GENERIC TERMS OF REFERENCE FOR PROVINCIAL PTC



TERMS OF REFERENCE

PROVINCIAL PHARMACEUTICAL AND THERAPEUTICS COMMITTEE

Name

This entity shall be known as the XXX Provincial Pharmacy and Therapeutics Committee (PTC).

Definitions

ABC analysis: Classification of inventory items into three categories (A,B, and C) according to the value of their annual usage. This classification is useful for analysing drug consumption and utilization, comparing actual versus planned purchases, justifying procurement budgets, guiding procurement patterns, and setting priorities for stock management. Class A items are the 10 to 20 per cent of items that account for 75 to 80 per cent of funds spent; class B items are the items with intermediate usage rates; class C items are the vast majority of items with low, individual usage and which accounts for 5 to 10 per cent of funds spent.

Adverse drug reaction (ADR): A harmful or unintended response in a human or animal to a medicine that occurs at any dosage. It can also result from lack of efficacy of a medicine, off-label use, overdose, misuse, or abuse.

Drug versus medicine: The word drug is often replaced by medicine after a resolution of the National Essential Medicine Committee

Executive authority: Member of the Executive Council for Health

Evidence-based: A process of independent and objective decision making based on consideration of objective data.

Formulary: A list of medicines that are approved for use in the health care system by authorized prescribers and dispensers

Health district: A clearly defined geographical or administrative area for the implementation of primary health care services and whose boundaries coincide with district and metropolitan municipal boundaries.

Medical practitioner: A person registered as such under the Health Professions Act, 1974; also includes interns

Medicine utilization review (MUR): A method evaluating and re-examining the use of drugs to determine the appropriateness of the drug therapy. A study of drug prescriptions to evaluate appropriateness and cost-effectiveness by comparing actual drug use to predetermined standards; formerly known as drug utilization review.

Personal information: Includes, but is not limited to, information identifiable to an individual that relates to a person's health, finances, education, business, use or receipt of governmental services, other activities, names, addresses, telephone numbers, social security numbers, driver's license numbers, financial profiles, credit card numbers, financial identifiers, and other identifying numbers.

Rational medicine use (RMU): In 1985, the World Health Organization (WHO) in Nairobi defined rational use as follows: the rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community; formerly known as rational drug use.

Standard treatment guidelines (STGs): A systematically developed collection of statements designed to assist medical practitioners and patients in making decisions about appropriate health care for specific clinical circumstances.

Therapeutic equivalence

- 1) A medicine is considered therapeutically equivalent to another medicine if both medicines—
 - (a) Are pharmaceutically equivalent, i.e., contain the same amount of active substances in the same dosage form, meet the same or comparable standards, and are intended to be administered by the same route
 - (b) Display the same effects with respect to efficacy and safety when administered in the same molar dose
- 2) Therapeutic equivalence is determined from comparative bioavailability, pharmacodynamic, clinical, or in vitro studies that meet the requirements and accepted criteria for bioequivalence as determined by the Executive Council for Health.

Acronyms and Abbreviations

ADR	adverse drug reaction
AMR	antimicrobial resistance
DOH	Department of Health
EML	essential medicines list
INN	international non-proprietary name
MUR	medicine utilization review
NEMLC	National Essential Medicines List Committee
PTC	pharmacy and therapeutics committee
RMU	rational medicine use
STG	standard treatment guideline
VEN	vital, essential, and non-essential (analysis)

Purpose of the Provincial PTC

The purpose of the committee is to:

- 1) Promote, in XXX Province, access to quality medicines that are safe and cost effective
- 2) Provide a peer review mechanism for the oversight of institutional and district PTCs
- 3) Develop governance systems to guard against the introduction of perversities and conflicts of interest
- 4) Institute systems for the promotion of RMU
- 5) Publish a provincial formulary that is compliant with all relevant policies
- 6) Institute and implement systems for access to non-formulary medicines
- 7) Develop and maintain medicines safety systems
- 8) Develop and maintain medicine procurement systems that are compliant with relevant policy and statutory requirements and optimise cost efficiencies.
- 9) Contribute toward the development of the national essential medicines list (EML) through the development of peer review mechanisms
- 10) Apply evidence-based medicine and pharmaco-economic principles in the review of applications for new formulary and essential medicines items
- 11) Contribute toward the development of the medicine's budget that takes into consideration epidemiological and standard of care considerations
- 12) Evaluate, through available evidence, the effectiveness of medicines within a class or classes

Accountability of the Provincial PTC

The Provincial PTC is appointed by the head of the Department of Health and will provide him or her with quarterly reports regarding its various functions as determined by the terms of reference. To this end, the Provincial PTC will establish indicators to gauge its performance. All policies and formularies emanating from the Provincial PTC's work will be submitted to the head of Department of Health for approval prior to implementation.

Authority to Act

Authority to act is provided by the Constitution of South Africa:

- 1) Section 217(1) of the Constitution states that an organ of the state must procure goods and services, such as medicines, in accordance with a system that is fair, equitable, transparent, competitive, and cost-effective. These five principles of procurement apply to all procurement phases, starting with the planning stage through to contract maintenance. In terms of medicines and other pharmaceuticals, the Provincial PTC offers the best opportunities for compliance with the law.
- 2) Section 33(3)c of the Constitution and its attendant legislation, the Promotion of Administrative Justice Act, requires an effective process with the least waste of effort.

Principles

The following principles will govern the functioning of the Provincial PTC:

- 1) The primary function of the Provincial PTC is to ensure appropriate availability of medicines for use at different levels of health services within the province.
- 2) The basis of selection of these medicines would be:
 - a) Safety and quality
 - b) Efficacy
 - c) Rational need and use
 - d) Cost-effectiveness
 - e) Affordability
- 3) Selection of medicines for use in the public sector is not based on cost alone, but rather on cost-effectiveness and affordability. Ineffective, substandard medicines will not be selected.
- 4) For appropriate and rational use of the selected medicines, a standard treatment guideline (STG) indicating the position of the medicine in the management algorithm should be provided prior to addition to the formulary.

- 5) Procurement should be undertaken in accordance with the selection as soon as possible, once the head of the department or a designate has signed off on the decision. This will be reflected in the minutes of the deliberations.
- 6) An official circular informing all end-users will be sent through institutions' structures, informing them of the Provincial PTC's decisions and requesting them to implement the policies.
- 7) In accordance with the national Department of Health (DOH) medicines policy, the availability of selected drugs should be designated with institutional and prescribers' levels.
 - a) The DOH has divided services according to the following levels:
 - i. Primary care or level 1 services – clinics, community health centres, and 24- hour health centres
 - ii. Hospital-level care or level 2 services – district and regional hospitals
 - iii. Tertiary and quaternary care or level 3 services – academic or central hospitals
 - b) The levels of prescribers are defined according to the National Essential Medicines List and Standard Treatment Guidelines.
- 8) To support drug utilization for each of these levels of care, the national essential medicines program has developed formularies:
 - a) Primary-care level (latest edition 2010)
 - b) Paediatric (not yet available) and adult hospital-level books (latest edition 2012)
 - c) Tertiary-level list of drugs (undergoing review; information is available through the secretariat at the National Department of Pharmaceutical Services).
- 9) The decisions of the national essential medicines program for all levels of health care must be adopted in totality. There will be a link between decisions adopted at the Provincial PTC and the National Essential Drug Programme and vice versa.
- 10) The adoption of decisions from the DOH's National Essential Drug Programme is based on the premise that decisions reached by the national committee have undergone the necessary scrutiny of the evidence-based process and would allow congruency in drug utilization for the entire country. Should decisions at the national level not be acceptable to the Provincial PTC, then evidence for a variance in opinion should be presented to the Provincial PTC. If supported, then a full motivation will be sent to the National Essential Drug List Committee (NEDLC).
- 11) Motivations for addition of non-EML medicines to the formulary must be submitted with evidence to the Provincial PTC Formulary Subcommittee; if deemed appropriate, the submission will be presented to the full Provincial

PTC. If supported by the PTC, the information must then be sent to the NEDLC. Should NEDLC delay responding to the submission, then the product may be purchased on a named-patient basis while awaiting feedback.

- 12) Implementation of an essential medicine program should result in:
 - a) 80 per cent of drug expenditures for the province will be directed at primary and hospital levels, according to the essential medicines formulary
 - b) 10-15 per cent of expenditures will support tertiary services
 - c) 5 per cent of expenditures will be on medicines not mentioned in the essential medicine program

- 13) In accordance with this proposed expenditure and to make the process function efficiently, the Provincial PTC should attempt to ensure that no or limited stock-outs of essential medicines are experienced. When prioritizing availability, essential medicines for primary health care must take precedence over hospital-level medicines, and availability of medicines at level 2 should take priority over availability of medicines at level 3.

- 14) Accountability should be ensured by appropriate governance structures, especially by the financial administrative section of the province.

- 15) There should be no influence within the Provincial PTC by the pharmaceutical or equipment industry. Names of members on this committee should be kept confidential as well as all discussions. Minutes of the meeting should therefore not reflect individual names when items are discussed.

- 16) An ABC analysis of medicines utilized in the province should be carried out regularly and items with incongruent use must be highlighted and investigated at different institutions.

- 17) The Safety and Quality Subcommittee is tasked to regularly review any adverse events related to medicines within the province or reported in the literature and bring these matters to the urgent attention of the Provincial PTC.

- 18) The selection of members to serve on the Provincial PTC must be in accordance with the need for functioning of this committee so that decisions reached would be insightful. Where conflicts of interest are declared, the Chair would decide whether the member could participate in the discussions; however, the member will be asked to recuse him or herself during the voting process.

Objectives

The main objectives of the XXX Provincial PTC shall be to:

- 1) Establish a protocol for the selection of medicines within the therapeutic classes already approved by the National Essential Medicines List Committee (NEMLC)
- 2) Establish a protocol for the approval of repackaged medicines and revise the list annually
- 3) Establish procedures and protocols for the compilation of a XXX procurement catalogue based upon the current provincial formulary and prevailing tenders
- 4) Establish procedures and protocols to monitor and evaluate compliance with the procurement, distribution, and use of medicines
- 5) Quantify provincial needs for medicines that appear on the current approved formulary in accordance with the national tender cycle
- 6) Establish and participate in quality assurance activities relating to procurement, distribution, and use of medicine
- 7) Design RMU interventions, including regulatory and educational activities, to ensure safe and cost-effective prescribing practices
- 8) Design programs aimed at patients to promote safety and RMU including adherence
- 9) Develop a policy for the establishment of local PTCs and monitor their functioning
- 10) Establish a budget and protocol for the purchase of medications for academic purposes, including investigational and clinically initiated trials

Functions

- 1) Establish governance systems that guard against conflicts of interest and perversities in the prevailing environment
- 2) Participate in the compilation and peer review of the national EML and its associated STGs
- 3) Review the EML and DOH's STGs and, where relevant, adapt local STGs and protocols
- 4) Launch new editions of the EML and the associated provincial formulary; for new medicines, institute rational prescribing measures, such as educational and managerial interventions

- 5) Establish uniform systems for applications to add and remove medicines from the formulary with an attendant administrative screening protocol
- 6) Establish evidence-based and pharmaco-economic-based systems for the review of applications for new essential medicines
- 7) Peer-review applications in accordance with the systems established in (6) and, where supported, submit applications to the NEDLC for approval
- 8) Establish a system for the application and review of named-patient medicines
- 9) Review the named-patient approvals granted by institutional PTCs in accordance with an established roster
- 10) Prepare and monitor a budget for medicines based on consumption and morbidity to facilitate implementation of the provincial formulary
- 11) Compile and prepare a provincial formulary
- 12) Develop medicine usage review programmes to ensure maximum patient benefit on the most cost-effective basis
- 13) Implement local PTCs and monitor their functionality
- 14) Establish and maintain a system for:
 - a) Approval of the purchase of medication for academic purposes including investigationally initiated trials
 - b) Approval of repackaged medicine
 - c) Compilation of a procurement catalogue based upon the current provincial formulary and prevailing tenders
 - d) Reporting quality problems and withdrawing defective products
 - e) Programme for Reporting medicine safety problems (medicine errors, ADRs)
 - f) Review of the items on tender and verification of the estimates

Monitoring and Reporting

To assist the Provincial PTC in executing its mandate, the following reports will be required:

- 1) All Provincial PTC indicators
- 2) Antimicrobial resistance (AMR)
- 3) Medicines utilisation reviews
- 4) ADR and medication error trends
- 5) Named-patient medicines procurement
- 6) Financial data
 - a) ABC analysis
 - b) Percentage of medications outside the EML and percentage outside the formulary by consumption
 - c) Percentage of medicines out of stock, including cumulative number of days out of stock
 - d) Percentage of medicines bought out of tender

Membership Requirements for the Provincial PTC

- 1) The committee shall consist of up to 25 members appointed by the Head of the Department of Health, including the following ex-officio members with full voting rights:
 - a) Chief director, Health Services Support (Chair; 1)
 - b) Head of Pharmaceutical Services in the province (1)
 - c) Manager of the Medical Supplies Depot (1)
 - d) NEMLC representatives (2)
- 2) Other members of the NEMLC or its technical committees can serve on the Provincial PTC as technical advisors, when required.
- 3) Members shall sign a code of conduct and accept the terms of reference; failure to comply may result in disciplinary action that could lead to the termination of the appointment.
- 4) Different areas of expertise must be represented on the PTC, and members must have public sector experience; the number of members that must be knowledgeable in each area is:
 - a) Evidence-based medicine (2)
 - b) Primary health care (2)
 - c) Secondary health care (2)
 - d) Tertiary health care (2)
 - e) RMU (3)
 - f) PTC (2)
 - g) Medical supply management (2)
 - h) Financial management (1)
 - i) Good Pharmacy Practice (2)
 - j) AMR (2)
- 5) Committee members shall not use the name of the committee in any publication, meeting, negotiation, or promotion without prior approval of the head of the DOH.
- 6) The Provincial PTC and its subcommittees may co-opt persons from specific specialties as they deem necessary, to assist in the finalization of a matter on the agenda; such co-opted persons shall have no voting powers.

Appointment Period

- 1) Members, excluding ex-officio members as mentioned above, shall be appointed to a term of three years and the Head of Department of Health may, after due consideration, extend the term beyond the three-year cycle.
- 2) A member may be re-appointed for two consecutive terms (of a three-year cycle) and will become eligible for re-appointment after an absence of one cycle.
- 3) Vacancies will be reviewed in line with the skills base requirements, and appointments will be made when necessary.

Resignation, Termination, and Leave of Absence

- 1) Membership will be reviewed if any member is absent without a valid apology for more than two consecutive meetings.
- 2) The Chair, supported by elected members, will investigate any wrong doing or misconduct by members; the Chair may then recommend to the Head of Department of Health that the membership be suspended or terminated.
- 3) A member may resign by submitting a written notice to the Chair.
- 4) The Chair may resign by submitting a written notice to the Head of Department of Health.
- 5) Members should inform the Chair of a leave of absence prior to a meeting; in the case of sabbatical leave, the members should inform the Chair three months in advance.

Establishment of Subcommittees and Task Teams

The Provincial PTC, in the execution of its functions, may constitute subcommittees or task teams by means of establishment of specific terms of reference.

The following subcommittees will be established in accordance with the terms of reference:

- Formulary
 - Medicine Rational Utilization
 - Procurement Advisory
 - Safety and Quality (includes ADR monitoring)
- 1) Such subcommittees shall be under the leadership of and chaired by a Provincial PTC member or such other person designated by the Provincial PTC, who shall ensure compliance with the terms of reference.
 - 2) No member or group shall have authority to amend or alter the terms of reference, adopt any action contrary to the committee, remove any member, or take any action on behalf of the Provincial PTC.
 - 3) Any member of any group may be removed by the Provincial PTC whenever the best interests of the committee or the state will be best served by such removal.
 - 4) Each subcommittee shall appoint its own Chair and secretary from among its members.

Chair of the Committee

The Chair shall:

- 1) Play a leadership role in developing and implementing an effective Provincial PTC and sound policies and procedures
- 2) Possess a comprehensive knowledge of the selection, procurement, management, and rational use of medicines
- 3) Have leadership and management skills to direct and foster open and collegial discussion among all committee members while maintaining focus on the issues at hand
- 4) Have respect for committee members from diverse backgrounds, perspectives, and sources of expertise and promote a culture of respect among committee members and key stakeholders
- 5) Be able to function in a team, often under stressful circumstances
- 6) Have the courage and confidence to uphold decisions

Functions of the Chair

- 1) Conduct the Provincial PTC meetings in accordance with the annual schedule
- 2) Facilitate the Provincial PTC's discussion of the agenda points to arrive at a consensus
- 3) Upon arrival at consensus, summarise the decision and call for members to propose and second the adoption of the motion
- 4) If a consensus cannot be reached, the final decision on how to resolve the matter will reside with the Chair
- 5) Facilitate the development and maintenance of policies and guidance documents with advice and consultation from all relevant stakeholders
- 6) With the assistance of the secretariat, finalise all Provincial PTC documents for submission to the Head of Department of Health

Secretariat

The Directorate of Pharmaceutical Services will supply the resources for the secretariat.

Functions of the Secretariat

- 1) Develop and maintain an annual schedule for the meetings of the Provincial PTC
- 2) Convene and make all the necessary logistics arrangements for the meetings
- 3) Advise the Provincial PTC on administrative and regulatory matters
- 4) Compile draft minutes of the meeting in consultation with the Chair
 - a) Draft minutes will be circulated within 30 working days after the meeting
 - b) Minutes of the previous meeting will be adopted at the beginning of the next meeting
- 5) Coordinate and facilitate any research required for the Provincial PTC to perform its functions
- 6) Compile relevant documents to be tabled at the Head of Department meetings
- 7) Maintain information regarding the performance of the Provincial PTC

Standing Items on the Provincial PTC Agenda

- 1) Declaration of Conflict of Interest
- 2) Minutes
- 3) Matters arising
- 4) Feedback on NEMLC meeting
- 5) Safety, quality assurance, and ADR reports
- 6) MUR
- 7) ABC and VEN analyses
- 8) Budget vs. expenditures
- 9) Local (institutional) PTC reports
- 10) Formulary
- 11) Named-patient report
- 12) Drug supply management report

Urgent Matters

The committee will appoint four members who, together with the Chair, shall constitute the executive committee. Urgent matters will be attended to by the executive committee and then ratified by the full PTC at the next meeting.

The following will be considered as urgent matters:

- 1) When public health will be compromised if an item is not approved
- 2) Resistance to an antimicrobial agent listed on the formulary has become evident
- 3) Matters regarding the non-approval of an item at a lower level when a patient's life is in danger

Attendance at Meetings

- 1) The Provincial PTC shall meet quarterly.
- 2) The appointed members are expected to volunteer and apply their knowledge of current clinical practices during discussions. Matters discussed during sessions must remain confidential.
- 3) The appointed members are expected to attend personally (no substitutions) and all apologies must be submitted in writing. (Apologies per e-mail will be permitted.) The member will be permitted to participate via teleconference at the discretion of the Chair.
- 4) Members are expected to be conversant with the agenda and documents provided before the scheduled meeting to ensure active participation.

Voting and Quorum

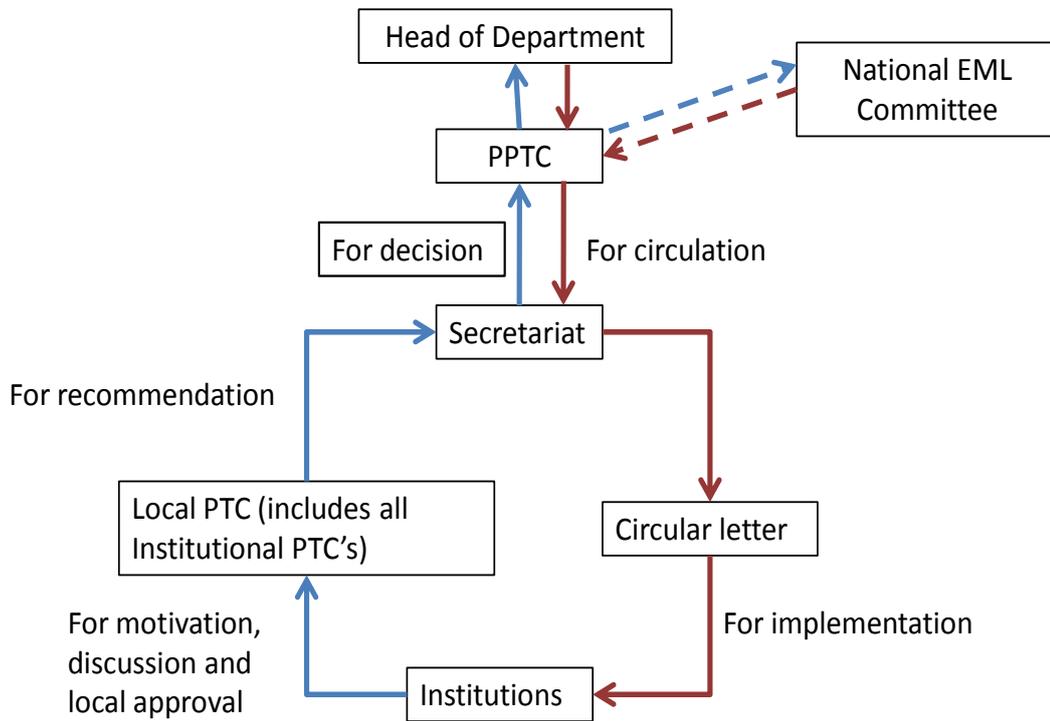
- 1) A quorum shall be deemed to be 60 per cent of members.
- 2) All business of the Provincial PTC shall be transacted by motion or resolution, which may be made by any member in attendance, including the Chair, and shall require a seconder.
- 3) Voting on motions or resolutions shall be by a show of hands, unless a member asks that the roll be called and that the vote of each member be recorded.
- 4) Each member of the Provincial PTC shall have one vote on each matter submitted to a vote of the committee. The Chair shall be a voting member of the committee.
- 5) A majority of 80 per cent of those voting shall be considered a quorum which is required for all matters.
- 6) The secretariat has NO vote.
- 7) When a member recuses himself or herself from participating on any matter, that person will not be counted for purposes of determining a quorum.

Decision Implementation

The Chair of the Provincial PTC signs the minutes after acceptance by a proposer and seconder.

The secretariat will extract the relevant information and decisions and then circulate for implementation.

Communication Strategy



Amendment of Terms of Reference of the XXX Provincial PTC

Terms of reference should be reviewed within a five-year cycle by the Directorate of Pharmaceutical Services and submitted to the Head of Department of Health for ratification and approval.

The terms of reference of the Provincial PTC were duly adopted at the meeting of the Provincial PTC on the

_____ (day) of _____ (month), _____ (year)

Signed by

.....
Chair **Date**

Approved by

.....
Head of Department **Date**

ANNEX B. GENERIC TERMS OF REFERENCE FOR DISTRICT PTC



TERMS OF REFERENCE

XXX DISTRICT PHARMACEUTICAL AND THERAPEUTICS COMMITTEE

Name

This entity shall be known as the XXX District Pharmaceutical and Therapeutics Committee (PTC).

Definitions

ABC analysis: Classification of inventory items into three categories (A,B, and C) according to the value of their annual usage. This classification is useful for analysing drug consumption and utilization, comparing actual versus planned purchases, justifying procurement budgets, guiding procurement patterns, and setting priorities for stock management. Class A items are the 10 to 20 per cent of items that account for 75 to 80 per cent of funds spent; class B items are the items with intermediate usage rates; class C items are the vast majority of items with low, individual usage and which accounts for 5 to 10 per cent of funds spent.

Adverse drug reaction (ADR): A harmful or unintended response in a human or animal to a medicine that occurs at any dosage. It can also result from lack of efficacy of a medicine, off-label use, overdose, misuse, or abuse.

Drug versus medicine: The word drug is often replaced by medicine after a resolution of the National Essential Medicine Committee

Executive authority: Member of the Executive Council for Health

Evidence-based: A process of independent and objective decision making based on consideration of objective data.

Formulary: A list of medicines that are approved for use in the health care system by authorized prescribers and dispensers

Health district: A clearly defined geographical or administrative area for the implementation of primary health care services and whose boundaries coincide with district and metropolitan municipal boundaries.

Medical practitioner: A person registered as such under the Health Professions Act, 1974; also includes interns

Medicine utilization review (MUR): A method evaluating and re-examining the use of drugs to determine the appropriateness of the drug therapy. A study of drug prescriptions to evaluate appropriateness and cost-effectiveness by comparing actual drug use to predetermined standards; formerly known as drug utilization review.

Personal information: Includes, but is not limited to, information identifiable to an individual that relates to a person's health, finances, education, business, use or receipt of governmental services, other activities, names, addresses, telephone numbers, social security numbers, driver's license numbers, financial profiles, credit card numbers, financial identifiers, and other identifying numbers.

Rational medicine use (RMU): In 1985, the World Health Organization (WHO) in Nairobi defined rational use as follows: the rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community; formerly known as rational drug use.

Standard treatment guidelines (STGs): A systematically developed collection of statements designed to assist medical practitioners and patients in making decisions about appropriate health care for specific clinical circumstances.

Therapeutic equivalence

- 3) A medicine is considered therapeutically equivalent to another medicine if both medicines—
 - (c) Are pharmaceutically equivalent, i.e., contain the same amount of active substances in the same dosage form, meet the same or comparable standards, and are intended to be administered by the same route
 - (d) Display the same effects with respect to efficacy and safety when administered in the same molar dose
- 4) Therapeutic equivalence is determined from comparative bioavailability, pharmacodynamic, clinical, or in vitro studies that meet the requirements and accepted criteria for bioequivalence as determined by the Executive Council for Health.

Acronyms and Abbreviations

ADR	adverse drug reaction
DOH	Department of Health
EDL	Essential Drug List
EML	Essential Medicine List
MUE	medicine use evaluation
MUR	medicine utilization review
PTC	Pharmaceuticals and Therapeutics Committee
RMU	rational medicine use
STG	standard treatment guideline
VEN	vital, essential, and non-essential (analysis)
WHO	World Health Organization

Purpose of the District PTC

To advise all categories of health workers at XXX District on issues relating to therapeutics and medicines use and selection in order to promote the rational, cost-effective, and safe use of medicines in accordance with the national standard treatment guidelines (STGs).

Accountability of the District PTC

The District PTC is appointed by XXX and will provide him or her with quarterly reports regarding its various functions as determined by the terms of reference. To this end, the District PTC will establish indicators to gauge its performance. All policies and formularies emanating from the District PTC's work will be submitted to the XXX for approval prior to implementation.

Authority to Act

Authority to act is provided by the Constitution of South Africa:

- 1) Section 217(1) of the Constitution states that an organ of the state must procure goods and services, such as medicines, in accordance with a system that is fair, equitable, transparent, competitive, and cost-effective. These five principles of procurement apply to all procurement phases, starting with the planning stage through to contract maintenance. In terms of medicines and other pharmaceuticals, the District PTC offers the best opportunities for compliance with the law.
- 2) Section 33(3)c of the Constitution and its attendant legislation, the Promotion of Administrative Justice Act, requires an effective process with the least waste of effort.

Principles

The following principles will govern the functioning of the District PTC:

- 1) The primary function of the District PTC is to ensure appropriate availability of medicines for use at different levels of health services within the district.
- 2) An official circular informing all end-users will be sent through institutions' structures, informing them of the District PTC's decisions and requesting them to implement policies.
- 3) The decisions of the Provincial PTC must be adopted in totality. There will be a link between decisions adopted at the District PTC and the Provincial PTC and vice versa.
- 4) Motivations for addition of non-EML and non-provincial formulary medicines to the formulary must be submitted with evidence to the Provincial PTC Formulary Subcommittee; if deemed appropriate, the submission must be presented to the full Provincial PTC.
- 5) Accountability should be ensured by appropriate governance structures.
- 6) There should be no influence within the District PTC by the pharmaceutical or equipment industry. Names of members on this committee should be kept confidential as well as all discussions. Minutes of the meeting should therefore not reflect individual names when items are discussed.
- 7) An ABC analysis of medicines utilized in the district should be carried out regularly and items with incongruent use must be highlighted and investigated at different institutions.
- 8) A regular review of any adverse events related to medicines reported locally within the district or reported in the literature should be carried out and brought to the urgent attention of the District PTC.
- 9) The selection of members to serve on the District PTC must be in accordance with the need for functioning of this committee so that decisions reached would be insightful. Where conflicts of interest are declared, the Chair would decide whether the member could participate in the discussions; however, the member will be asked to recuse him or herself during the voting process.

Objectives

The main objectives of the District PTC shall be to:

- 1) Design RMU interventions, including regulatory and educational activities, to ensure safe and cost-effective prescribing practices

- 2) Promote patient safety by monitoring, assessing, reporting, and minimizing adverse drug reactions (ADRs) and medication errors
- 3) Design programs aimed at patients to promote safety and RMU including adherence
- 4) Support the establishment of PTCs in hospitals and monitor their functioning
- 5) Develop, review, and adapt standard treatment guidelines or protocols for the district based on the national Essential Medicines List (EML)
- 6) Develop and maintain a formulary based on the South African Essential Drug List (EDL; primary and hospital) and compliant with all relevant policies
- 7) Ensure that medicine procurement systems are compliant with relevant policies and statutory requirements and that cost efficiencies are optimised
- 8) Monitor expenditures of drugs to be sure that they are in line with current budgets
- 9) Establish governance systems that guard against conflicts of interest and perversities in the prevailing environment

Functions

- 1) Conduct operational research (MUR) to support RMU
- 2) Initiate educational programs in matters relating to drug therapy
- 3) Develop and enforce standard guidelines on drug promotion for representatives visiting institutions
- 4) Develop and maintain a district formulary based on the South African EDL (primary and hospital) and compliant with all relevant policies
- 5) Support research activities on new medicines used in hospitals by reviewing protocols and evaluating evidence-based data
- 6) Collect, monitor, and process reports of ADRs
- 7) Liaise with the Ethics Committee regarding on-going trials in line with legal requirements
- 8) Keep up to date with all newly published work and be aware of new evidence-based developments
- 9) Promote comments from prescribers in the compilation and peer review of the chapters of the national EML and its associated STGs

10) Review the EML and National Department of Health's (DOH) STGs and, when relevant, adapt local STGs and protocols

11) Establish a system for the application and review of named-patient medicines

Monitoring and Reporting

To assist the Provincial PTC in executing its mandate, the following reports will be required:

- 1) All District PTC indicators
- 2) Antimicrobial resistance
- 3) Medicines utilisation reviews
- 4) ADR and medication error trends
- 5) Named-patient medicines procurement
- 6) Financial data
 - a) ABC analysis
 - b) Percentage of medications outside the EML and percentage outside the formulary by consumption
 - c) Percentage of medicines out of stock, including cumulative number of days out of stock
 - d) Percentage of medicines bought out of tender

Membership Requirements for the District PTC

- 1) The committee shall consist of up to 25 members appointed by the district chief director of the DOH, including the following ex-officio members with full voting rights:
 - a) Health district manager (Chair; 1)
 - b) District pharmacy manager (1)
 - c) Manager of the regional pharmacy (1)
 - d) Provincial PTC representative (1)
 - e) Sub district managers (1 for each subdistrict)
- 2) Other members of the Provincial PTC or its technical committees can serve on the District PTC as technical advisors, when required.
- 3) Members shall sign a code of conduct and accept the terms of reference; failure to comply may result in disciplinary action that could lead to the termination of the appointment.
- 4) Different areas of expertise must be represented on the PTC, and members must have public sector experience; the number of members [to be decided by each district] that must be knowledgeable in each area is:
 - a) Evidence-based medicine (x)

- b) Primary health care (x)
 - c) Secondary health care (x)
 - d) RMU (x)
 - e) PTC (x)
 - f) Medical supply management (x)
 - g) Financial management (x)
 - h) Good Pharmacy Practice (x)
 - i) Infectious diseases (x)
 - j) Pharmacovigilance (x)
- 5) Committee members shall not use the name of the committee in any publication, meeting, negotiation, or promotion without prior approval of the Head of the DOH.
- 6) The District PTC and its subcommittees may co-opt persons from specific specialties as they deem necessary, to assist in the finalization of a matter on the agenda; such co-opted persons shall have no voting powers.
- 7) Each member shall be responsible for representing the interest of the district and shall not:
- a) Act in a manner that is inconsistent with their participation, membership, function, and role in the committee
 - b) Expose themselves to any situation involving the risk of a conflict of interest between their professional and personal interests
 - c) Use their position or any information entrusted to them or obtained in the course of their involvement in the committee to enrich himself/herself or his/her relatives
 - d) Act in a way that may compromise the credibility, transparency, workings, and integrity of the committee
- 9) Every member must disclose to the Chief Director of the district any financial or other interest in the pharmaceutical industry before accepting the appointment to the committee.
- 10) Members must also disclose any interest acquired after their appointment. These interests may include, but are not limited to, any gifts, sponsored foreign trips, funding for clinical trials, research, attendance at conferences, hospitality, and any other benefit of a material nature received by him/her or by a member of their family.
- 11) Upon making the disclosure, the member may be asked to excuse himself/herself from the meeting to enable the committee to discuss the matter to determine whether the member should be excluded by virtue of conflict of interest.
- 12) Any disclosure and decision of the committee regarding determination of further participation in the discussion by the member with a conflict of interest must be recorded in the minutes.

Appointment Period

- 1) Members, excluding ex-officio members as mentioned above, shall be appointed to a term of three years and the Chief Director may, after due consideration, extend the term beyond the three-year cycle.
- 2) A member may be re-appointed on two consecutive terms (of a three-year cycle) and will become eligible for re-appointment after an absence of one cycle.
- 3) Vacancies occasioned will be reviewed in line with the skills base requirements and appointments will be made when deemed necessary.

Resignation, Termination, and Leave of Absence

- 1) Membership will be reviewed if any member is absent without a valid apology for more than two consecutive meetings.
- 2) The Chair, supported by elected members, will investigate any wrong doing or misconduct by members; the Chair may then make a recommendation to the Chief Director, which may result in suspension or termination.
- 3) A member may resign by submitting a written notice to the Chair.
- 4) The Chair may resign by submitting a written notice to the Chief Director.
- 5) Members need to inform the Chair of a leave of absence prior to a meeting; in the case of sabbatical leave, the members need to inform the Chair three months in advance.

Establishment of Subcommittees and Task Teams

The District PTC in the execution of its functions may constitute subcommittees or task teams by means of establishment of specific terms of reference:

The following subcommittees will be established in accordance with the terms of reference:

- Medicine Rational Utilization
 - Procurement Advisory
 - Safety and Quality (includes ADR monitoring)
- 1) Such subcommittees shall be under the leadership of and chaired by a District PTC member or such other person designated by the District PTC, who shall ensure compliance with the terms of reference.
 - 2) No member or group shall have authority to amend or alter the terms of reference, adopt any action contrary to the committee, remove any member, or take any action on behalf of the District PTC.

- 3) Any member of any group may be removed by the District PTC whenever the best interests of the committee or the state will be best served by such removal.
- 4) Each subcommittee shall appoint its own Chair and secretary from among its members.

Chair of the Committee

The Chair shall:

- 1) Play a leadership role in developing and implementing an effective District PTC and sound policies and procedures.
- 2) Possess a comprehensive knowledge of the selection, procurement, management, and rational use of medicines
- 3) Have leadership and management skills to direct and foster open and collegial discussion among all committee members while maintaining focus on the issues at hand
- 4) Have respect for committee members from diverse backgrounds, perspectives, and sources of expertise and promote a culture of respect among committee members and key stakeholders
- 5) Be able to function in a team, often under stressful circumstances
- 6) Have the courage and confidence to uphold decisions

Functions of the Chair

- 1) Conduct the District PTC meetings in accordance with the annual schedule
- 2) Facilitate the District PTC's discussion of the agenda points to arrive at a consensus
- 3) Upon arrival at consensus, summarise the decision and call for members to propose and second the adoption of the motion
- 4) If a consensus cannot be reached, the final decision on how to resolve the matter will reside with the Chair
- 5) Facilitate the development and maintenance of policies and guidance documents with advice and consultation from all relevant stakeholders
- 6) With the assistance of the secretariat, finalise all District PTC documents for submission to the Chief Director

Secretariat

District Pharmaceutical Services will supply the resources for the secretariat.

Functions of the Secretariat

- 1) Develop and maintain an annual schedule for the meetings of the District PTC
- 2) Convene and make all the necessary logistics arrangements for the meetings
- 3) Advise the District PTC on administrative and regulatory matters
- 4) Compile draft minutes of the meeting in consultation with the Chair
 - a) Draft minutes will be circulated within seven working days after the meeting
 - b) Minutes of the previous meeting will be adopted at the beginning of the next meeting
- 5) Conduct operational research as required for the committee to perform its functions
- 6) Ensure that the decisions made by the committee are submitted to the Chief Director of the district
- 7) Correlate and circulate all pertinent material for meetings to all members and their task teams
- 8) Report committee activities to the Provincial PTC as per the provincial reporting template and indicators

Standing Items on the District PTC Agenda

- 1) Declaration of Conflict of Interest
- 2) Minutes
- 3) Matters arising
- 4) Feedback on Provincial PTC meeting
- 5) Safety, quality assurance, and ADR reports
- 6) ABC and VEN analyses
- 7) MURs
- 8) Motivation for additions to and deletions from the district formulary
- 9) Budget vs. expenditures
- 10) Drug supply management report
- 11) PTC performance report

Urgent Matters

The committee will appoint four members who, together with the Chair, shall constitute the executive committee. Urgent matters will be attended to by the executive committee and then ratified by the full PTC at the next available meeting.

The following will be considered as urgent matters:

- 1) Resistance to an antimicrobial agent listed on the formulary has become evident
- 2) Out of stock of a vital item in a facility

Attendance at Meetings

- 1) The District PTC shall meet every other month.
- 2) The appointed members are expected to volunteer and apply their knowledge of current clinical practices during discussion. Matters discussed during sessions must remain confidential.
- 3) The appointed members are expected to attend personally (no substitutions) and all apologies must be submitted in writing. (Apologies per e-mail will be permitted.) The member will be permitted to participate via teleconference at the discretion of the Chair.
- 4) Members are expected to be conversant with the agenda and documents provided before the scheduled meeting to ensure active participation.

Voting and Quorum

- 1) A quorum shall be deemed to be 60 per cent of members.
- 2) All business of the District PTC shall be transacted by motion or resolution, which may be made by any member in attendance, including the Chair, and shall require a seconder.
- 3) Voting on motions or resolutions shall be by a show of hands, unless a member asks that the roll be called and that the vote of each member be recorded.
- 4) Each member of the District PTC shall have one vote on each matter submitted to a vote of the committee. The Chair shall be a voting member of the committee.
- 5) A majority of 80 per cent of those voting shall be considered a quorum which is required for all matters.
- 6) The secretariat has NO vote.

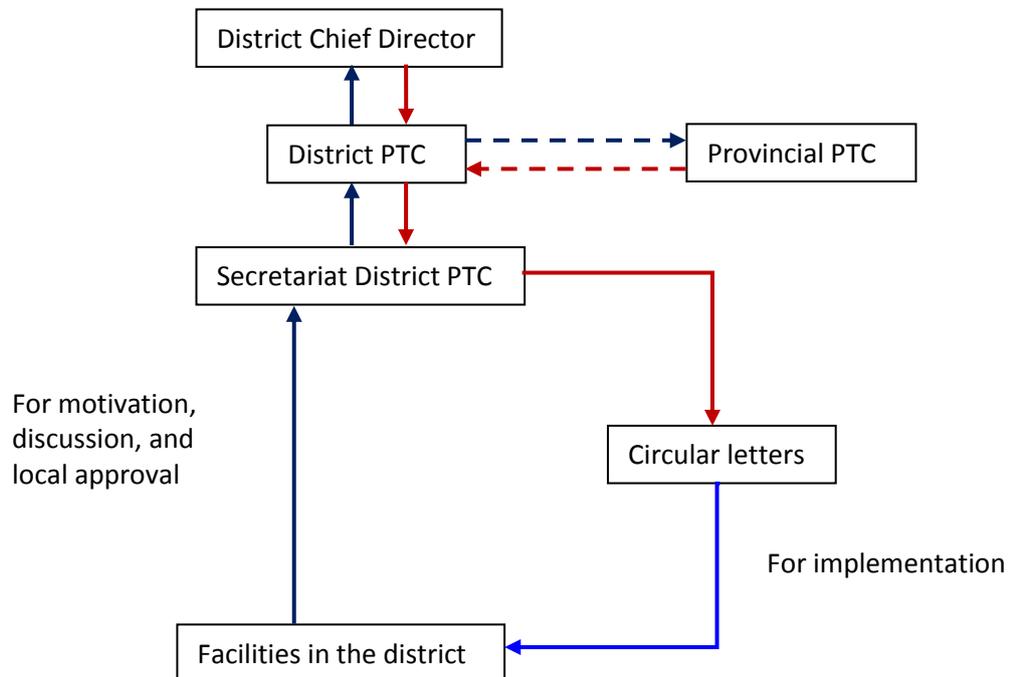
- 7) When a member recuses himself or herself from participating on any matter, that person will not be counted for purposes of determining a quorum.

Decision Implementation

The Chair of the District PTC signs the minutes after acceptance by a proposer and a seconder.

The secretariat will extract the relevant information and decisions and then circulate for implementation.

Communication Strategy



Amendment of Terms of Reference of the District PTC

Terms of reference should be reviewed within a five-year cycle by the District Pharmacy Manager and submitted to the Chief Director for ratification and approval.

The terms of reference of the District PTC were duly adopted at the meeting of the District PTC on the

_____ (day) of _____ (month), _____ (year)

Signed by

.....
Chair **Date**

Approved by

.....
Chief Director **Date**

ANNEX C. GENERIC TERMS OF REFERENCE FOR HOSPITAL PTC



TERMS OF REFERENCE

XXX HOSPITAL PHARMACY AND THERAPEUTICS COMMITTEE

Name

This entity shall be known as the XXX Hospital Pharmacy and Therapeutics Committee (PTC).

Definitions

ABC analysis: Classification of inventory items into three categories (A,B, and C) according to the value of their annual usage. This classification is useful for analysing drug consumption and utilization, comparing actual versus planned purchases, justifying procurement budgets, guiding procurement patterns, and setting priorities for stock management. Class A items are the 10 to 20 per cent of items that account for 75 to 80 per cent of funds spent; class B items are the items with intermediate usage rates; class C items are the vast majority of items with low, individual usage and which accounts for 5 to 10 per cent of funds spent.

Adverse drug reaction (ADR): A harmful or unintended response in a human or animal to a medicine that occurs at any dosage. It can also result from lack of efficacy of a medicine, off-label use, overdose, misuse, or abuse.

Drug versus medicine: The word drug is often replaced by medicine after a resolution of the National Essential Medicine Committee

Executive authority: Member of the Executive Council for Health

Evidence-based: A process of independent and objective decision making based on consideration of objective data.

Formulary: A list of medicines that are approved for use in the health care system by authorized prescribers and dispensers

Health district: A clearly defined geographical or administrative area for the implementation of primary health care services and whose boundaries coincide with district and metropolitan municipal boundaries.

Medical practitioner: A person registered as such under the Health Professions Act, 1974; also includes interns

Medicine utilization review (MUR): A method evaluating and re-examining the use of drugs to determine the appropriateness of the drug therapy. A study of drug prescriptions to evaluate appropriateness and cost-effectiveness by comparing actual drug use to predetermined standards; formerly known as drug utilization review.

Personal information: Includes, but is not limited to, information identifiable to an individual that relates to a person's health, finances, education, business, use or receipt of governmental services, other activities, names, addresses, telephone numbers, social security numbers, driver's license numbers, financial profiles, credit card numbers, financial identifiers, and other identifying numbers.

Rational medicine use (RMU): In 1985, the World Health Organization (WHO) in Nairobi defined rational use as follows: the rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community; formerly known as rational drug use.

Standard treatment guidelines (STGs): A systematically developed collection of statements designed to assist medical practitioners and patients in making decisions about appropriate health care for specific clinical circumstances.

Therapeutic equivalence

- 5) A medicine is considered therapeutically equivalent to another medicine if both medicines—
 - (e) Are pharmaceutically equivalent, i.e., contain the same amount of active substances in the same dosage form, meet the same or comparable standards, and are intended to be administered by the same route
 - (f) Display the same effects with respect to efficacy and safety when administered in the same molar dose
- 6) Therapeutic equivalence is determined from comparative bioavailability, pharmacodynamic, clinical, or in vitro studies that meet the requirements and accepted criteria for bioequivalence as determined by the Executive Council for Health.

Acronyms and Abbreviations

ADR	adverse drug reaction
AMR	antimicrobial resistance
CEO	chief executive officer
DUR	drug utilization review
EDL	Essential Drug List
EML	Essential Medicine List
INN	international non-proprietary name
MUE	medicine use evaluation
MUR	medicine utilization review
PTC	Pharmacy and Therapeutics Committee
RMU	rational medicine use
STG	standard treatment guidelines
VEN	vital, essential and non-essential (analysis)
WHO	World Health Organization

Purpose of the Hospital PTC

The purpose of the committee is to:

- 1) Promote rational medicine use (RMU) by all prescribers at XXX Hospital
- 2) Promote the implementation and use of the national Essential Medicines Lists (EMLs)
- 3) Develop, review, and adapt standard treatment guidelines (STGs) and protocols from the hospital-level EML
- 4) Formulate and implement policies and guidelines pertaining to RMU within the hospital
- 5) Monitor expenditures of medicines so they are in line with the current budgets
- 6) Conduct operational research to support RMU
- 7) Initiate educational programmes in matters relating to medicine therapy
- 8) Develop and maintain a medicines safety system through collection, monitoring, and reporting of adverse drug reactions (ADRs)
- 9) Develop and enforce governance systems to guard against the introduction of perversities and conflicts of interest
- 10) Develop and maintain a hospital formulary based on the South African national EML, aligned with the Gauteng Provincial Formulary and compliant with all relevant policies

- 11) Apply evidence-based medicine and pharmaco-economic principles in the review of applications for additions to and deletions from the hospital formulary
- 12) Develop and enforce standard operating procedures on medicine promotion when representatives visit institutions
- 13) Support research activities by reviewing protocols and evaluate evidence-based data related to new medicines used in the hospital
- 14) Liaise with the Ethics Committee regarding on-going drug trials to ensure compliance with legal requirements

Accountability of the Hospital PTC

The Hospital PTC is appointed by the Chief Executive Officer (CEO) of the hospital and will provide him or her with quarterly reports regarding its various functions as determined by the terms of reference. To this end, the Hospital PTC will establish indicators to gauge its performance. All policies and formularies emanating from the PTC's work will be submitted to the CEO for approval prior to implementation.

Authority to Act

Authority to act is provided by the Constitution of South Africa:

- 1) Section 217(1) of the Constitution states that an organ of the state must procure goods and services, such as medicines, in accordance with a system that is fair, equitable, transparent, competitive, and cost-effective. These five principles of procurement apply to all procurement phases, starting with the planning stage through to contract maintenance. In terms of medicines and other pharmaceuticals, the Provincial PTC offers the best opportunities for compliance with the law.
- 2) Section 33(3)c of the Constitution and its attendant legislation, the Promotion of Administrative Justice Act, requires an effective process with the least waste of effort.

Principles

The following principles will govern the functioning of the Hospital PTC:

- 1) The primary function of the Hospital PTC is to ensure appropriate use of medicines in the hospital
- 2) The decisions of the national essential medicines program for all levels of health care must be adopted in totality

- 3) The adoption of decisions from the Department of Health's National Essential Drug Programme is based on the premise that decisions reached by the national committee have undergone the necessary scrutiny of the evidence-based process and would allow congruency in the drug utilization for the entire country. Should decisions at the national level not be acceptable to the Hospital PTC, then evidence for a variance in opinion should be presented to the Provincial PTC. If supported, then a full motivation will be sent to the National Essential Drug List Committee (NEDLC).
- 4) Motivations for addition of non-EML medicines to the formulary must be submitted with evidence to the Provincial PTC formulary subcommittee; if deemed appropriate, the submission will be presented to the full Provincial PTC. If supported by the PTC, the information must then be sent to the NEDLC. Should NEDLC delay responding to the submission, then the product may be purchased on a named-patient basis while awaiting feedback.
- 5) There should be no influence within the Hospital PTC by the pharmaceutical or equipment industry. Names of members on this committee should be kept confidential as well as all discussions. Minutes of the meeting should therefore not reflect individual names when items are discussed.
- 6) An ABC analysis of medicines utilized in the hospital should be carried out regularly and items with incongruent use must be highlighted and investigated at different institutions
- 7) Reports on adverse events related to medicines used at the hospital will be sent to the Safety and Quality Subcommittee of the Provincial PTC.
- 8) The basis of selection of medicines would be:
 - a) Safety and quality
 - b) Efficacy
 - c) Rational need and use
 - d) Cost-effectiveness
 - e) Affordability
- 9) The selection of members to serve on the Hospital PTC must be in accordance with the need for functioning of this committee so that decisions reached would be insightful. Where conflicts of interest are declared, the Chair would decide whether the member could participate in the discussions; however, the member will be asked to recuse him or herself during the voting process
- 10) An official circular informing all end-users will be sent through institutions' structures, informing them of the Hospital PTC's decisions and requesting them to implement policy.

Objectives

The main objectives of the XXX Hospital PTC shall be to:

- 1) Design RMU, interventions including regulatory and educational activities, to ensure safe and cost-effective prescribing practices
- 2) Design programs aimed at patients to promote safety and RMU including adherence
- 3) Establish procedures and protocols to monitor and evaluate compliance with the procurement, distribution, and use of medicines
- 4) Quantify the hospital's needs for medicines that appear on the current approved formulary in accordance with the national tender cycle
- 5) Participate in quality assurance activities relating to procurement, distribution, and use of medicine
- 6) Establish a protocol for the selection of medicines within the therapeutic classes already approved by the National EML Committee and the Provincial PTC

Functions

- 1) Develop medicine usage review programmes to ensure maximum patient benefit on the most cost-effective basis
- 2) Adapt local STGs and protocols to ensure compliance with national STGs
- 3) Develop educational programmes for the launch of the new editions of the EML and the associated provincial formulary; for new medicines, institute rational prescribing measures, such as educational and managerial interventions
- 4) Establish and maintain a system for reporting on medicine safety (medicine errors, ADRs)
- 5) Establish governance systems that guard against conflicts of interest and perversities in the prevailing environment
- 6) Compile and prepare a hospital formulary
- 7) Establish uniform systems for applications to add and remove medicines from the formulary with an attendant administrative screening protocol
- 8) Establish evidence based medicine and pharmaco-economic-based systems for the review of applications for new essential medicines

- 9) Peer-review applications in accordance with the systems established in (8) and, where supported, submit applications to the Provincial PTC for approval
- 10) Prepare and monitor a budget for medicines based on consumption and morbidity to facilitate implementation of the hospital formulary

Monitoring and Reporting

To assist the Hospital PTC in executing its mandate, the following reports will be required:

- 1) All PTC indicators
- 2) Antimicrobial resistance
- 3) Medicines utilisation reviews
- 4) ADR and medication error trends
- 5) Named-patient medicines procurement
- 6) Financial data
 - a) ABC analysis
 - b) Percentage of medication outside the EML and percentage outside the formulary by consumption
 - c) Percentage of medicines out of stock to including accumulative number of days out of stock
 - d) Percentage of medicines bought out of tender

Membership Requirements for the Hospital PTC

- 1) The committee shall consist of up to 25 members appointed by the CEO, including the following ex-officio members with full voting rights:
 - a) Clinical director (Chair; 1)
 - b) Financial director (1)
 - c) Nursing representatives (1)
 - d) Provincial PTC representative (for tertiary and quaternary hospitals)
- 2) Other members of the Provincial PTC or its technical committees can serve on the Hospital PTC as technical advisors, when required.
- 3) Members shall sign a code of conduct and accept the terms of reference; failure to comply may result in disciplinary action that could lead to the termination of the appointment.
- 4) Different areas of expertise must be represented on the Hospital PTC, and must have public sector experience; the number of members [to be decided by each hospital] that must be knowledgeable in each area is:
 - a) Psychiatry (x)
 - b) Infectious disease (x)
 - c) Microbiology (x)

- d) ICU (x)
 - e) Anaesthesiology (x)
 - f) Pulmonary (x)
 - g) Paediatrics (x)
 - h) Geriatrics (x)
 - i) Renal/PDU (x)
 - j) Pharmacology (x)
 - k) Orthopaedics (x)
 - l) Oncology (x)
 - m) Internal medicine (x)
 - n) Gynaecology (x)
- 5) Committee members shall not use the name of the committee in any publication, meeting, negotiation, or promotion without prior approval of the CEO.
- 6) The Hospital PTC and its subcommittees may co-opt persons from specific specialties as they deem necessary, to assist in the finalization of a matter on the agenda; such co-opted persons shall have no voting powers.
- 7) Each member shall be responsible for representing the interest of the institution and shall not:
- a) Act in a manner that is inconsistent with their participation, membership, function, and role on the committee
 - b) Expose themselves to any situation involving the risk of a conflict of interest between their professional and personal interests
 - c) Use their position or any information entrusted to them or obtained because of their involvement in the committee to enrich himself/herself or his/her relatives
 - d) Act in a way that may compromise the credibility, transparency, workings, and integrity of the committee
- 8) Every member must disclose to the CEO of the institution any financial or other interest in the pharmaceutical industry before accepting an appointment to the committee.
- 9) Members must also disclose any interest acquired after their appointment. These interests may include, but are not limited to, any gifts, sponsored foreign trips, funding for clinical trials, research, attendance at conferences, hospitality, and any other benefit of a material nature received by him or her or by a family member.
- 10) Upon making the disclosure, the member may be asked to excuse himself/herself from the meeting to enable the committee to discuss the matter to determine whether or not the member is excluded by virtue of conflict of interests.
- 11) Any disclosure and decision of the committee regarding determination of further participation in the discussion by the member with a conflict of interest must be recorded in the minutes.

Appointment Period

- 1) Members, excluding ex-officio members as mentioned above, shall be appointed to a term of three years and the CEO may, after due consideration, extend the term beyond the three-year cycle.
- 2) A member may be re-appointed for two consecutive terms (of a three-year cycle) and will become eligible for re-appointment after an absence of one cycle.
- 3) Vacancies occasioned will be reviewed in line with the skills base requirements and appointments will be made when necessary.

Resignation, Termination, and Leave of Absence

- 1) Membership will be reviewed if any member is absent without a valid apology for more than two consecutive meetings.
- 2) The Chair, supported by elected members, will investigate any wrong doing or misconduct by members; the Chair may then recommend to the CEO that the membership be suspended or terminated.
- 3) A member may resign by submitting a written notice to the Chair.
- 4) The Chair may resign by submitting a written notice to the CEO.
- 5) Members should inform the Chair of a leave of absence prior to a meeting; in the case of sabbatical leave, the members should inform the Chair three months in advance.

Establishment of Subcommittees and Task Teams

The Hospital PTC, in the execution of its functions, may constitute subcommittees or task teams.

The following subcommittees will be established in accordance with the terms of reference:

- Medicine Rational Utilization Subcommittee
 - Pharmacovigilance Subcommittee (includes ADR monitoring)
- 1) Such subcommittees shall be under the leadership of and chaired by a Hospital PTC member who shall ensure that there is compliance with the terms of reference.
 - 2) No member or group shall have authority to amend or alter the terms of reference, adopt any action contrary to the committee, remove any member, or take any action on behalf of the Hospital PTC.

- 3) Any member of any group may be removed by the Hospital PTC whenever the best interests of the committee or the state will be best served by such removal.
- 4) Each subcommittee shall appoint its own Chair and secretary from among its members.

Chair of the Committee

The Chair shall:

- 1) Play a leadership role in developing and implementing an effective Hospital PTC and sound policies and procedures
- 2) Possess a comprehensive knowledge of the selection, procurement, management, and rational use of medicines
- 3) Have leadership and management skills to direct and foster open and collegial discussion among all committee members while maintaining focus on the issues at hand
- 4) Have respect for committee members from diverse backgrounds, perspectives, and sources of expertise and promote a culture of respect among committee members and key stakeholders
- 5) Be able to function in a team, often under stressful circumstances
- 6) Have the courage and confidence to uphold decisions

Functions of the Chair

- 1) Conduct the Hospital PTC meetings in accordance with the annual schedule
- 2) Facilitate the Hospital PTC's discussion of the agenda points to arrive at a consensus
- 3) Upon arrival at consensus, summarise the decision and call for members to propose and second the adoption of the motion
- 4) If a consensus not being reached, the final decision on how to resolve the matter will reside with the Chair
- 5) Facilitate the development and maintenance of policies and guidance documents with advice and consultation from all relevant stakeholders
- 6) With the assistance of the secretariat, finalise all Hospital PTC documents for submission to the CEO

Secretariat

The hospital pharmacy will supply the resources for the secretariat.

Functions of the Secretariat

- 1) Develop and maintain an annual schedule for the meetings of the PTC
- 2) Convene and make all the necessary logistics arrangements for the meetings
- 3) Advise the Hospital PTC on administrative and regulatory matters
- 4) Compile draft minutes of the meeting in consultation with the Chair
 - a) Draft minutes will be circulated within seven working days after the meeting
 - b) Minutes of the previous meeting will be adopted at the beginning of the next meeting
- 5) Follow-up on the committee's action plan and inform the committee of its progress
- 6) Conduct operational research as required for the committee to perform its functions
- 7) Ensure that the decisions taken by the committee are submitted to the CEO
- 8) Correlate and circulate all pertinent material for meetings to all members and their task teams
- 9) Report on committee activities to the Provincial PTC as per provincial reporting template and indicators

Standing Items on the Hospital PTC Agenda

- 1) Declaration of Conflict of Interest
- 2) Minutes
- 3) Matters arising
- 4) Feedback on Provincial PTC meeting (for tertiary and quaternary hospitals)
- 5) ADRs, medication error reports
- 6) ABC and VEN analyses
- 7) MUR
- 8) Motivation for additions to and deletions from institution formulary
- 9) Budget vs. expenditures
- 10) Drug supply management report
- 11) PTC performance report

Urgent Matters

The committee will appoint four members who, together with the Chair, shall constitute the executive committee. Urgent matters will be attended to by the executive committee and then ratified by the full PTC at the next available meeting.

Attendance at Meetings

- 1) The Hospital PTC shall meet every other month
- 2) The appointed members are expected to volunteer and apply their knowledge of current clinical practices during discussions. Matters discussed during sessions must remain confidential.
- 3) The appointed members are expected to attend personally (no substitutions) and all apologies must be submitted in writing. (Apologies per e-mail will be permitted.)
- 4) Members are expected to be conversant with the agenda and documents provided before the scheduled meeting to ensure active participation.

Voting and Quorum

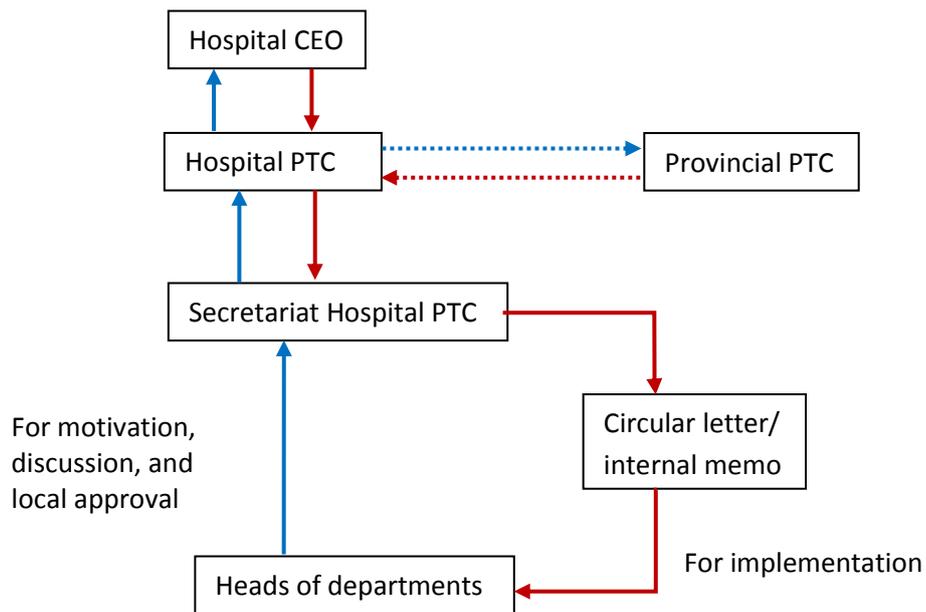
- 1) A quorum shall be deemed to be 65 per cent of members.
- 2) All business of the Hospital PTC shall be transacted by motion or resolution, which may be made by any member in attendance, including the Chair, and shall require a seconder.
- 3) Voting on motions or resolutions shall be by show of hands, unless a member asks that the roll be called and that the vote of each member be recorded.
- 4) Each member of the Hospital PTC shall have one vote on each matter submitted to a vote of the committee. The Chair shall be a voting member of the committee.
- 5) A majority of 80 per cent of those voting shall be considered a quorum which is required for all matters.
- 6) The secretariat has NO vote.
- 7) When a member recuses himself or herself from participating on any matter, that person will not be counted for purposes of determining a quorum.

Decision Implementation

The Chair of the Hospital PTC signs the minutes after acceptance by a proposer and seconder; the secretariat will extract the relevant information and decisions and then circulate for implementation.

It is the responsibility of each Head of Department to ensure implementation of the decisions taken by the PTC.

Communication Strategy



Amendment of Terms of Reference of the Hospital PTC

Terms of reference should be reviewed within a 5 year cycle by the responsible pharmacist and submitted to the Chief Executive Officer for ratification and approval.

The terms of reference of the PTC were duly adopted at the meeting of the PTC on the

_____ (day) of _____ (month), _____ (year)

Signed by

.....

Chair

Date

Approved by

.....

Chief Executive Officer

Date

ANNEX D. DECLARATION OF INTERESTS GUIDANCE DOCUMENT



PHARMACY AND THERAPEUTICS COMMITTEE (PTC) DECLARATION OF INTERESTS GUIDANCE DOCUMENT

A Code of Practice for Pharmacy and Therapeutics Committee Members

Background

A conflict of interest exists when an individual's secondary interests, (e.g., personal, financial) interfere with or influence judgments regarding the individual's primary interests (e.g., patient welfare, education, research integrity). There is evidence demonstrating the association of financial ties with a breakdown in the integrity of decision-making processes. From a public perspective, the type of conflict most likely to affect the public's trust is a financial conflict where the expert tends to gain financially from a particular decision, although other competing interests, such as professional advancement, are also important. Conflict of interest policies are designed to protect the integrity of decision-making processes through disclosure and transparency.

1. Introduction

This code of practice guides the XXX Pharmacy and Therapeutics Committee (PTC) members, members of subcommittees, and any working groups that the committee may, from time to time, establish. This code describes the circumstances in which these individuals should declare an interest in the health care industry.

2. Scope and Definitions

2.1 Scope

This code applies to the Chair, PTC members, and members of subcommittees appointed by the XXX Department of Health. This also includes temporary members and members of any working groups that the committee may, from time to time, establish.

2.2 Definitions

Pharmaceutical industry: Companies, partnerships, or individuals who are involved with the manufacture, sale, or supply of medicines, as defined in the Medicines and Related Substances Act (Act 101 of 1965), that are or may be used by state institutions; this also applies to trade associations representing companies involved with such products

Professional organisations: Colleges, health professional associations and societies, and universities

Members: PTC and all its subcommittees

Administrative unit: Department or organisation with which the member has an employment relationship with managerial responsibilities

Employees: Full- and part-time employees of the XXX Department of Health

Conflict of interest: Occurs when the member, his/her partner (a spouse or other person with whom s/he has a similar close personal relationship), or the administrative unit with which the expert has an employment relationship has a financial or other interest that could unduly influence the expert's position with respect to the subject matter being considered

Apparent conflict of interest: Occurs when the existence of an interest could result in the expert's objectivity being questioned by others

Potential conflict of interest: An interest which any reasonable person may believe should be reported

3. Types of Interest

The following is intended as a guide to the kinds of interest that should be declared. When a member or employee is uncertain as to whether an interest should be declared, he or she should seek guidance from the Chair of the PTC or from the Chair of the relevant committee or subcommittee.

If members have interests not specified in these notes, but which they believe could be regarded as influencing their advice, these interests should be declared. However, neither members nor the PTC are under an obligation to search out links between companies of which they could not reasonably be expected to be aware or links between organisations in which they have a connection or interest and another company or organisation.

Different types of financial or other interests, whether personal or with the administrative unit with which the member has an employment relationship, can be envisaged; the following list, which is not exhaustive, is provided as guidance.

- 1) A financial interest (e.g., shares or bonds) in a commercial entity with an interest in the subject matter of the meeting or work (except share holdings through general mutual funds or similar arrangements where the expert has no control over the selection of shares)
- 2) A proprietary interest in a substance, technology, or process (e.g., ownership of a patent) to be considered in, or otherwise related to the subject matter of, the meeting or work
- 3) An employment, consultancy, directorship, or other position during the past four years, whether or not in any commercial entity, that has an interest in the subject matter of the meeting or work, or an on-going negotiation concerning prospective employment or other association with such commercial entity
- 4) Paid work or research during the past four years commissioned by a commercial entity with interests in the subject matter of the meetings or work
- 5) Any paid work or research involving the product or comparator
- 6) Payment or other support covering a period within the past four years, or an expectation of support for the future, from a commercial entity with an interest in the subject matter of the meetings or work, even if it does not convey any benefit to the expert personally, but benefits his/her position or administrative unit (e.g., a grant or fellowship or other payment for the purpose of financing a post or consultancy)
- 7) Access to classified or proprietary information concerning the product or comparator that the member cannot disclose to the committee
- 8) Service on a body that has previously pronounced on the product or participated in the development of a guideline involving the product

Sponsorship to attend international conferences is usually accepted as insignificant if:

- It falls within the individual's scope of practice
- Accommodation is in keeping with travel requirements and the duration of the conference
- The spouse was not sponsored

The members are reminded that, with respect to the above, an interest in a competing substance, technology, or process, or an interest in or association with work for or in support of a commercial entity with a direct competitive interest must similarly be disclosed.

It is recognised that individuals may have some interaction with the pharmaceutical industry; although this should be declared, it does not preclude membership in the Provincial PTC and its subcommittees.

4. Interests of the Chair

The Chair of the PTC and the Chairs of any of the subcommittees should not have any current personal interests in the pharmaceutical industry.

5. Declaration of Interests

Committee members must declare interests prior to each meeting by submitting the Declaration of Interest form.

Only the name of the company and the nature of the interest are required. The amount of any salary, fees shareholding, grant, etc., need not be disclosed. An interest is current if the member has an on-going financial involvement with the pharmaceutical industry or if the member, department, or organisation for which he or she has managerial responsibility is in the process of carrying out work for the pharmaceutical industry.

The committee secretariat will ensure that the Declaration of Interest has been received upon appointment and then annually thereafter. Any relevant conflict of interest will be discussed with the Chair of the committee and tabled at the PTC annually or as the need arises.

At the onset of meetings, the Chair of the committee will ask all members to sign a Declaration of Interest and ask members to disclose any changes in their status. The request for declaration of conflict of interest will be recorded in the minutes as will relevant changes and the deliberation of the committee to this effect.

6. Handling of Declared Conflicts of Interests at Committee Meetings and Participation by Members

A determination should be made as whether the declared conflict of interest is:

- Insignificant
- Potentially significant
- Clearly significant

Furthermore, discussion should be lead with respect to weighing the importance of the expert's contribution against the nature and extent of the interest. Significant financial interest can be defined as anything of monetary value that would reasonably appear to be affected by the outcome of a proposed decision. Such interests include, but are not limited to:

- Salary or other payments for services (e.g., consulting fees, principal investigator fees, honoraria)
- Equity interests (e.g., stocks, stock options, or other ownership interests; this does not include interest in mutual funds where the individual has no control over the selection of holdings)
- Intellectual property rights (e.g., patents, patents in which the investigator has a financial interest, copyrights, and royalties from such rights)

The Chair, in consultation with the committee, may rule that:

- The member may participate in all facets of the meeting provided the interests are recorded and the member provides an undertaking that the said conflicts or relationships will not bias or otherwise influence their involvement in the decision. Furthermore, members will be required to limit recommendations to those based on the best available evidence and that such recommendations be consistent with generally accepted medical practice. These are usually insignificant conflicts of interest.
- The member's involvement is limited with respect to the affected agenda item to exploratory discussions. Once the committee has arrived at a point where they are in a position to vote on the affected agenda item, the committee member(s) will be asked to recuse themselves from the meeting. Final deliberations will be entertained in the absence of the affected parties and a decision taken. This involves those with a potential conflict of interest that the committee deems to offer significant expert insight that would benefit the decision. The abstinence of the member(s) is to be recorded in the minutes.
- The member is excluded from participation in the proceeding of the specific meeting. These are usually members with significant conflict of interest pertaining to a product.

7. Record of Interests

A record is kept at the provincial office for Pharmaceutical Services of the names of individuals who have declared their interests:

- On appointment, as the interest first arises, or through the annual declaration and the nature of the interest
- At meetings, giving dates, names of relevant products and companies, details of the interest declared, and whether the member took part in the proceedings

8. Publication

Information disclosed on this form and agreements with members may be made available to third parties if compelled in terms of the Rules of Court pursuant to litigation or by virtue of the provisions of the Promotion of Access to Information Act, 2000 (Act 2 of 2000). The latter requires the protection of personal information and contains procedures that require consultation with the person to whom the information relates. Therefore, in the event of compulsory disclosure, this will not take place without prior consultation with the affected party.

ANNEX E. CONFIDENTIALITY GUIDANCE DOCUMENT



PHARMACEUTICAL AND THERAPEUTICS COMMITTEE (PTC) CONFIDENTIALITY GUIDANCE DOCUMENT

A Code of Practice for PTC Members

Background

Confidentiality and transparency are not mutually exclusive. A balance needs to be struck between managing risk while maintaining the appropriate degree of transparency required for sound technical decision-making and protection of constitutional rights. A risk is any event that affects the performance and viability of the review program and/or its external stakeholders. In terms of leaked information, the risk broadly translates into:

- Loss of credibility
- Decisions made externally on draft material
- Reluctance of members to participate in the process and/or loss of momentum of the review
- Negative impacts upon the procurement process of the government
- Negative business consequences for various parties including suppliers

In addition to the product of the review, which is in the public domain, any member of the public may utilize the Promotion of Access of Information Act (PAIA) to obtain information, provided such requests are reasonable and have been made in compliance with the administrative procedure detailed in the PAIA.

1. Introduction

This code of practice guides the XXX Pharmacy and Therapeutics Committee (PTC) members, members of subcommittees, and any working groups that the committee may, from time to time, establish. This code describes the circumstances in which

these individuals should maintain confidentiality regarding the decisions of the committee and its source documents.

2. Scope and Definitions

2.1 Scope

This code applies to the Chair, PTC members, and members of subcommittees appointed by the XXX Department of Health; this also includes temporary members and members of any working groups that the committee may, from time to time, establish.

2.2 Definitions

Pharmaceutical industry: Companies, partnerships or individuals who are involved with the manufacture, sale, or supply of medicines, as defined in the Medicines and Related Substances Act (Act 101 of 1965), that are or may be used by state institutions; this also applies to trade associations representing companies involved with such products

Professional organisations: Colleges, health professional associations and societies, and universities

Members: PTC and all its subcommittees

Administrative unit: Department or organisation with which the member has an employment relationship with managerial responsibilities.

Employees: Full- and part-time employees of the XXX Department of Health

Confidential business information: Commercial or financial information considered confidential because disclosure may:

- Impair the Government's ability to obtain necessary information in the future
- Cause substantial harm to the competitive position of the individual or business entity that provided the information

Proprietary information: Information or data belonging to an owner or proprietor, who may have exclusive rights to the manufacture and sale of a specific item

Trade secret: Any formula, pattern, device, or information that is used in business that provides a competitive advantage

Sensitive information: Information or data in which disclosure, loss, misuse, alteration, or destruction of may adversely affect national security or other Government interests

Promotion of Access Information Act (PAIA): Section 32 (1) (a) of the Constitution of the Republic of South Africa Act, No. 108 of 1996 provides that everyone has a right of access to any information held by the state and any information held by another person that is required for the exercise or protection of any rights. PAIA, No. 2 of 2000 is the national legislation that was enacted to give effect to the constitutional right of access to information.

Internal stakeholders: Those subcommittees or task teams constituted by the XXX PTC with established terms of reference

External stakeholders: All stakeholders that have not been designated as internal or who have been granted access to the documentation in terms of a resolution of the XXX PTC.

3. Types of Information that are Considered Confidential

The following is intended as a guide to the types of information and situations that should remain confidential. When a member or employee is uncertain as to whether information should be disclosed to an external party, he or she should seek guidance from the Chair of the PTC or from the Chair of the relevant committee or subcommittee. Alternatively, the interested party should be referred to the provincial Department of Health's information officer appointed under the terms of the PAIA and the relevant manual published by this officer. Further guidance as to implementation of PAIA, such as grounds for refusal, can be found at <http://www.doj.gov.za/paia/paia.htm>.

Different types of confidential information can be envisaged; the following list, which is not exhaustive, is provided as guidance.

- Identity of a reviewer; the review of motivations for access to non-EML medicine follows a process of consensus seeking grounded in evidence-based principles, and hence the decision of the committee is that of a collective and not an individual. Disclosure of an individual's identity poses certain risks which include:
 - Exposure of the review process to potential undue pressures from external stakeholders and parties with vested interests which may discredit the objectivity and impartiality of the review process and introduce conflict of interests
 - The reviewer's unwillingness to participate in future reviews
- Proprietary information; although the review process does not routinely utilize information that may be considered proprietary, any such information that is supplied to the committee should enjoy the protection of the appropriate level of confidentiality.

Leaked information poses a specific list of risks as it may, for example:

- Prolong the review process through the introduction of subjective information by individuals with a vested interest prior to the finalization of the evidence-based consensus process.
- Provide a competitor a business advantage to a potential supplier in which case it would be considered a trade secret.
- Be implemented as a policy prior to finalization of the consensus-seeking process.

Leaked information is any information that an individual has access to which is not in the public domain. This includes all documents that are actively being reviewed by the XXX PTCs or its task teams or subcommittees, unless approved for external consultation as contemplated in the terms of reference. In its resolution of acceptance of a technical document, the XXX PTC should declare the level of confidentiality and for documents approved for consultations, the scope of the consultation.

4. Interests of the Chair

The Chair of the PTC is the individual responsible for compiling information to be communicated to the information officer for disclosure in terms of any approved PAIA application. The PTC Chair may consult with the secretariat or the Chair of the relevant subcommittee in the compilation of such documentation. The affected committee should be informed of such disclosure and should be furnished with a copy for their reference. The nature, but not necessarily the details of communication with internal and external stakeholders, should be declared as part of the proceedings of the affected committee. In meetings with stakeholders on technical matters, the relevant Chair of the subcommittee will act as the spokesperson supported by any member of the committee who has agreed to such a meeting and members of the secretariat. The secretariat may meet with stakeholders to discuss matters that are of a procedural or administrative nature or to clarify a technical matter that requires expertise available in the secretariat, provided that the member of the secretariat has been present in the relevant deliberations.

5. Maintenance of Confidentiality

Committee members should be provided with a copy of the confidentiality policy and must sign a confidentiality agreement upon appointment and annually thereafter.

The committee secretariat will provide the members with the policy and ensure that the confidentiality agreement has been received upon appointment and then annually thereafter.

All source documentation must comply with relevant copyright provisions and should remain confidential unless approved by the XXX PTC. During the review, strict confidentiality must be maintained on all draft documents until consensus has been reached at the level of the PTC that such a document may be released for

consultation or public consumption. Members of the subcommittee must note that consensus and approval by the subcommittee does not lift the confidentiality restriction until such time as the PTC has pronounced on the matter. A reviewer may, however, consult with experts in accordance with the terms of reference and in consultation with the relevant committee. Where such consultation requires the disclosure of any significant sections of technical documents, the recipient must sign a confidentiality agreement. When the restriction is lifted, the expert should be informed of such.

For the purpose of confidentiality, the restriction refers to information contained in the document whether it is disclosed verbally, electronically, or as hard copy.

The maintenance of confidentiality also requires procedural safeguards. Final minutes tabled at the PTC should not identify individuals, although the working version may have transient reference to individuals (by initials) in order to track contributions that are outstanding. Although the minutes adopted by the committee may have residual reference to these initials, their removal is considered mandatory and administrative.

All materials related to the review process must be stored in a secure manner to prevent unauthorized access. They must be transmitted by electronic carriers. When documentation is no longer required, it must be destroyed by burning or shredding or returned to the secretariat for destruction.

When a member is faced with a request for information by an external stakeholder, and the request has merit or is in the interest of public health, the member should consult the Chair of the relevant subcommittee who will refer the matter to the Chair of the PTC, unless the aforementioned has delegated such powers.

A copy of the confidentiality policy should be available to any member of the public who expresses an interest in accessing information or who is of the opinion that the agreement has been transgressed.

6. Handling of Disclosure of Confidential Information

A determination should be made as to whether the disclosure was:

- 1) Outside of the provision of this policy
- 2) Inadvertent
- 3) Clearly in disregard of this policy

Furthermore, discussion should be lead with respect to the harm or potential harm such a disclosure may have for the review process, individuals who have contributed, or the government.

The Chair, in consultation with the committee, may rule that the member:

- 1) Reviews the policy, discusses it with the Chair, and signs a new confidentiality agreement

- 2) Takes corrective measures to prevent further inadvertent disclosures
- 3) Is excluded from participation of meetings and/or consultation

7. Record of Interests

The secretariat should keep a record of individuals who signed agreements on appointment, as the need first arises, or annually thereafter.

8. Publication

Information disclosed on this policy and agreements with members may be made available to third parties if compelled in terms of the Rules of Court pursuant to litigation or by virtue of the provisions of the Promotion of Access to Information Act, 2000 (Act 2 of 2000). The latter requires the protection of personal information and contains procedures that require consultation with the person to whom the information relates. Therefore, in the event of compulsory disclosure, this will not take place without prior consultation with the affected party.

ANNEX F. DECLARATION OF INTERESTS FORM



_____ PHARMACY AND THERAPEUTICS COMMITTEE

DECLARATION OF INTERESTS

Membership and participation in the _____ Pharmacy and Therapeutics Committee (and its subcommittees) require measures to ensure that the best possible assessment of scientific evidence is achieved in an independent atmosphere free of either direct or indirect pressures. Thus, to assure the technical integrity and impartiality of the committees' work, it is necessary to avoid situations in which financial or other interests might affect the outcome of that work. Each member is therefore requested to review the _____ PTC's guidance document on declaration of interest prior to undertaking this declaration.

SECTION A

Declaration: Have you or your partner (a spouse or other person with whom you have a similar, close personal relationship) any knowledge of an interest (as defined in the PTC guidance document on declaration of interests) in the subject matter of the meeting or work in which you will be involved, which may be considered as constituting a real, potential, or apparent conflict of interest?

Yes No **If yes, please give details in section B.**

Declaration: Does your department or organisation for which you have an employment relationship with **managerial responsibilities** have any knowledge of an interest (as defined in the PTC guidance document on declaration of interests) in the subject matter of the meeting or work in which you will be involved, which may be considered as constituting a real, potential, or apparent conflict of interest?

Yes No **If yes, please give details in section B.**

SECTION B

If you answered “yes” to either question in section A, you must complete the following table.

Details of Relevant Financial Relationship(s) (include all those that apply)	
Name of organisation(s)	Nature of what was received/interest

I hereby declare that the disclosed information is correct and that no other situation of real, potential, or apparent conflict of interest is known to me. I undertake to inform you of any change in these circumstances, including if an issue arises during the course of the meeting or work itself.

_____/_____/_____
Member’s signature Member’s printed name Date

TO BE COMPLETED BY THE CHAIR OF THE COMMITTEE

In consultation with the committee, I have reviewed this declaration of interest and deemed there to be (circle one)

No Insignificant Potentially significant Clearly significant
conflict of interest.

_____/_____/_____
Chair’s signature Chair’s printed name Date

ANNEX G. CONFIDENTIALITY DECLARATION FORM



PHARMACY AND THERAPEUTICS COMMITTEE

DECLARATION OF CONFIDENTIALITY

I hereby declare that:

- a) I have taken cognisance of the provisions of the Protection of Information Act, 1982 (Act 84 of 1982), especially sections 2, 3, and 4 thereof;
- b) I understand that I may not divulge any information of whatever nature, which I have obtained or may obtain by virtue of my official duties, to any unauthorised person, whether verbally or in writing without prior approval of the Head of Department: _____, an official duly authorised by him/her;
- c) I understand that the above-mentioned directives and provisions remain in force, not only during my term of office, but also after the termination of my services with _____ and
- d) I am fully aware of the serious consequences that may result from breaking or violating the above-mentioned directives and provisions.

Member's signature Member's printed name Date / /

Witnesses

1 _____

2 _____

ANNEX H. NOMINATION FORM



XXX PHARMACEUTICAL AND THERAPEUTICS COMMITTEE

NOMINATION FORM

I, _____ I.D. number/PERSAL number _____ hereby
nominate _____ I.D number/PERSAL number _____
for the category _____

Brief motivation:

Signature

Date

ANNEX I. STANDARDISED CV TEMPLATE



GAUTENG PROVINCE

HEALTH
REPUBLIC OF SOUTH AFRICA

Curriculum Vitae

1. Personal details:

Name and surname	
Designation: Mr./Mrs./ Ms./Dr./Prof., etc.	
Work address	
Contact information	Tel no.
	Fax no.
	Mobile no.
	Email address

2. Academic and Professional Qualifications:

Year	Institution	Qualification and field of study

3. Health Professionals Council of South Africa (HPCSA)/South African Pharmacy Council (SAPC)/South African Nursing Council registration number:

4. Current personal medical malpractice insurance details [medical and dental practitioners]:

5. Past and current work experience:

Date	Institution	Position held

6. Pharmacy and Therapeutics Committee experience in the last 5 years:

7. Peer-reviewed publications in the past 3 years and any other major publications:

9. Any additional information:

Signature: _____

Date: _____

ANNEX J. REPORTING TEMPLATE FOR LOCAL PTCS



REPORTING TEMPLATE FOR PTC MEETINGS

Name of PTC:	
Date of meeting:*	
List of attendees:	
Apologies:	
1. Resolutions:	
2. Actions implemented (findings, corrective interventions developed, and results):	
3. Unresolved matters that need input or discussion at GPPTC level:	
4. List of items outside EML procured for previous period:	
5. Red flags in facility pharmacy (e.g., human resource implications, stock availability):	
6. ADR reporting and product quality issues:	
7. Cost drivers (top 10) or ABC analysis:	
8. Report of expired medicines:	
9. Interventions undertaken to support the rational medicines use:	

***Please include a copy of the PTC meeting minutes with this report. Please submit this report to the regional PTC secretariat for submission to the GPPTC.**

ANNEX K. LOCAL PTCS M&E INDICATORS



Indicators to Measure Functionality of Local PTCS

Indicator*	Definition	Data source	Target
Process indicators			
Does the PTC have documented and up to date TORs?	<p>TORs must include the following to be considered valid:</p> <ul style="list-style-type: none"> • Description of members • Appointment process • List of functions • Authority of the committee • Policy and procedures for declaration of interest • Communication strategy <p>TORs must have been submitted to Pharmaceutical Services</p>	TORs document	Yes
Does the PTC have a documented strategic plan?	Strategic plan must include M&E plan	Strategic plan document	Yes
Percentage of PTC members who attend at least 75% of meetings per annum	<ul style="list-style-type: none"> • Numerator – number of members who attend at least 75% of meetings • Denominator – total number of members of PTC 	Minutes of meetings	100%
Decisions are clearly documented	Decision is documented in the minutes of the meeting. Reasons for the decision taken are included in the minutes	Minutes of meetings	Yes
Decisions are communicated to stakeholders	Stakeholders includes health care personnel, management, and persons responsible for in-service training	Minutes of meetings, supplementary lists, communication to stakeholders	Yes

Guidelines for Implementation of PTCs in Gauteng Province

Indicator*	Definition	Data source	Target
Does the PTC have guidelines on the information required in applications to add medicines to the national/provincial formulary?	Guidelines must include evidence of efficacy, safety, cost-effectiveness and relevance to local context	Application guidelines	Yes
Output indicators			
Number of meetings of PTC held per annum	Meeting of PTC at which a quorum of members was present	Minutes of meetings	At least 4 meetings per year
Number of submissions approved/ number of submissions tabled at PTC	At level of district or institutional PTC, 'approved' refers to when agreement is reached to refer submission to next level of PTC	Minutes of meetings	TBD
Does the PTC review cases of mortality thought to be due to preventable ADRs and/or medication errors?	Cases where a patient is suspected of dying because of a preventable ADR – such cases may be referred to the committee by an individual practitioner or by a Morbidity and Mortality Committee of an institution	Minutes of meetings	Yes
Number of copies of ADR reports forwarded to the national data base per annum per 1000 patients	A copy of the report of an ADR submitted to the national data base must be submitted to Pharmaceutical Services	<ul style="list-style-type: none"> • ADR reports (numerator) • Patient numbers – head counts – information management (denominator) 	TBD
No. of MURs done per annum	A MUR is a method evaluating and re-examining the use of drugs to determine the appropriateness of the drug therapy. A study of drug prescriptions to evaluate appropriateness and cost-effectiveness by comparing actual drug use to predetermined standards; formerly known as drug utilization review.	Minutes of meetings, copies of MUR reports	TBD
Outcome indicators			
Medicine expenditure per capita/patient	<ul style="list-style-type: none"> • Numerator – total amount spent on medicine in the province/district/ institution • Denominator – total no. of patients treated in the province/district/institution 		TBD
Expenditure on non-EDL medicines as a total of medicines expenditure	<ul style="list-style-type: none"> • Numerator – expenditure on non-EDL medicines • Denominator – total expenditure on medicine 	Stock management system	TBD
Percentage of prescriptions in accordance with STGs (frequency is ad hoc)	<ul style="list-style-type: none"> • Numerator – no. of prescriptions in accordance with STGs • Denominator – total number of prescriptions assessed 	Prescriptions	100%

*For all indicators, frequency is annually, except as noted.

ANNEX L. ACTION PLAN TEMPLATE



XXX Pharmaceutical and Therapeutics Committee

Action plan for 20__-20__

Objectives of the PTC

As per the terms of reference, the main objectives of the PTC shall be to:

- 1.
- 2.
- 3.

Rationale behind the action plan

Outcomes

Outputs

Output indicators

Outcomes indicators

Year 1 action plan Gantt chart

Activities	Q1	Q2	Q3	Q4
Summary activity 1				
Activity 1.1				
Activity 1.2				
Activity 1.3				
Activity 1.4				
Activity 1.5				
Summary activity 2				
Activity 2.1				
Activity 2.2				
Activity 2.3				
Activity 2.4				
Activity 2.5				
Assess impact of activity 1				

ANNEX M. GAUTENG PROVINCE MOTIVATION FORM FOR INCLUSION OF NEW MEDICINE ON NEML



GAUTENG PROVINCE

HEALTH
REPUBLIC OF SOUTH AFRICA

Motivation Form for Inclusion of a New Medication on the National Essential Medicines List

Section 1: Medication details			
Generic name (or international non-proprietary name):			
Proposed indication:			
Prevalence of condition (based on epidemiological data, if any):			
Prescriber level:			
Primary health care 1	Medical officer 2	Specialist 3	Designated specialist 4

Section 2: Evidence and motivation		
2.1 Estimated benefit		
Effect measure		
Risk difference (95% CI)		
NNT		
2.2 Motivating information (level of evidence based on the SORT system)		
A. New product: High-quality systematic reviews or peer-reviewed, high quality, randomised, controlled trials (level 1)		
Author	Title	Journal ref.
B. Older product with weaker evidence base: Poor-quality controlled trials or high-quality observational studies (level 2)		
Author	Title	Journal ref.
2.3 Cost considerations		
Have you calculated the cost?	YES	NO
Daily cost	Cost minimisation	Cost-effectiveness analysis
Other relevant cost information if available:		
Author	Title	Journal ref.
2.4 Additional motivating comments		
2.5 Strength of recommendation taxonomy		
Section 3: Motivator's details		
PTC title:		Date submitted:

ANNEX N. GUIDELINES FOR MOTIVATION FOR INCLUSION OF NEW MEDICINE ON NEML¹⁷

GUIDELINES FOR THE MOTIVATION OF A NEW MEDICINE ON THE NATIONAL ESSENTIAL MEDICINES LIST

Section 1: Medication details

- » Generic name
A fundamental principle of the Essential Drug Programme is that of generic prescribing. Most clinical trials are conducted using the generic name.
- » Proposed indication
There will usually be many registered indications for the medication. However, this section should be limited to the main indication which is supported by the evidence provided in section 2.
- » Prevalence of the condition in South Africa
This information is not always readily available. However, it is an important consideration in the review of a proposed essential medicine.
- » Prescriber level
Here the proposed prescriber level should be included. If more than one level is proposed each relevant box should be ticked.

Section 2: Evidence and motivation

- » Estimated benefit
 - Effect measure: this is the clinical outcome that was reported in the clinical trial such as BP, FEV₁, CD₄, VL etc.
 - Risk benefit: this should be reported in the clinical trial and, in most cases, includes the 95% confidence level (95% CI). Absolute risk reduction, also termed risk difference, is the difference between the absolute risk of an event in the intervention group and the absolute risk in the control group.
 - Number Need to Treat (NNT): gives the number of patients who need to be treated for a certain period of time to prevent one event. It is the reciprocal of the absolute risk or can be calculated using the formula below.

Calculations

	Bad outcome	Good outcome	Total patients
Intervention group	a	c	a + c
Control group	b	d	b + d

Measure	Equation
Absolute risk:	$[b/(b+d)] - [a/(a+c)]$
Number needed to treat	$\frac{1}{[b/(b+d)] - [a/(a+c)]}$
Relative risk	$[a/(a+c)] \div [b/(b+d)]$
Odds ratio	$\frac{[a/(a+c)] \div [c/(a+c)]}{[b/(b+d)] \div [d/(b+d)]} = (a/c) \div (b/d)$

Reference - Aust Prescr 2008;31:12-16)

¹⁷ National Department of Health Republic of South Africa, 2012. Hospital Level Adults, Standard Treatment Guidelines and Essential Medicines List. Page xxix

- » Motivating information (**Level of evidence based on the SORT system**)
- The National Essential Drug List Committee has endorsed the adoption of the SORT system for categorising levels of evidence. This system¹ contains only three levels:

Level I	Good quality evidence	Systematic review of RCTs with consistent findings High quality individual RCT
Level II	Limited quality patient orientated evidence	Systematic review of lower quality studies or studies with inconsistent findings Low quality clinical trial Cohort studies Case-control studies
Level III	Other	Consensus guidelines, extrapolations from bench research, usual practice, opinion, disease-oriented evidence (intermediate or physiologic outcomes only), or case series

A: Newer product: for most newer products, level 1 evidence such as high quality systematic reviews or peer-reviewed high quality randomised controlled trials should be identified and referenced in the space provided.

B: Older products: many of these products were developed prior to the wide use of randomised controlled trials. However, there maybe level 1 evidence where the product was used as the control arm for a newer product. If no level 1 evidence can be identified, then level II data from poorer quality controlled trials or high quality observational studies should be referenced in the space provided.

- » Cost considerations
- Where a published reference supporting the review of cost is available comments should be made regarding its applicability to the South African public sector environment.
 - Possible unpublished information that can be included:
 - o Cost per daily dose or course of therapy – for long term or chronic therapy such as hypertension the usual daily dose should be calculated (Dose x number of times a day) and converted into the number of dosing units e.g. tablets. This is then used to calculate the cost per day. For medications used in a course of therapy such as antibiotics this is then multiplied by the number of days in the course of therapy.
 - o Cost minimisation is used where there is evidence to support equivalence and aims to identify the least costly treatment by identifying all the relevant costs associated with the treatment.

¹ Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician*. 2004;69:550-6.

- Cost-effectiveness analysis is used to compare treatment alternatives that differ in the degree of success in terms of the therapeutic or clinical outcome. By calculating a summary measurement of efficiency (a cost-effectiveness ratio), alternatives with different costs, efficacy rates, and safety rates can be fairly compared along a level playing field.

Where any of these have been performed tick the relevant block and send as an attachment with all the calculations. If possible, the spread sheet should be supplied electronically.

Section 3: Motivator's Details

The receipt of all submission will be acknowledged. In addition, all decisions with supporting arguments will be communicated where appropriate. This section therefore forms a vital link between the motivator and the decision making process.

ANNEX O. CHECKLIST TOOL FOR GUIDING FORMULARY DECISION MAKING¹⁸

Box 1. Checklist Tool for Guiding Formulary Decision Making

A. Evidence of need

Is there a compelling need to add the drug to our formulary?

- What is the prevalence and importance of the condition the drug is intended to treat? What is the relevance of this drug to our population? Are there special subpopulations for which there may be a compelling need?
- What are the demonstrated shortcomings of existing therapy? Is there evidence that this drug overcomes problems in safety, efficacy, acceptability, or convenience that characterize existing therapy?
- What role does this drug play in addressing this need? What are the US Food and Drug Administration (FDA), European Medicines Agency (EMA), or other international agencies' approved indications? What other claims for the drug are being made?
- What other therapeutic approaches (including non-drug alternatives) might reasonably be pursued instead?
- Is the drug needed for all the venues/settings for which it is being requested (e.g., for both inpatient and outpatient formulary use)?

B. Efficacy

What is the evidence to support the claims for this drug?

- What is the quality and strength of the evidence supporting the efficacy claims? How well designed are these studies?
- Are the claims (both on- and off-label) being made for this drug supported by the data presented?
- How relevant is the population in the published studies to our population and patients in whom it is likely to be used? Were patients like those we treat included in the clinical trials used to gain FDA, EMA, or other governmental regulatory approval, and will the drug's use likely be similar to patients where benefit is proven?
- To what extent are the benefits based on surrogate measures (i.e., hemoglobin A1c, low-density lipoprotein [LDL], serum sodium) rather than clinically relevant outcomes (e.g., mortality, quality of life, strokes)?
- Does the published (or unpublished) literature contain conflicting evidence about efficacy? Is there suggestion of selective publication, or selective sharing of only more favorable studies by those advocating formulary addition.
- What is the "marginal efficacy" – efficacy above and beyond other therapeutic alternatives?
- Do the efficacy studies use proprietary or manufacturer-developed scales that may bias the findings to give favorable results (e.g., specialized, manufacturer-developed quality of life instruments targeted to be responsive to the effects of a particular drug)?

C. Safety

What safety issues need to be considered?

- Is there a potential for look-alike, sound-alike name errors raised by or reported for this drug?
- Are there safety issues surrounding the administration or preparation requirements?
- What is the adequacy of the experience with the drug? What are the number and types of patients studied? How long has the drug been used to assure there is a demonstrated safety track record (since many adverse effects only appear after 5–10 years of use)?
- Are there suggestions of early warning signals (either in the literature, unpublished studies or reports, or theoretical concerns based on class effects) of potential safety concerns (e.g., reports of hepatotoxicity, nephrotoxicity, or drug drug interactions, QT prolongation) that may be a red flag, cautioning against moving too quickly to approve the drug?
- What patient monitoring or other special precautions (e.g., pregnant women, renal insufficiency, government-mandated risk evaluation and mitigation strategies [REMS in US]), are needed or required to use the drug safely? How difficult will it be for practitioners to comply with needed monitoring, and how likely are they to perform adequately?
- How strong is the evidence of this drug's safety compared to other drugs in its class, or other drugs for the same indication currently on the market? What are the anticipated types of adverse events? How do the frequency, severity, preventability, and ameliorability of these adverse events compare across alternative drugs for this indication?

D. Misuse impact potential

If placed on the formulary, what is the potential for misuse or overuse?

- Is the drug subject to intensive marketing to either consumers or prescribers for questionable and/or off-label indications that may lead to excessive or inappropriate use?
- Is there evidence or worry that the drug will be subject to excessive or unrealistic patient demand and expectation? Are there concerns that advertising, including direct-to-consumer in countries where this exists, will play a role in patient demand? Are industry-funded patient advocacy groups aggressively lobbying for the drug, possibly creating pressures for premature or overuse?
- Is there uncertainty or difficulty in accurately diagnosing the condition that is the indication for this drug, leading to potential overuse or inappropriate use of the drug?
- Are there concerns for widespread "off-label" usage?
- Might the expansion of indications to new manufacturer-promoted syndromes play a role in this drug's usage and potential for

¹⁸ Schiff GD, Galanter WL, Duhig J, Koronkowski MJ, Lodolce AE, et al (2012) A Prescription for Improving Drug Formulary Decision Making. PLoS Med 9(5):e1001220. Doi:10.1371/journal.pmed.1001220

overuse?

- Is there experience (in our institution or published literature) with similar drugs and situations suggesting there may be overuse of this agent?
- Is there evidence that any of the active ingredients in the drug is addictive or habit forming?

E. Cost Implications

Can we justify the cost of this drug?

- How much will it cost? Are there other relevant costs such as additional preparation, storage, administration, monitoring, or other downstream costs beyond simple acquisition costs?
- What is the cost and burden of additional monitoring requirements in safely using this drug?
- What are the comparative costs of other alternatives (e.g., are generics available?)
- Will a competitor/comparable drug soon become available generically?
- If there is an added cost associated with using this drug, is there a significant clinical benefit that justifies the added expense?
- What other pricing issues (rebate deals, market share or exclusivity requirements, some of which may not be transparent) may impact purchasing this drug for our institution or patients? Will the price be raised later once we switch over to this drug ("bait and switch" pricing tactics)?
- What are re-imbursalment cost ramifications? What costs will be covered by private or public insurers versus what costs will be borne by the institution or patients (as co- or full pay)?
- What costs are involved in switching patients currently on another drug that we may be substituting this medication for (additional visits, monitoring)?
- Is pill-splitting a possibility for cost savings? Is it easy, safe, desirable?
- How do the acquisition and above additional costs compare to evidence of cost savings (reduction in admissions, other expenditures)?

F. Decision-making information, calculations, timing, and process

What is the strength and quality of evidence and information available to the Committee?

- What is the source (i.e., from pharmaceutical sales representative versus independent review), completeness, timeliness, and quality of the information the Committee has available to make a decision at this time?
- Has an independent drug monograph review been prepared for the Committee (e.g., by a pharmacist or drug information service)? If yes: Are the monograph and other information upon which decisions are being made adequate, or are there unanswered questions (such as those raised in this document) that require additional information?
- Are there reviews by other formulary or guideline committees or international drug bulletins whose judgments and decisions can also help inform our discussion and decision?
- Are there outstanding questions that may be answered by additional information (e.g., pending research trials) that may warrant deferring a decision?

What is the status and quality of the review process and use at our institution?

- Has the drug previously been reviewed by our formulary Committee? If yes what were the issues raised in prior review, discussion, and decision? Was the process a fair and high quality group decision?
- Have there been significant numbers of non-formulary requests for this drug at our institution or plan? If yes, what are utilization and safety experiences and issues surrounding its non-formulary use? What are the pros and cons of keeping non-formulary status for now?
- Have the requisite subcommittees and key and knowledgeable specialists been consulted, how have they weighed in on the decision?
- Has there been undue influence or bias impacting the decision-making process? Have all conflicts of interest (financial, research funding) been disclosed related to the requester, committee members, or involved with evaluating this drug's formulary status (e.g., desire to please a high income-generating clinician)?
- What is desirability of approval now versus delaying approval pending additional information?
- Which clinicians should be permitted to use this drug and in what clinical venue?
- Should there be restrictions (e.g., clinical prior approval or other mechanisms) placed on this medication (based on indication, safety, clinical, or cost outcomes)? If so, what should they be and how easily can they be operationalized and made to work effectively minimizing administrative burdens?
- Are there guidelines and/or electronic clinical decision support alerts that could help ensure safe and appropriate use of this medication; how can they best be operationalized?

ANNEX P. SECTION 21 APPLICATION FORM

MEDICINES CONTROL COUNCIL



SECTION 21 APPLICATION

COUNCIL'S RESPONSIBILITIES AND LIABILITY WHEN PERFORMING ITS FUNCTION IN TERMS OF SECTION 21 OF ACT 101 OF 1965

In terms of this Section the Authority/Council may authorize the sale of unregistered orthodox medicine, complementary medicine, and veterinary medicine or device for certain purposes.

21. (1) The authority may in writing authorize any person to sell during a specified period to any specified person or institution a specified quantity of orthodox medicine, complementary medicine, veterinary medicine or device, which is not registered.
21. (2) Any orthodox medicine, complementary medicine, veterinary medicine or device sold in pursuant to any authorization under sub-section (1) and in such a manner and during such period as the Authority may in writing determine.
21. (3) Authority may at any time by notice in writing withdraw the authorization granted in terms of sub-section (1) if effect is not given to any determination made in terms of sub-section (2)

An applicant who wishes to sell an unregistered medicine must be fully informed and be able to respond if his request is not successful.

Section 21 mandates the Authority to approve the use of unregistered medicine. The Authority, therefore, is required to address the following requirements of Section 21.

- Authorise sales
- Specify the period of sale
- Specify the purchaser or institution
- Specify the quantity of medicine
- Determine the purpose for the use of such medicine
- Determine the manner of use
- Determine the period of use
- Withdrawal of the authority to sell or use

THE AUTHORISATION OF THE USE OF UNREGISTERED MEDICINE UNDER SECTION 21 OF ACT 101 OF 1965

1. Objective: The objective of Section 21 of this policy is to determine how an unregistered medicine can be authorized under Section 21.
2. Responsibility: The Authority shall delegate the administration of the control of the execution to the appropriate qualified person (Clinical Pharmacologist or Medicine Control Officer)
3. Source document Section 21 of Act 101 of 1965

4. Policy

- 4.1 The Authority shall in writing authorize any person to sell during a specified period up to (six months) to any specified person or institution a specified quantity of any medicine, which is not registered.
- 4.2 All applicants must submit the following information:
 - (a) Name, street address and telephone number of the applicant/medical practitioner²
 - (b) Registration number of the prescriber
 - (c) Name and address of the patient
 - (d) Diagnosis of the patient
 - (e) Dose, frequency and route of administration of the product
 - (f) Number and frequency of repeats
 - (g) Concomitant medication
 - (h) Name and (Generic) of the product
 - (i) Motivation why an unregistered product is to be used
 - (j) Reasons for not using similar registered product/current regimen
 - (k) Urgent applications can be handled by telephone in case of an emergency but the above mentioned information must be supplied before an authorization number is supplied. A telephonic request must be followed up in writing within 48 hours.
- 4.3 Requests can only be repeated after a follow-up reports have been submitted to the supplier and the Authority.
- 4.4 In case of long term treatment a follow-up report must be submitted every six months. A new authorization number must be obtained every six months.
- 4.5 The officer designated must confirm the authorization in writing.
- 4.6 The patient must be fully informed that the drug is not registered with the authority.
- 4.7 The patient must be fully informed about the possible benefits and risks of the product.
- 4.8 The patient must sign the informed consent. In case of a minor the parent or guardian must sign the informed consent.
- 4.9 If approved, the product shall only be used for the treatment of the patient in such a manner and for the approved period only. No other patient may receive the authorized unregistered medicine.
- 4.10 All adverse events or unexpected events must be reported to the Authority.
- 4.11 At the termination of treatment a full case report shall be submitted to the Authority
- 4.12 The Authority shall in writing withdraw any such authorization.
- 4.13 All unused unregistered products shall be returned to the supplier for disposal according to the requirements of the Authority.
- 4.14 Information about the basic efficacy, safety and quality about the product must be supplied to the authority.
- 4.15 Where the product is used for the clinical trial, the MBR1 form must include the formula of the final product in terms of a dosage unit:

- a) Specifications of the final product namely *viz* the name of the specification, limits of criteria of acceptance of all physical, chemical and where applicable microbial parameters.
 - b) The laboratory responsible for the final lot release locally. At least an identification and assay must be done if the product is imported.
 - c) Stability data derived from the product stored at room temperature (at least nine months), and elevated conditions (3 months) in tabulated form. The date of manufacture, batch number, batch size and container must be stated.
- 4.16 The Chief Executive Officer, when the Authority is not sitting, refers, as far as possible, all matters and report there on to the next meeting of Council.
- 4.17 An exemption will be given for investigational and comparator medicines which:
- a) are new chemical entities
 - b) are new or different dose forms, delivery systems and formulations of established medicines, which
 - c) does not have consent to be sold in the Republic of South Africa

The Authority may grant the approval after receiving approval from an accredited ethics committee for the study protocol and the justification and validity of the study protocol

C. PARTICULARS OF THE PATIENT

1. Title: First Names: Surname:
2. Age: Gender: Weight: Height:
3. Occupation:
4. Residential Address:
5. Work or postal Address:
6. Telephone number (office hours):
7. Cellular phone number:
8. Diagnosis (Reason for the application to use unregistered medication; full description including severity, staging and prognosis where applicable)
9. Details of current treatment regimen for the above diagnosis (C No. 8.). Include medicinal, surgical and other treatment
10. Concomitant disease/s (full description including severity, staging and prognosis where applicable):
11. Current treatment regimen/s for the above concomitant disease/s (C. 10)
12. Please specify which of, and the doses of the above treatment regimens (sections C 9 & 12 above) that will be continued together with the unregistered medication/device.
13. Informed Consent obtained for the use of the unregistered medicine/device on the patient: Yes or No
Please attach a completed valid informed consent form

12. Motivation for the use of the unregistered medication/device (do not repeat the indication and reasons listed in Sections C No. 8 & D No. 11)

13. Have you or any other person or institution applied to the MCC for the use of the same or other unregistered medicine/device for the same patient in the past? Yes or No. If yes, specify and supply the MCC approval number.

14. I hereby certify that:

- the use of this unregistered medication/device is purely for the management of the patient's disease and not research,
- data collected during treatment of the patient with the unregistered medication/device, may only be used for research after obtaining specific approval from the patient and the MCC, and that the MCC will be supplied with the results (published and unpublished) of such research
- a copy of this application form and consent form will be made available on request to the patient and any registered health care professional who may be involved in the treatment of the above patient.

Signed:(Applicant)

Date:

E. INFORMED CONSENT FORM

I _____ (full names of the patient) voluntarily agree to be treated with a medication, namely _____ which is not registered in South Africa, _____ name of doctor, practice, hospital) for _____ (name of the disease).

I confirm that I have been fully informed and my questions answered by _____ (name of applicant, i.e. prescribing doctor) about my disease (for which a section 21 application is being made), its cause, severity, prognosis, available (in South Africa) registered treatment options and the reasons for the current state of my illness and the unregistered medication and application to use a medication that is not registered in S.A., and that:

- the medication is not registered in South Africa) and that this implies that the quality, effectiveness and safety of this medication have not been verified by the Medicines Control Council (MCC) of South Africa (S.A.)
- the medication will only be supplied to, and used by and on me once specific approval has been obtained from the MCC of S.A.
- the medication _____ (generic and trade names) is approved for the treatment of _____ (my disease) in _____ (name of the country from which the medication is to be imported), or (the medication is in an advanced stage of development [at least phase III trial] in South Africa and or _____ (country of origin) and that its quality, effectiveness and safety are well documented and within legally and scientifically acceptable levels)
- appropriate measures will be taken to prevent, monitor and manage the unwanted effects on me of the unregistered medication
- _____ (name of doctor) will comply with all regulations of the MCC, laws (S.A. and foreign) and conditions of approval of use of this unregistered medication/device and accordingly ensure continued availability and supply of the medication
- use of the unregistered medication on and by me is for managing my disease and not for medical research
- any information collected by _____ (name of applicant), his/her employer, successor or any other person other than the MCC or its legal representative, may be used for research purposes upon receipt of specific written separate informed consent from me, my guardian or person responsible for my affairs after my death
- I will be free to stop using the medication at any time and that I will inform my (treating) doctor accordingly.

Full Names of patient/guardian:

Signature of patient/Guardian:

Date:

Name of doctor (applicant):

Signature of doctor:

Date:

Name of witness:

Signature of witness:

Date:

F. PROGRESS REPORT FORM

Initial

Follow-up

Final

4 *F. 1. Particulars of the Treating Doctor/Pharmacist*

Title: Initials: Surname

Email Address: Telephone no. Fax No:

Postal Address:

F. 2. Patient Particulars:

Title: Initials: Surname:

Age: Gender: Weight: Height:

Phone No: Cell No:

5 F. 3. Particulars of the unregistered Medication

MCC Section 21 Approval No:

Disease for which the unregistered medicine was used:

Generic Name of the medicine: Trade Name:

Dosage that has been given to the patient: (Amount, Route, Frequency and Duration of administration)

Date of commencement of treatment with unregistered medicine:

Date last used: or ongoing treatment

6 F. 4. Outcome of treatment F. 4.1. Therapeutic effect

Excellent assessed Good Satisfactory No effect Not

Brief description/comments:

F 4.2. Adverse drug reaction(ADR) to the unregistered medication

None or Present

If Present: local or systemic Severity: Mild Moderate
 Severe

Description of ADR including results of laboratory and/or other investigations and management

Outcome of ADR: Resolved Ongoing Resulted in disability Resulted in death

MEDICINES CONTROL COUNCIL



SECTION 21 APPLICATION FEES

To all Section 21 applicants:

Please note that as from 19 December 2003, an application fee of R200 **per named patient** is payable before your application is evaluated. This is in accordance with Government Regulation Gazette Vol. 462, No. 25837 regarding fees payable to the Registrar (Medicines and Related substances control Act 101, of 1965) published on 19 December 2003.

Should you require **emergency stock** please state the following in your application:

- 1) Exact quantity of emergency stock required for the next six-month period.
- 2) Dosage per patient.
- 3) Exact number of patients you intend treating with emergency stock (i.e. Quantity in question 1 divided by dosage in question 2).

The total fee payable for emergency stock is **R200** multiplied by the **exact number of patients** you intend treating with emergency stock.

Please note that only cheques made out to the **Medicines Control Council** are acceptable means of payment.

Also note that the banking details of the MCC will be available very soon to enable electronic transfers and deposits to be made. You will be updated on the MCC website: www.mccza.com.

To speed up the approval process, please submit the cheque with your application to:

Medicines Control Council
Ground Floor North
Civitas Building
Andries Street
Pretoria
0002

Faxed applications will be processed only if proof of receipt of cheque by reception of Medicines Control Council is submitted with the application. Please state patients' names and/or numbers of patients and exact quantities of drugs required for that respective cheque payment.

7 SECTION 21 CONTACT DETAILS				
CONTACT DETAILS	Fax: 012 395 8775	Tel: 012 395 8241	E-mail: munbos@ health.gov.za	Civitas Building, Pretoria
QUERY TYPE				
Written query	X		X	
Application submission	X			X
Application form is available on the website www.mccza.com				
Telephonic queries		X Between 10h00 and 12h00 on week days		

Yours faithfully

REGISTRAR OF MEDICINES

ANNEX Q. MCC ADR AND PRODUCT QUALITY REPORTING FORM

MEDICINES CONTROL COUNCIL



ADVERSE DRUG REACTIONS REPORTING FORM

Version 1: Released for implementation	May 2003
Version 2: Released for implementation	November 2004
Version 3: Updated contact details	April 2011

ADVERSE DRUG REACTION AND PRODUCT QUALITY PROBLEM REPORT FORM

(Identities of reporter and patient will remain strictly confidential)

 <p>health Department: Health REPUBLIC OF SOUTH AFRICA</p>	<p>NATIONAL ADVERSE DRUG EVENT MONITORING CENTRE NADEMC</p> <p>The Registrar of Medicines Private Bag X 828 Pretoria , 0001</p> <p style="text-align: right;">Fax: (021) 448-6181 Tel : (021) 447-1618</p> <p style="text-align: center;">In collaboration with the WHO International Drug Monitoring Programme</p>
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PATIENT INFORMATION

Name (or initials): Patient Reference Number:
 Sex: M F Age: DOB:/...../..... Weight (kg) Height (cm)

ADVERSE REACTION / PRODUCT QUALITY PROBLEM (tick appropriate box)

Adverse reaction and/or Product Quality problem Date of onset of reaction:/...../.....
 Time of onset of reaction:hour.....min

Description of reaction or problem (Include relevant tests/lab data, including dates):

1. MEDICINES / VACCINES / DEVICES (include all concomitant medicines)

Trade Name & Batch No. (Asterisk Suspected Product)	Daily Dosage	Route	Date Started	Date Stopped	Reasons for use

ADVERSE REACTION OUTCOME (Check all that apply)

<input type="checkbox"/> death <input type="checkbox"/> disability <input type="checkbox"/> congenital anomaly <input type="checkbox"/> required intervention to prevent permanent impairment/damage	<input type="checkbox"/> life-threatening hospitalisation <input type="checkbox"/> Other.....	<p>Reaction abated after stopping medicine: <input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> N/A</p> <p>Event reappeared on rechallenge: <input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> Rechallenge not done</p>	<p>Recovered: <input type="checkbox"/> Y <input type="checkbox"/> N</p> <p>Sequelae: <input type="checkbox"/> Y <input type="checkbox"/> N</p> <p>Describe Sequelae:..... </p>
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COMMENTS: (e.g. Relevant history, Allergies, Previous exposure, Baseline test results/lab data)

2. PRODUCT QUALITY PROBLEM:

Trade Name	Batch No	Registration No	Dosage form & strength	Expiry Date	Size/Type of container

Product available for evaluation?: Y N

REPORTING HEALTHCARE PROFESSIONAL:

NAME: QUALIFICATIONS:.....
 ADDRESS:
 Signature Date
 Postal Code: TEL: (.....).....

This report does not constitute an admission that medical personnel or the product caused or contributed to the event.

ADVICE ABOUT VOLUNTARY REPORTING

Report adverse experiences with:

- medications (drugs, vaccines and biologicals)
- medical devices (including in-vitro diagnostics)
- complementary / alternative medicines (including traditional, herbal remedies, etc.)

Please report especially:

- adverse drug reactions to newly marketed products
- serious reactions and interactions with all products
- adverse drug reactions which are not clearly reflected in the package insert.

Report product quality problems such as:

- suspected contamination
- questionable stability
- defective components

- poor packaging or labelling
- therapeutic failures

Report even if:

- you're not certain the product caused the event
- you don't have all the details

Important numbers:

Investigational Products and Product Quality Problems:

- fax: (012) 395-9201
- phone: (012) 395-9341

Adverse Events Following Immunisation:

- fax: (012) 395 8905
- phone: (012) 395 8914/5

Confidentiality: Identities of the reporter and patient will remain strictly confidential.

Your support of the Medicine Control Council's adverse drug reaction monitoring programme is much appreciated. Information supplied by you will contribute to the improvement of medicine safety and therapy in South Africa.

PLEASE USE ADDRESS PROVIDED BELOW - JUST FOLD IN THIRDS, TAPE and MAIL

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Posgeld sal deur die geadresseerde betaal word

No Postage stamp necessary if posted in the Republic of South Africa
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DEPARTEMENT VAN
GESONDHEID**

**REGISTRAR OF MEDICINES
REGISTRATEUR VAN MEDISYNE**

**PRIVATE BAG / PRIVAATSAK
X828
PRETORIA
0001**

ANNEX R. DEPARTMENTAL PRODUCT QUALITY COMPLAINT FORM

Enquiries: Mrs. Nomsa Sithole
Bank of Lisbon Building Room 1201
Tel. No.: (011) 355-3584

Enquiries: Mrs. S. Van Dyk
Medical Supplies depot
Tel: (011) 628 9003

DISPOSABLE- SURGICAL SUNDRY-ITEMS ON TENDER

Note: You are requested to complete the following form in bold print using black ink. Any incomplete forms will be returned to the hospitals.

COMPLETE IN DUPLICATE – KEEP ONE COPY FOR RECORD PURPOSES.

1.) Hospital: _____ **Date:** _____

Tel: _____

Fax: _____

Address: _____

2.) Name of person who reported complaint: (Print) _____

2.1) Rank: _____

2.2) Department: _____

2.3) Contact Telephone Number: _____

2.4) Signature: _____

Item Description: _____

Trade Name: _____

Code Number: _____

Contract Number: _____

Enquiries: Mrs. S. Van Dyk
Medical supplies depot
Tel: (011) 628 9003

PHARMACEUTICAL ITEMS ON TENDER

Note: You are requested to complete the following form in bold print using black ink. Any incomplete forms will be returned to the hospitals.

COMPLETE IN DUPLICATE – KEEP ONE COPY FOR RECORD PURPOSES.

1.) Hospital: _____ Date: _____

Tel: _____

Fax: _____

Address: _____

2.) Name of person who reported complaint: _____

2.1) Rank: _____

2.2) Department: _____

2.3) Contact Telephone Number: _____

2.4) Signature: _____

Item: _____

Description: _____

Trade Name: _____

Code Number: _____

Contract Number: _____

Batch: _____

Exp. Date: _____

Firm: _____

Complaint:

Head of Department: (Signature) _____

Head of Department: (Print) _____

Contact Telephone Number: _____

Date: _____

Pharmacist in charge: _____

Senior clinical Executive: (Signature) _____

Senior clinical Executive: (Print) _____

Date: _____

ANNEX S. MUE DATA COLLECTION TOOL TEMPLATE



Medicine Use Evaluation

Background

Objectives of the evaluation

Review period:

Method:

- Retrospective or Prospective

Analysis:

- Percentage of prescriptions compliant with STG

Thresholds:

Submission:

Data Collection Tool

Name of medicine being reviewed										
Name of institution										
Patient number										
Ward										
Data collector's initials										
Date data collected										
Patient chart number										
Patient gender										
Patient age at time of prescription										
Patient weight at time of prescription										

Annex S. MUE Data Collection Tool Template

Name of medicine being reviewed										
Name of institution										
Patient number										
Diagnosis (tick)										
List EML indications for medicine under review										
Other (please provide detail)										
Lab test with results										
Lab test recommended in STGs										
Other (detail and results)										

Name of medicine being reviewed										
Name of institution										
Patient number										
Dosage										
Dose										
Frequency										
Route of administration										
Duration of treatment										
Outcome assessment										
Length of hospitalisation (days)										
Recovered										
Died										
Unchanged										
Lost to follow up										
Outcome unknown										

ANNEX T. GUIDELINES FOR ADR REPORTING



GUIDELINE FOR REPORTING ADVERSE DRUG REACTIONS AND PRODUCT QUALITY PROBLEMS

What is pharmacovigilance?

Pharmacovigilance is defined as the science and activities concerned with the detection, assessment, understanding and prevention of adverse reactions to medicines. The ultimate goal of pharmacovigilance is to improve the safe and rational use of medicines, thereby improving patient care and public health.

What is an adverse drug reaction?

An adverse drug reaction (ADR) is defined as a response to a medicine which is harmful and unintended, including lack of efficacy, and which occurs at any dosage and can also result from overdose, misuse or abuse of a medicine.

The purpose of ADR reporting is to reduce the risks associated with drug prescribing and administration and to improve patient care and safety.

Who should report ADRs?

All health care workers, including doctors, dentists, pharmacists, nurses and other health professionals should report all suspected adverse reactions to medicines (including vaccines, X-ray contrast media, traditional and herbal remedies), especially when the reaction is unusual, potentially serious or clinically significant. Report ADRs even if you are uncertain if the medicine is responsible for causing the reaction.

What types of reactions should be reported?

- All ADRs of newly marketed drugs or new drugs added to the Essential Drugs List
- All serious ADRs that:
 - Are considered to be life-threatening
 - Require patient hospitalisation or prolongation of existing hospitalisation

- Result in persistent or significant disability or incapacity
- Cause congenital anomalies/birth defects
- Are considered clinically important
- Result in death

- ADRs that are not clearly stated in the package insert

- Unusual or interesting ADRs

- All ADRs or poisonings to traditional or herbal remedies

What product quality problems should be reported?

- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging or labelling
- Therapeutic failures
- Expired batches

How do I know if a patient's condition is an ADR?

You should consider the following six factors when an ADR is suspected:

- 1) **What exactly is the nature of the reaction?** (try to describe the reaction as clearly as possible and where possible provide an accurate diagnosis)

- 2) **Did the reaction occur in a reasonable time relationship to starting treatment with the suspected drug?** (some reactions occur immediately after being given a medicine while others take time to develop)

- 3) **Is the reaction known to occur with the particular drug as stated in the package insert or other reference?** (If the reaction is not documented in the package insert, it does not mean that the reaction cannot occur with that particular medicine)

- 4) **Did the patient recover when the medication was stopped?** (some reactions can cause permanent damage, but most reactions are reversible if the medication is stopped in time)

- 5) **Did the patient take the medication again after the reaction occurred (i.e. rechallenge). If so, did the same reaction occur again?** (In most situations it is not possible or ethical to rechallenge the patient with the same medicine. But if such information is available or if such a rechallenge is necessary, it is a very strong indicator that the medicine is responsible for the reaction)

- 6) **Can this reaction be explained by other causes (e.g. underlying disease/s; other drug/s; toxins or foods)?** (It is essential that the patient is thoroughly investigated to decide what the actual cause of any new medical

problem is. A drug-related cause should be considered, especially when other causes do not explain the patient's condition)

In most cases there is some level of uncertainty as to whether the drug is directly responsible for the reaction. Many of the questions above may remain unanswered or may be contradictory but the reaction should still be reported. A well-documented report which includes information about all the above-mentioned questions can provide the first signal of a previously unknown problem.

How can I prevent ADRs from occurring in my patients?

Some ADRs are unavoidable and cannot be prevented. However, most ADRs can be prevented by following the basic principles of rational use of medicines that are described in these guidelines. In addition, careful monitoring of patients during therapy will avoid further worsening of ADRs that are detected.

How do I report an ADR or product quality problem?

All ADRs and product quality problems should be reported on the ADR/product quality form available through the pharmacy at your institution and should be completed in as much detail as possible.

Particular attention should be paid to the following when completing the reporting form:

- Patient details: Patient identifier (name, initials or reference number), gender, age, date of birth, weight and height.
- Date and time of onset of reaction
- Description of the reaction or problem, providing relevant history, allergies, previous exposure and clinical and laboratory data.
- Medication history, including all **concomitant** and **over-the-counter** medicines.
- Outcome of the reaction.
- Product quality reports: Trade name, batch number, registration number, dosage form and strength, expiry date and size/type of container.
- Details of reporter: Name, qualifications, contact details and institution.

Completed forms should be returned to the Head of the Pharmacy of the institution where the patient was treated OR the District Pharmacist in the case of reports from primary health care facilities.

The Head of the Pharmacy or the District Pharmacist will submit the reports to the Regional PTC secretariat, who will then submit the reports to the Safety and Quality

Sub-Committee of Gauteng Provincial PTC using the following email address or fax number:

For attention: Christina Ntlhane
Email: Magalane.Ntlhane@gauteng.gov.za
Fax: 086 724 4618

All completed reports received will be acknowledged and feedback provided to the reporter, where indicated. Reports will also be forwarded to the Medicines Control Council and relevant health programmes, as appropriate, by the Safety and Quality Sub-Committee of the Gauteng Provincial PTC.

What will happen to my report?

The information obtained from your reported reactions promotes the safe use of medicines on a local and national level. A well-completed ADR/product quality form submitted by you could result in any of the following:

- Additional investigations into the use of the medication.
- Educational initiatives to improve the safe use of the medication.
- Appropriate package insert changes by the MCC to include the potential for the reaction reported by you.
- Changes in the scheduling or manufacture of the medicine to make the medicine safer.

Will reporting have negative consequences on the health worker or the patient?

This ADR report does not constitute an admission that you or any other health professional contributed to the event in any way. Feedback on the outcome of the report, together with any important or relevant information relating to the reaction you have reported, will also be sent to you as appropriate. The details of your report will be evaluated and stored confidentially. The names of the reporter and the patient appearing in the report will be removed before any details about a specific ADR are used or communicated to others. The information obtained from your report will not be used for commercial purposes. The information is only meant to improve our understanding of the medicines we use in the country.

Report an ADR today, and save a life tomorrow!