REPUBLIC OF KENYA

MINISTRY OF HEALTH

PHARMACY AND POISONS BOARD

GUIDELINES FOR THE ESTABLISHMENT OF THE QUALIFIED PERSON FOR PHARMACOVIGILANCE

DECEMBER 2018

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Abbreviations

ADE	Adverse drug Event
FDA	Food and Drugs Authority
GVP	Good Pharmacovigilance Practice
MAH	Market Authorisation Holder
MIPV	Medicines Information and Pharmacovigilance
PBRER	Periodic Benefit Risk Evaluation Report
PPB	Pharmacy and Poisons Board
PSMF	Pharmacovigilance System Master File
PSUR	Periodic Safety Update Report
QMS	Quality Management Systems
QPPV	Qualified Persons for Pharmacovigilance
SPC	Summary of Product Characteristics

Definition of Terms

In these guidelines, unless the context otherwise states:

Adverse Events	Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.
Adverse Drug Reaction	A response to a medicinal product which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological conditions.
Board	The Pharmacy and Poisons Board
Health Technologies	Application of organized knowledge and skills in the form of devices, medicines, vaccines, procedures and systems developed to solve a health problem and improve quality of lives.
International Conference Harmonization (ICH)	Technical requirements for registration of pharmaceuticals for human use.
Local Technical Representatives (LTR)	A person or company appointed by the manufacturer or the Marketing Authorization Holders to import, receive as donation, distribute or sell a medicinal product in Kenya.

Manufacturer	A person or a body who sells a product under their own name, or under a trademark, design, trade name or other name or mark owned or controlled by the person or the body, and who is responsible for designing, manufacturing, assembling, processing, labeling, packaging, refurbishing or modifying the product, or for assigning to it a purpose, whether those tasks are performed by that person or on their behalf.
Marketing Authorization Holders	A person or company authorized by the Board to manufacture, import, receive as donation, distribute or sell a medicinal product in Kenya.
Medical Products	Any products used to diagnose, treat or care for Patients.
Periodic Benefit-Risk Evaluation Report (PBRER)	An update of the world-wide marketing experience of a medicinal product at defined times with focus on formal evaluation of benefit in special population at defined times during post-registration period.
Periodic Safety Update Reports (PSURs)	A regular update of the world-wide safety experience of a medicinal product at defined times during post-registration period.
Pharmacovigilance	The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

Qualified Person for Pharmacovigilance (QPPV)	An individual named by a Marketing Authorization Holder (MAH) as the main person responsible for ensuring that the company (the MAH) meets its legal obligations for monitoring of the safety and quality of the product marketed in Kenya.
Risk Management Plan	A systematic approach and set of Pharmacovigilance activities and interventions designed to identify, characterize, prevent or minimize risks relating to medicinal products, and the assessment of effectiveness of those interventions and how these risks will be communicated to the Board and the general population.
Urgent Safety Restriction	an interim change, due to new information having a bearing on the safe use of the medicinal product, to the product information concerning particularly one or more of the following items in the summary of product characteristics: the indications, posology, contraindications, special warnings and special precautions for use and undesirable effects. In rare cases the changes may also relate to quality problems requiring a change of the SmPC labeling or Package Leaflet.

Acknowledgement

The Pharmacy and Poisons Board acknowledges the contribution of the following in the research and compilation of these guidelines from the Ministry of Health, our stakeholders and Partners

We take this early opportunity to thank all the, pharmaceutical manufacturers, distributors, retailers and respondents who offered their valuable contributions to the editing of this guideline.

List of contributors

The Pharmacy and Poisons Board acknowledges the immense contribution of the following for their research, compilation and commitment in developing this guideline.

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Preface

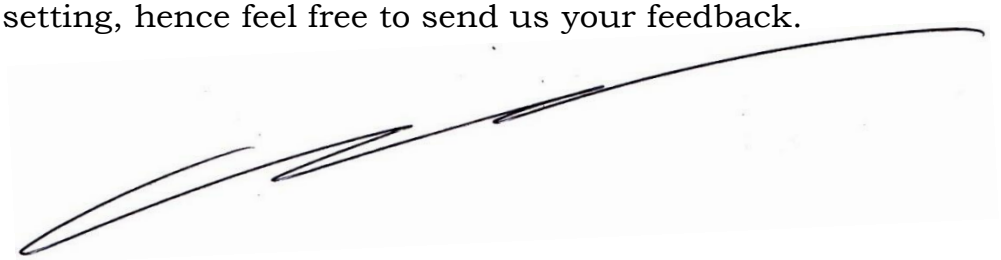
The Pharmacy and Poisons Board (PPB) is the authority mandated, by Cap 244 of the Laws of Kenya, to regulate the Practice of Pharmacy and the manufacture and trade in drugs and poisons.

The Pharmaceutical Industry has seen rapid growth since the enactment of Act. To date, over 23,419 products have been registered for the Kenyan Market. Despite their obvious benefits, they are known to have a possibility of causing adverse events which can be serious or even fatal. The safety and quality of these medical products and health technologies must continuously be monitored by key players in the industry to ensure patients safety.

In order to continuously monitor the quality and safety of the marketed products in Kenya, the Pharmacy and Poisons Board has been actively involved in designing tools and guidelines for detection and reporting of suspected quality and safety issues related.

In order to engage and involve the Pharmaceutical Industry this document has been developed to provide guidance for the establishment of Qualified Persons for Pharmacovigilance (QPPV) by Market Authorization Holders in order to enhance safety monitoring of their products.

This is the first version of QPPV guideline and we undertake to continuously review it and incorporate up-to-date practices, as may be necessary for our setting, hence feel free to send us your feedback.



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Foreword

Medical Products and Health Technologies have significant benefits to our lives and lead to significant reduction in morbidity and mortality. However, even though their beneficial effects cannot be over emphasized, they have a potential for producing adverse or unwanted events no matter how skillfully they are used.

The Pharmacy and Poisons Board (the National Medicines Regulatory Authority in Kenya) has been implementing strategies aimed at ensuring that products used in Kenya are safe, efficacious, of good quality and are supplied and handled by qualified personnel. Safety and efficacy surveillance of medical product and health technologies by Market Authorization Holders has in the past not been emphasized. To address this, the Pharmacy and Poisons Board has developed guidelines for the establishment of qualified persons for Pharmacovigilance (QPPV). The QPPV is necessary to ensure that MAH are actively involved in monitoring of safety and quality of medical products and health technologies.

This document sets out to guide Market Authorization Holders on the operations of the QPPV and all MAHs are encouraged to actively participate in pharmacovigilance to monitor and report all quality and safety related to their medical products and health technologies to help safeguard the health of all Kenyans.

Dr. Fred M. Siyoi,

Chief Executive Officer, Pharmacy and Poisons Board

Legal framework

The regulation for the conduct of pharmacovigilance activities is governed according to Pharmacy and Poisons Act, Cap 244 Laws of Kenya Subsidiary Legislation, Pharmacy and Poisons (Registration of Drugs) Rules charted out in the mission "to protect the health of the public by regulating the profession of pharmacy and ensuring quality, safety and efficacy of medical products and health technologies".

Executive summary

The Pharmacy and Poisons Board as the National Medicines Regulatory Authority in Kenya has the responsibility of ensuring quality, safety and efficacy of medical products and health technologies. This guideline describes the obligations of the Marketing Authorization Holder to set up a pharmacovigilance system master file through establishment of a qualified persons for pharmacovigilance in order to ensure they collect, collate and evaluate information about suspected adverse reactions and quality problems of products it puts into the Kenyan market. These guidelines apply to all entities that have authorization to put medical products and health technologies into the Kenyan market.

MAH will be required to have a QPPV person at his disposal who will meet specific required qualifications as stipulated in the guideline. The QPPV will be the contact person between the Board and MAH and hence will perform all the roles of a QPPV. From time to time as will be stipulated in the Good Pharmacovigilance Practice Guidelines, the Board will carry out pharmacovigilance inspections at the MAH offices and at the outsourced offices in order to ensure compliance with the law and this guideline.

Regulatory sanctions shall be applied to the MAH, local representative, manufacturer and/or the QPPV in the case of non-compliance to the regulations in these guidelines.

The sanctions will depend on whether the non-compliance will be critical, major or minor.

Introduction

The World Health Organization has defined pharmacovigilance as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem. The ultimate goal of pharmacovigilance is to improve the safe and rational use of medicines, thereby improving patient care and public health.

The Pharmacy and Poisons Board as the National Medicines Regulatory Authority in Kenya has the responsibility of ensuring quality, safety and efficacy of medical products and health technologies. Marketing Authorization Holders/Manufacturers as owners of these products in Kenya have the responsibility of ensuring that their products in the Kenyan market meet the highest standard of quality, safety and efficacy. The Marketing Authorization Holders/Manufacturers shall be responsible for the products they import for as long as they are in the Kenyan market.

This guideline describes the obligations of the Marketing Authorization Holder to set up a pharmacovigilance system master file through establishment of a qualified persons for pharmacovigilance in order to ensure they collect, collate and evaluate information about suspected adverse reactions and quality problems of products it puts into the Kenyan market. The ultimate goal is to ensure that medical products and health technologies put on the Kenyan market are safe, efficacious, of good quality, and continue to provide a satisfactory benefit-risk balance.

These guidelines have been adapted mainly from the European Medicines Agency's guidelines for Good Pharmacovigilance Practices (GVP), which currently provide the most comprehensive description of best practices in safety monitoring and reporting for marketing authorization holders. Regionally adaptations include the Ghana FDA guidelines for establishment of QPPV.

The guidelines provide detailed guidance for marketing authorization holders on establishing and maintaining a pharmacovigilance system including its quality management, pharmacovigilance system master file, adverse reaction reporting, risk management, post authorization safety studies, risk communication and pharmacovigilance audit.

This document is to be used in conjunction with other existing relevant medical products and health technologies guidelines and policies in the country. The requirements outlined herein are to be considered general guides, to be adapted

to ensure the marketing authorization holder achieves compliance with regulatory objectives.

These guidelines are hereby promulgated for information, guidance and strict compliance by the Pharmaceutical Industry including local representatives appointed by Marketing Authorization Holders/Manufacturers whose products have been given marketing authorization in Kenya on the requirements and responsibilities of Qualified Person for Pharmacovigilance especially when dealing with post marketed medicines safety and quality related issues.

Scope

These guidelines apply to all entities that have authorization to put medical products and health technologies into the Kenyan market. The marketing authorisation holders include but are not limited to Pharmacy and Poisons Board (PPB) license holders, individuals, public and private institutions, local and international manufacturers, importers/parallel importers and donors of medical products and health technologies.

These guidelines apply to products whose authorisation to market or distribute include requirements for active safety monitoring.

The products include but are not limited to:

a) Products with less than ten (10) years post marketing experience elsewhere or five (5) years Kenya
b) Advanced therapeutic products such as tissue, cell or gene-based products
c) Products that are subject to risk management plan in any other country
d) Orphan medicinal products
e) Products that have received accelerated or conditional marketing approval in any country
f) Products for use solely in special populations such as children, pregnant mothers and the elderly
g) Products that act via the immune system such as cytokines and monoclonal antibodies
h) Any other product based on benefit risk assessment of the Agency

The Pharmacy and Poisons Board also requires a marketing authorization holder to adhere to these guidelines where the PPB identifies safety concerns in the course of post marketing surveillance.

This does not discharge the marketing authorization holder off the responsibility of monitoring the safety and quality of all its medicinal products through the established pharmacovigilance systems required by the Board.

Requirements

General Requirements

The Marketing Authorization Holder (MAH) shall permanently and continuously have at his/her disposal an appropriately qualified person responsible for Pharmacovigilance (QPPV) residing in Kenya.
The MAH should:

a. Ensure provision of training in Pharmacovigilance to the QPPV
b. Ensure that the QPPV has sufficient authority to:
c. Implement pharmacovigilance activities as listed in Section
d. Participate in Risk Management Planning when necessary
e. Participate in the preparation of regulatory action in emerging safety concerns (e.g. variations, urgent safety restrictions, and, as appropriate, communication to Patients and Healthcare Professionals)
f. Act on MAH's behalf including liaising with the Board
g. Ensure that there are appropriate processes, resources, communication mechanisms and access to all relevant information for the fulfillment of the QPPV's responsibilities and tasks.
h. Ensure that the QPPV has sufficient authority to influence the performance of the quality system and the pharmacovigilance activities of the marketing authorization holder (section 4)

Information to be submitted to the Board by the MAH
The MAH shall submit the following information, via an official letter, to the Board relating to the QPPV:

Curriculum vitae including key information on the job description of the QPPV, contact details including but not limited to the name, telephone, fax and e-mail, postal and official working address as well as emergency contact details, Description of the responsibilities guaranteeing that the QPPV has sufficient authority over the pharmacovigilance system in order to promote, maintain and improve compliance including the reporting structure. Any change or update to the above shall be communicated to the Board within thirty calendar days.

Specific Requirements

Qualifications of QPPV

a. The qualified person for pharmacovigilance (QPPV) shall have minimum requirement of a Bachelor's Degree in Pharmacy, with additional certificate/diploma/fellowship or post graduate training in good pharmacovigilance practices (GVP) from institutions recognized by Pharmacy and Poisons Board.
b. The qualified person responsible for Pharmacovigilance shall in addition receive a mandatory refresher GVP trainings facilitated by the MAH in accredited/recognized institutions by the Board.
c. The refresher trainings should be carried out at least once in two years and evidence of the same submitted to PPB.
d. Have knowledge of applicable Kenyan safety monitoring legislation and guidelines and international standards for good pharmacovigilance practices.
e. Within the first five years of acting as QPPV, in addition to the GVP training, the occupant of this role must have completed at the least a master's program in pharmacovigilance and pharmacoepidemiology in institutions recognized by the board and certification provided to the board.
f. Demonstrate GVP knowledge in the implementation of activities stipulated in the MAHs pharmacovigilance system master file
g. The QPPV shall have current/valid practice license from Pharmacy and Poisons Board as the QPPV pharmacist and must be prominently displayed at the MAHs premises.
h. The QPPV should be qualified by pertinent training or experience relevant to their assigned responsibilities.

Roles and Responsibilities of QPPV

The qualified person responsible for pharmacovigilance should be available at all time when needed and be at the marketing authorization holder's disposal permanently and continuously.

The QPPV should reside and operate in Kenya.

Back-up procedures in the case of absence of the QPPV should be in place and should be accessible through the QPPV's contact details.

The QPPV should ensure that the back-up person has all necessary information to fulfil the role.

The QPPV shall be responsible for;

a) The establishment and maintenance of the marketing authorization holder's pharmacovigilance system master file and therefore should have sufficient authority to influence the performance of the quality system and the good pharmacovigilance standards and to promote, maintain and improve compliance with the legal requirements. Hence, the QPPV should have access to the pharmacovigilance system master file (PSMF) at all times.
b) Having oversight over the functioning of the pharmacovigilance system in all relevant aspects including quality management system (e.g. standard operating procedures, contractual arrangements, database operations, compliance data regarding quality, completeness and timeliness of expedited reporting and submission of periodic update reports, audit reports and training of personnel in relation to pharmacovigilance).
c) The QPPV shall act as a single point of contact for the Board on all matters relating to the product safety and quality of their marketed products including pharmacovigilance inspections.
d) Preparing, reviewing and implementing company SOPs for PV activities in the country.
e) The QPPV should be aware of the validation status of the adverse reaction database if applicable, including any failures that occurred during validation and the corrective actions that have been taken to address the failures. The QPPV should also be informed of significant changes that are made to the database (e.g. changes that could have an impact on pharmacovigilance activities).

f) The QPPV may delegate specific tasks, under supervision, to appropriately qualified and trained individuals, for example, acting as safety experts for certain products, provided that the QPPV maintains system oversight and overview of the safety profiles of all products. Such delegation should be documented.

g) Establishing and maintaining a system which ensures that information about all suspected adverse drug reactions/events (or spontaneous post-marketing events) which are reported to the personnel of the marketing authorization holder, including to medical representatives, is collected, collated, processed and evaluated and forwarded to the Board in line with the timelines stipulated by the Board.

h) Preparing and submitting the following to the Board through established channels:
   i. Adverse Events to Medical Products and Health Technologies
   ii. Periodic Safety Update Reports and Periodic Benefit-Risk Evaluation Reports (PSUR/PBRER)
   iii. Company-sponsored pre- and post-registration study reports
   iv. Risk Management Plans (RMPs)
   v. Ongoing pharmacovigilance evaluation during the post-registration period. The report should be submitted to PPB as soon as possible after the evaluation.

i) Ensuring that any request from the Board for additional information deemed necessary for the evaluation of the risk-benefit ratio of a marketed product, is provided to the Board fully and promptly.

j) Overseeing the safety profiles of the company's marketed products and any emerging safety concerns.

k) Ensuring that all personnel involved in pharmacovigilance activities, which may include customer service and sales representatives etc. have their specific duties recorded in a written description and have adequate authority to carry out their responsibilities.

l) Ensuring that all personnel involved in pharmacovigilance activities should be aware of the principles of pharmacovigilance that affect them, and all personnel shall receive relevant training.

m) Ensuring that competent persons are appointed to carry out their duties and functions in their absence.

n) Ensuring that Qualified health care professional possessing adequate experience and education (e.g. QPPV and medical affairs staff), should be available to evaluate information in respect of potential ADEs, assesses the seriousness, expectedness and reportability of ADEs and determine if the ADE report qualifies for expedited reporting.
o) Ensuring that training is provided prior to implementation of new or revised procedures. Records of training should be maintained.
p) Have an oversight of the PMS activities of the MAHs products registered in the country.

Outsourcing of QPPV

The Marketing Authorization Holders/Manufacturers can outsource the services of QPPV. Under such arrangement, the following conditions apply;
All the provisions in this guideline including the QPPV being a resident in Kenya, be accredited and recognized by the Pharmacy and Poisons Board.

If the QPPV is employed by a third party, even if the usual working address is an office of the marketing authorization holder, this should be indicated and the name of the company the QPPV works for provided.

The Marketing Authorization Holder should nevertheless retain the full responsibility for the completeness and accuracy of the pharmacovigilance system master file. The ultimate responsibility for the fulfilment of all pharmacovigilance tasks and responsibilities as well as the quality and integrity of the pharmacovigilance system always remain with the Marketing Authorization Holder.

In addition, the outsourcing company should supply the Board with a copy of the contract with the outsourced company clearly indicating the roles and responsibilities of each party. A description of the subcontracted activities and/or services should be included in the pharmacovigilance system master file (PSMF) and a list of the subcontracts should be included in an annex to the PSMF, specifying the product(s) organization may be subject to inspection at the discretion of the PPB.

The QPPV working at the outsourced companies shall supply the Board with the valid annual practice license.

Timelines for safety reporting

The following reporting timelines shall be applicable when submitting reports to the board

a) **Local fatal adverse events** shall be reported within 7 calendar days
b) **Serious (non-fatal) local events** shall be reported within 15 calendar days
c) **Non-serious local reports** shall be reported within 30 calendar days
d) **All foreign fatal, serious (non-fatal) and non-serious reactions** of medicines registered in Kenya shall be reported as per regular timelines within the Periodic Safety Update Report (PSUR) / Periodic Benefit-Risk Evaluation Report (PBRER) as indicated below:

- Routinely upon request
- every 6 months from authorization until the product is placed in the market
- every 6 months for the first two years on the market
- annually for the next two years
- thereafter every 3 years

Submission of safety reports

The safety reports shall be sent through E2b (the international standard for transmitting medicine adverse event reports specified by the (ICH)) format or any other format as shall be communicated by the Board.

The reports should be uploaded at **www.pv.pharmacyboardkenya.org**

The reports submitted will be treated with utmost confidentiality as required by the existing Kenyan Laws.

Pharmacovigilance Inspections

From time to time as will be stipulated in the Good Pharmacovigilance Practice Guidelines, the Board shall carry out pharmacovigilance inspections at the MAH offices and at the outsourced offices in order to ensure compliance with the law and requirements of this guideline.

Pharmacovigilance audit activities will serve to verify by examination and evaluation of objective evidence, the appropriateness and effectiveness of the implementation and operation of a pharmacovigilance system, including its quality system for pharmacovigilance activities.

Routine inspections will be done every two years. More frequent inspections may be performed on case to case basis or less depending on other considerations like risk-based inspections.

Sanctions

The following regulatory sanctions shall be applied to the MAH, local representative, manufacturer and/or the QPPV in the case of non-compliance to the regulations in these guidelines. They will be informed of non-compliance and advised on how this can be remedied. The sanctions will depend on the classification of the non-compliance as being be critical, major or minor.

Critical (CR): a deficiency in one or more pharmacovigilance processes or practices that represents a serious violation of applicable legislative requirements and /or guidance and/or leads to a seriously deficient pharmacovigilance system with a high level of risk to animal or public health.

Major (MA): a non-critical deficiency in the pharmacovigilance system, practices or processes that represents a violation of applicable legislative requirements and/or guidance and could potentially adversely influence or pose a risk to animal or public health.

Minor (MI): a deficiency in the pharmacovigilance system, practices or processes that represents a deviation from applicable legislative requirements and/or guidance and would not be expected to adversely affect or pose a risk to animal or public health**.**

Classification	Offence-examples	Sanction
Critical	Important safety warning omitted QPPV Non-compliance	1. Product recall 2. Suspension or revocation of MAH licensure 3. Re-inspection 4. Making public list of shames/blacklisting 5. Urgent safety restriction 6. Variation of MAH
Major	Change in prescribing information	1. Administrative fines 2. Non-compliance statement- 3. Infringement notice
Minor	Delays or non-submission of safety reports (PSUR/PBRERS)	1. Warning letters-The board may issue a formal warning reminding the MAH, local representative, manufacturer and/or the QPPV of their pharmacovigilance regulatory obligations 2. Delays in approvals of retention of products

Implementation Timeline

Marketing Authorization Holders/Manufacturers have 6 months (until 1st April 2019 to be fully compliant with this guideline though companies are encouraged to implement the guideline as soon as possible once they have been launched). Review will be done 6 months thereafter.

References

1. Guideline on Good Pharmacovigilance Practices (GVP) European Medicines Agency, EMA/816573/2011 Rev April 2013
2. Health Products and Food Branch Inspectorate Good Pharmacovigilance Practices (GVP) Guidelines GUI-0102
3. Ghana Food and Drugs Authority Guidelines for Selection of Qualified Person for Pharmacovigilance
4. National Agency for Food and Drug Administration and Control (NAFDAC),
5. Good Pharmacovigilance Practice Guideline 2016.