Botswana Medicines Regulatory Authority

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BOMRA
MEDICINES REGULATORY AUTHORITY

Approved By:

Lebogang Koitsiwe
Director,
Pharmacovigilance and Clinical Trials (Acting)

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Revision status sheet

Page	Changes made	Issue No	Process Owner (Title)	Initiated By (Name)	Reviewed By (Name)	Date
Whole Document	The guideline has been re-written to capture all aspects of PMS	1.0	Director, Pharmacovigilance and Clinical Trials	Wapapha Nthomiwa	Nonofo Thapelo	05/03/2026

1 Purpose

The guideline was developed for the purpose of having a standard and consistent way of conducting post-marketing quality surveillance (PMS) activities of medicines to find out information related to why, who, how, when and where to conduct the surveillance. Appropriate measures based on the findings of a risk-based approach are thereafter taken. As the study methods in the field of PMS continue to develop, there will be a need to regularly review the Guidelines to ensure that new methodologies are adapted in the assessment of BoMRA regulated products quality, safety and efficacy.

2 Scope

This guideline applies to conducting PMS activities, which evaluates the quality of marketed medicines through a surveillance program that includes sampling, laboratory testing and gathering sufficient data on the regulatory and usage status of the medicines. Although the type of surveillance study design used must be adopted on a case-by-case basis for products using specifically designed PMS protocols, the guideline defines the essential principles to be applied in a variety of situations. It further provides guidance for PMS activities involving authorized medicinal products in Botswana.

3 Definitions and abbreviations

3.1 Definitions

The following definitions shall apply;

3.1.1 Authority- Botswana Medicines Regulatory Authority (BoMRA)

3.1.2 Efficacy- The maximum ability of a medicine to produce the purported effect as determined by scientific methods, regardless of dosage forms.

3.1.3 Falsified- Medical products that deliberately/fraudulently misrepresent their identity, composition, or source.

3.1.4 Marketing authorization- An official document issued for the purpose of marketing or free distribution of a product after evaluation of safety, efficacy, and quality of the product.

3.1.5 Post-Marketing surveillance - Surveillance activities that occur following market approval of a medicine, including: maintenance of product authorization and/or registration of variations or renewals; regular inspections of manufacturers, wholesalers, distributors, and retailers; quality control testing; pharmacovigilance; promotion control; public reporting of poor-quality products; handling of market complaints; and removal and disposal of non-compliant products. It is typically considered a key regulatory function and refers to the set of comprehensive quality surveillance activities.

3.1.6 Quality assurance- An integrated system of activities involving planning, quality control, quality assessment, reporting, and quality improvement to ensure that a product or service meets defined standards of quality with a stated level of confidence.

3.1.7 Quality control - All measures taken, including the setting of specifications, sampling, testing, and analytical clearance, to ensure that raw materials, intermediates, packaging materials, and finished pharmaceutical products conform with established specifications for identity, strength, purity, and other characteristics.

3.1.8 Quality survey- Serves as a source of information about the quality of medicines available to patients at a point in time. However, quality surveys rely on laboratory testing and cannot offer complete assurance that medicines are safe and effective.

3.1.9 Regulatory decision - The range of actions taken against regulated persons or products by the Authority including denial, corrective notification, warning letter, suspension, revocation, detention, seizure and disposal of products, recall, withdrawal/suspension of marketing authorisation, and recommendation for prosecution.

3.1.10 Safety - The medicine should not present risks that are disproportionate to its benefits.

3.1.11 Sample - A product in given presentation (identified by its name, content of active pharmaceutical ingredient/s [API], dosage form, strength, batch number and manufacturer) collected at the specific sample collection site. It means that the same product characterized by the same name, content of APIs, dosage form, strength, batch and from the same manufacturer collected in two different sites represents two samples. Each sample must consist of the number of dosage units (e.g. tablets, capsules, ampoules, vials, bottles) required by the sampling plan.

3.1.12 Sampling plan - A sampling plan contains detailed identification of sites where samples will be collected, medicines to be sampled, minimum number of dosage units to be collected per sample, number of samples to be collected per medicine, and total number of samples to be collected in the area for which the sampling plan is prepared. It contains also detailed instructions for sample collectors.

3.1.14 Stakeholders - anyone person or entity involved in the supply chain, and use of medicinal products such as Market Authorization Holders, Distributors, marketing agencies, health care professionals and public.

3.1.15 Substandard product - Also called "out of specification," this term refers to authorized medical products that fail to meet either their quality standards or specifications, or both.

3.1.16 Unregistered product- Medical products that have not undergone evaluation and/or approval by a national or regional regulatory authority for the market in which they are marketed/distributed or used, subject to permitted conditions under national or regional regulation and legislation.

3.2 Abbreviations

3.2.1 ADE- Adverse drug effect

3.2.2 API- Active pharmaceutical ingredient

3.2.3 BoMRA- Botswana Medicines Regulatory Authority

3.2.4 GMP- Good Manufacturing Practice

3.2.5 GSMS - Global Surveillance and Monitoring System of WHO

3.2.6 LQAS - Lot quality assurance sampling

3.2.8 PMS – Post marketing surveillance

3.2.9 RB PMS - Risk-based post-marketing surveillance

3.2.10 SOP- Standard operating Procedure

3.2.11 WHO - World Health Organization

3.2.12 MedRS Tool - Medicines Risk based Surveillance Tool

3.2.13 MRSA - Medicines Related Substance Act

4 Method

4.1 Background

4.1.1 Good quality medicines are essential for efficient disease management. Substandard and falsified (SF) medicines can cause treatment failures, adverse reactions, increase morbidity and mortality, and contribute to the development of drug resistance. Vulnerable populations and patients with comorbidities are at particular risk of being harmed from receiving SF medicines. Poor-quality medicines also increase health care costs for both patients and the healthcare systems, wasting resources that could otherwise be used to benefit public health.

4.1.2 Medicines regulation is a complex process which is comprised of various regulatory instruments like authorization/registration for marketing following the assessment of product registration, inspection to ascertain manufacturers' compliance with the principles of good manufacturing practices (GMP) and approval of product information. It can also include post-marketing surveillance (PMS) activities, such as maintenance of products' authorization and/or registration through variations or renewals, regular inspections of manufacturers, wholesalers and retailers, quality control testing, use and disposal of medicines, pharmacovigilance, and implementation of regulatory actions in the event any quality problem has been found. When a product is publicly available, it is not possible to anticipate every conceivable side effect or adverse event that could occur in broad and diverse populations, and it may not be realistic

for manufacturers to foresee every manufacturing issue that could appear during full-scale operation.

4.1.3 Quality of medicines may easily deteriorate through improper handling during distribution or storage before they reach patients. Quality control/quality assurance (QA/QC) of medicines in the distribution system according to proper specifications is, therefore, an important prerequisite in ensuring optimal outcomes. Noting this, introducing quality survelliance of marketed products is thus vital in ensuring quality of medicines in circulation. It provides information on handling, storage and manufacturing conditions that affect quality of products so that corrective actions can be implemented.

4.1.4 For these reasons, Botswana Medicines Regulaltory Authority (BoMRA) considers PMS an important activity. PMS is inherent responsibility for the Authority stated in the BoMRA Medicines and Related Substance Act (MRSA) and its corporate strategy. The Authority's mission is to ensure that all medicinal products made available in the country are safe, effective and of good quality so that the health of the public is protected. On the other hand, the Authority alone cannot not create a robust PMS infrastructure. This is a multidimensional activity with shared responsibilities amongst the Authority, pharmaceutical manufacturers, importers, wholesalers, retailers and end users. It encompasses a series of regulations linked to product safety, efficacy, and quality and labelling, all of which must be considered as a holistic path to compliance.

4.1.5 Due to the complex nature of this activity, manufacturers are highly encouraged to structuring their PMS programs even before they make a regulatory market authorisation submission of their products because of the number of details needed to create a robust program.

4.1.6 Regulation of medicines is important in protecting the health and safety of the public. However, the approval process for new medicines or those already approved, and circulating cannot adequately predict the full extent of harmful or unexpected effects of a drug once it is on the market. As such, a PMS system is necessary for monitoring medicines in circulation. Such a system will be able to detect harmful and unexpected effects of medicines in a timely manner to avoid delays in follow-up and intervention measures. It also helps to improve the protection of health and safety of patients, users and others by reducing the likelihood of the same type of adverse incident being repeated in different places at different times.

4.1.7 Surveillance of medicines, therefore, plays an important role in discovering the actual status of products in terms of their safety, quality and efficacy that might present a risk to the users. As a result, the Authority may take appropriate measures of risk prevention or propose surveillance studies to further investigate the hazard and frequency of such occurrences related to safety, quality and efficacy of the products studied. This is very important to monitor continued safety, quality and efficacy of medicines. PMS is therefore critical in ensuring that medicines in the Botswana market continue to meet regulatory specifications.

4.2 Risk Based Approach to PMS (RB PMS)

The criteria on implementation of the risk-based approach to PMS shall follow the current WHO Prevention-Detection-Response (PDR) strategy on combating SFs as defined by the WHO. Below is a summary format of the PDR strategy to be implemented.

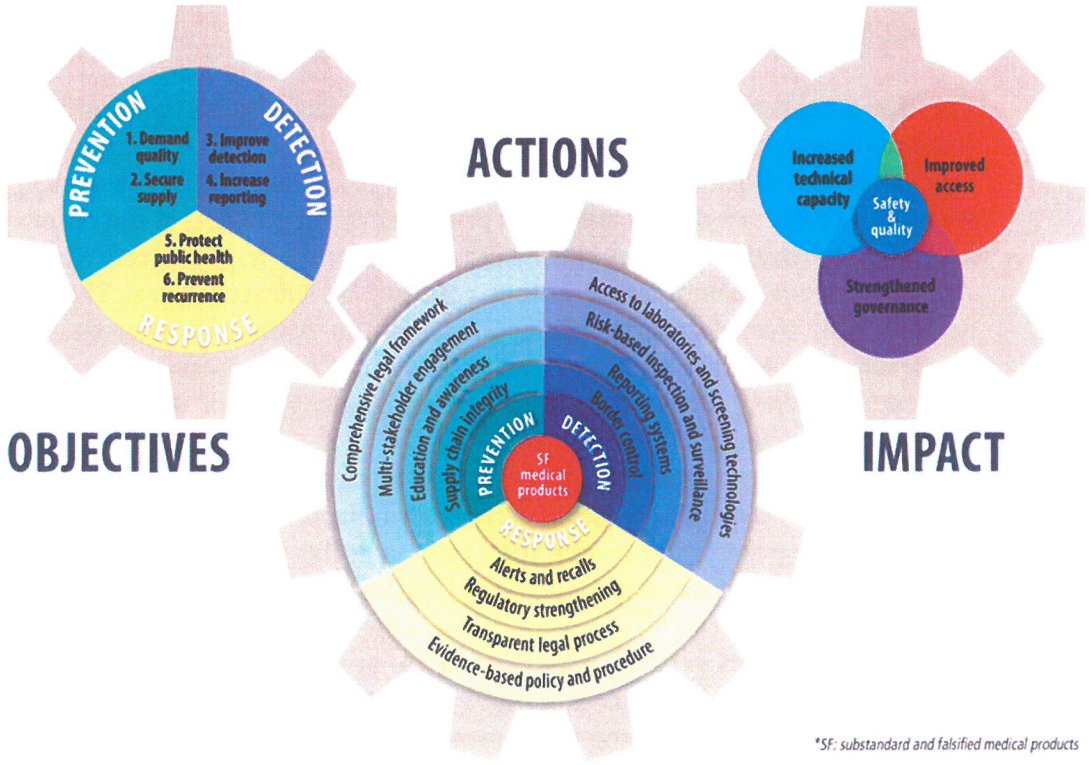

Figure 1: Objectives, Actions, and the Impact of Tackling SF Medical Products Using the PDR Strategy

The interaction between these various initiatives is needed to prevent, detect and respond to SF medical products with coordination across these sectors and disciplines. These initiatives interconnect and are the key elements that sets the PMS program.

a) **PREVENTION:** detection and response will not be necessary if the production of SF medical products or their access to the supply chain is prevented in the first place. Several programs will be developed under this initiative.

b) **DETECTION**: SFs medical products need awareness of the possible risk factors, programs that allow rapid exchange of information and trained staff with equipment to detect, do follow ups and take appropriate actions.
c) **RESPONSE:** The Authority will develop and strengthen the procedures and skills needed to keep a country's supply of medical products safe and effective, through the development of quality check programs under this initiative.

4.3 The PMS Program

The PMS program encompasses the pro-active (structured) and reactive (unstructured) collection of information on quality, safety and performance of medicines, medical devices, cosmetics, and related substances after they have been introduced in the market. Depending on the type of products under surveillance, the type of PMS program to implore will be determined by considering the objectives of the surveillance, which shall always be clearly defined and detailed. Any specific quality concerns to be investigated will be identified by one of the two programs i.e., structured or unstructured PMS, and clearly be addressed by the proposed method of investigational intervention.

It is therefore important to have all PMS stakeholders and consumers greatly involved to considerably improve the effectiveness of such a surveillance.

4.3.1 General objectives

The general objective of this guideline is to provide guidance on the surveillance of selected medicines that are available in the market, in selected areas at various levels of the distribution channels, with the aim of assessing the quality status of medicines and proposing appropriate actions.

4.3.2 Specific objectives

a) Ascertain medicines in the market conform with their authorised specifications.
b) To provide recommendations and various methodological approaches in conducting surveillance of quality of medicines.
c) Assist with identifying and testing of SF medicines.
d) To provide guidance in taking appropriate actions based on the surveillance findings e.g., following investigations of suspected quality defects of medicines.
e) To provide scientific evidence and enhance evidence based regulatory decisions.
f) To ensure market compliance to regulations on PMS

4.4 Activities of PMS

4.4.1 Main activities of PMS

PMS is a pro-active and reactive collection of information on products quality after they have been released into the market. As such, it is a post- registration procedure system to maintain the quality of the medicines whilst in the market.

Its main expected activities are as follows:

a) Collection of samples for selected medicines from the formal and/or informal market as per a defined protocol or in response to quality complaints about a medicine.
b) Testing of sampled medicines.
c) Taking regulatory decisions.
d) Implementation of corrective and preventive actions.
e) Follow up on regulatory decisions taken and recommendations.

4.5 PMS Committee(s)

Noting that SF medicines have a direct and huge effect on the public health, a well-structured PMS program is very important. Collaboration and coordinated activities among different departments and stakeholders such as different BoMRA, the Ministry of Health (MoH), Public Health Programs, manufacturers, importers, and the public all need to effectively coordinate. For this reason, BoMRA shall have an Internal PMS Committee that will work with an established National PMS Committee to coordinate the overall PMS activities. The Committees will involve all key players in this area of surveillance.

4.5.1 Composition of the Internal PMS Committee

a) Assigned relevant BoMRA officers.

4.5.2 Composition of the National PMS Committee

This Committee will consist of representatives of the following directorates and organizations;

a) Botswana Unified Revenue Service (BURS)
b) Ministry of Health
    i. Chief Pharmacist
    ii. Public Health Programs representative
    iii. Botswana Essential Drugs Action Program (BEDAP)
    iv. Central Medical Stores (CMS)
c) Community Pharmacist Association of Botswana (COPAB)
d) National Health Laboratory
e) Medical Aid representative
f) Botswana Pharmaceutical and Distribution Association – BoPHARMA (Distributors and Market Authorization Holders)
g) CMS - Logistics partner
h) Botswana Police Service (Criminal Investigations Department)
i) United Nations Children's Fund - (UNICEF)
j) World Health Organization (WHO)
k) Developmental Partners i.e., as per the National PMS Committee recommendation
l) Secretariat – BoMRA
m) Any other representative as approved by the Authority where necessary.

4.5.3 Roles and Responsibilities of Key Stakeholders

4.5.3.1 PMS Committee(s)

a) Provide guidance in the development and implementation of the PMS program.
b) Select medicinal products to be sampled, geographical regions for collection of samples and sampling strategies i.e., number of samples per site/sector/source.
c) Ensure that relevant regulatory actions and recommendations are implemented in respect of the outcome of PMS program.
d) Arrange training programs on PMS to both internal and external stakeholders.
e) Collect and analyse data and information generated through the PMS surveillance program.
f) Produce reports if required to relevant stakeholders such as BoMRA, donors, MAHs, MoH and public aimed at minimizing the risk to public health with respect to medical products on the market.
g) Monitor and evaluate implementation of the PMS program.
h) Assist in dissemination of the PMS results.

4.5.3.2 BoMRA - Medicine Quality Control Laboratory

a) Receive, store and retain samples.
b) Conduct confirmatory analysis on timely basis.
c) Prepare and submit the summary of analysis reports for possible regulatory actions.

4.5.3.3 Ministry of Health (Public Health programs)

a) Provide program-related medicines information and of SF medicines and products.
b) Support the implementation of the regulatory decision taken on specific public health programs.

4.5.3.4 Developmental Partners who provide technical and financial assistance to the PMS program

a) Provide technical and financial support in the implementation of PMS programs. e.g., supervisory visits and trainings.

4.5.3.5 Market Authorisation Holders (MAH), importers and wholesalers

a) Perform continuous monitoring of quality, safety, and efficacy of its manufactured or imported medicines as prescribed by the Authority or at the MAH/Importers/Wholesalers own will.
b) Report outcomes of the surveillance program(s) conducted by MAH/Importers/Wholesalers to the Authority especially where discrepancies are observed.

4.6 Handling SF medicines

Botswana is affiliated to the World Health Organization (WHO), and BoMRA participates in SF monitoring platforms such as technical working groups that combat SF medicinal products and monitoring of supply chains. Such platforms include active participation the Global Surveillance

Monitoring System (GSMS) and Rapid Alert systems. Such platforms inform the Authority on how to carry out risk based, and intelligence led PMS activities to minimize the SF penetration into the market.

4.6.1 PMS Structured Sampling

This is done as a planned and programmed exercise over a set period of time. The sampled selected medicines are then sent for compendial testing with the Laboratory. Subsequently, these inform Regulatory decisions the Authority needs to take and enforce. The process entails the following steps;

4.6.1.1 Selection of medicines to be surveyed

. The Authority may use the following criteria:

a) Newly introduced medicines on the market,
b) Medicines with limited safety and efficacy data,
c) Medicines with complex formulations,
d) Medicines known to have stability issues,
e) Medicines to which antimicrobial resistance is increasing,
f) Medicines in high demand,
g) Manufacturers or suppliers with previous quality issues,
h) The likelihood that SF medicines exist.

Furthermore, a series of risk factors can also be considered during selection of medicines as well such as;

a) Stability of medicines
b) GMP compliance (of manufacturers if known)
c) Distribution chain complexity
d) Extent of population exposure
e) Patient vulnerability
f) Dosage form complexity
g) Therapeutic risk
h) Extent of harm due to poor quality
i) Availability of the medicine during the surveillance period.
j) Safety and quality history of the product i.e., prior pharmacovigilance or medicine quality information
k) Extent of distribution and use of the medicine in the region
l) Manufacturing and distribution chain complexity
m) Therapeutic properties and risks such as safety margins, side effects, therapeutic failures, etc.

Furthermore, tools such as the Medicine Risk Assessment (MedRS) Tool can be used to select medicines, sample size and the specific sample collection sites, which for example, could be at BoMRA's Adverse Drug Reaction (ADR) Monitoring Centres. The tool has the capability to integrate

and automate the science and practice of a risk-based PMS into a single platform, enabling consistent implementation of risk-based surveillance approaches.

4.6.1.2 Selection of geographical areas for sampling

Areas with a high risk of compromised medicines will always be high risk areas to consider. The other criteria could include areas with poor storage conditions, poor access, high disease burden, population size, porous border zone, level of drug resistance, presence of illicit market, complexity of supply chain in the area and/or specific issues reported by prior inspections.

4.6.1.3 Types of sample collection sites (Sampling levels)

The following are different levels/points of entry to the market that will be considered during sample collection;

Level 1: Warehouse of Importers/ manufacturers, central and district medical stores, NGO central stores, procurement centres or other facilities supplied directly within various programs, central wholesalers and/or distributors.

Level 2: Wholesale, regional stores, districts stores

Level 3: Retailers: pharmacies, drug stores, Rural Drug Vendors, hospitals, speciality centres, health centres, clinics and health posts.

Level 4: Illegal outlets selling medicines outside the approved distribution system such as informal markets or unauthorized markets.

Level 5: virtual outlets that sell medicines via the Internet.

Sampling shall be performed in the public, private sectors and in informal markets such as tuck shops which are both licensed and unlicensed outlets depending on the surveillance objectives. These shall be identified by address and type of facility.

4.6.1.4 Sampling Designs

The Authority shall use various designs for the selection of sample collection sites and types. The choice shall depend on the objectives of the surveillance, the risks and consequences of inherent decision errors and biases and available resources. Such designs could be selected as a single type to follow or combined.

1. **Convenience sampling**

This is a non-probability sampling technique based on the discretion of the Authority. The sites, however, "would" not be selected just because of their convenient accessibility and proximity. The

Authority's Internal defined processes guiding the selection to best reflect the surveillance objectives will be pre-determined. Whenever convenience sampling will be done, the criteria of the sampling sites identified, types and the proportion of the outlets the selection represents will be clearly defined. This could be influenced by factors such as limitation of resources, funds or even availability samples.

2. Simple random sampling

Random sampling is a probability sampling technique that, if the sample size is sufficient, will give reliable estimates of samples to be collected against the probable available quantities on the market (i.e., with confidence intervals) of the prevalence of outlets selling possible poor-quality medicine. A representative sample size will be pre-determined by the risk-based sampling tools.

3. Stratified random sampling

Stratified sampling is a probability sampling technique where the Authority will divide outlets being investigated or sampled from, into different subgroups, then randomly select medicines to be sampled proportionally from these different subgroups. Stratified sampling will be used to adjust for potential differences, such as sales volume, type of customers, or geographical, trade and socioeconomic variables. Variables such as rural versus urban, private versus public outlets and one geographical area versus another will also be considered. As much as possible, sampling that is proportional to the number of outlets will mostly be considered and preferred as it is more efficient than a simple random sampling.

4. Lot quality assurance sampling (LQAS)

This is simpler, less expensive and needs smaller sample sizes. This technique will be used to determine whether the prevalence of outlets selling poor- quality medicines exceed a certain threshold. It's also important to determine whether a "section of a lot of medicines" meet the desired specifications without having to inspect the "entire lot".

5. Sentinel site monitoring

This involves following the quality of medicines in a particular locality over time. There are no common rules as to whether these sites will be chosen on the basis of potentially important variables such as rural versus urban, private versus public outlets, or sampling design, such as convenience or random samples or lot quality assurance sampling (LQAS). For instance, such monitoring could be done at BoMRA's Adverse Drug Reaction Monitoring Centres (AMCs).

4.6.1.5 Conducting Structured Sampling

4.6.1.5.1 Preparation of sampling plans detailing;

i. Number of dosage units/samples to be collected.
ii. Substitution criteria for facilities and medicines chosen.
iii. Training of samplers

iv. Storage and transportation of samples
v. Handing over samples for testing with the Laboratory
vi. Laboratory Testing as prescribed by the relevant monographs and methods. This shall be done in three (3) levels:
   a. Visual inspection
   b. Field-based tests by Minilab or other screening tools such as Rahman spectroscopy
   c. Compendial methods

4.6.1.5.2 Sampling Techniques

The Authority will identify the type of sampling technique to be followed depending on the surveillance objectives, the regulatory status of the target medicines, market intelligence of the medicine and attitude of the sellers. For example, knowledge of an outlet selling poor-quality medicines, understanding of the demand, health, legal and ethical implications associated with this medicine. As such, the Authority may implore explore either overt or covert sampling techniques.

a) *Overt sampling*: An outlet shall be informed about the surveillance objectives by the Authority as this is ***not*** a discreet exercise. Such engagement with the outlet would allow more data to be collected on poor-quality medicines, their risk factors, their origin, ultimately leading to a direct improvement in the medicine supply chain. This method could be used in circumstances such as where samples are collected at locations where patients are seen first by clinicians or in the public sector.

b) *Covert sampling*: For covert sampling, a mystery shopper could mimic a "normal shopper" from the community and will use a relevant standardised scenario to the medicines to be purchased. This technique will commonly be used in scenarios where there is need for samplers to conceal their identity. Mystery shoppers shall always be prepared to explain the real purpose of their visit to protect themselves if their identity is revealed.

4.6.1.6 Results or data analysis and communication

To allow proper interpretation, the data obtained during collection and testing of samples will be summarized and appropriately organized linking each sample with all the data gathered and ensuring consistency and security. Suitable precautions shall be taken to avoid errors. For analysis of large sets of data, statistical software's may be used.

After all the assessments and results are shared by the Laboratory, the PMS Committee(s) shall prepare a standard report based on the findings. Every report will contain a summary of the results and recommendations to guide the Authority in taking any regulatory actions should there be need.

4.6.1.6.1 Communication

The findings from surveillance, including measures taken, will be communicated to the relevant stakeholders and the public. Different mechanisms can be used to disseminate/communicate the PMS findings results. The following shall be taken into consideration:

a) Present results in different forums to raise awareness on quality of medicines under surveillance.
b) Publish in different bulletins, newsletters, magazines and other relevant printed materials.
c) Use different electronic medias, including radio and television.
d) Upload results to the Authority's website and other recognized websites.
e) Write and disseminate press releases with the results and contact information for follow-up.
f) Capture and collate results through online publicly available databases such as the Medicines Quality Database (http://www.usp.org/global- health/medicines-quality-database), WHO's - Global Surveillance Monitoring System (GSMS) and Rapid Alerts platforms.

4.6.1.7 Action

Depending on the data and findings by PMS program, the potential public health importance of the findings, the Authority may take a variety of actions, including, but not limited to;

a) Requesting additional information or clarification from market authorization holders.
b) Recall of products according to the BoMRA's guidelines of product recalling SF medicines.
    - Of note is that Manufacturers and importers shall have the responsibility to conduct this recall process.
c) Suspension or withdrawal of a product's marketing authorization.
d) Warning by BoMRA sent out to a list of institutions and any key persons dealing in/or prescribing the product.
e) Adequate and proportional sanctions, penalties and prosecution upon conviction for violations of the applicable legislation as per the MRSA and its related guidelines
f) Communicate with relevant stakeholders like regional and global health agencies, neighbouring countries and other relevant organizations such as National Regulatory Authorities.
g) Take regulatory actions in collaboration with relevant stakeholders such as Botswana Police Services (BPS), Botswana Unified Revenue Services (BURS), etc.
h) Take relevant legal actions in accordance with the administrative measures, complaint handling guidelines and other national laws.
i) For non-compliant products where the outcome dictates that the product in question be disposed, the latest version of BoMRA's guideline of Safe disposal of unwanted pharmaceuticals - BOMRA/IL/EN/P04/G01 shall be followed.

4.6.2 Conducting PMS Unstructured Sampling:

This is done on ad hoc basis and samples are picked based on the "*quality complaints*" received by BoMRA from the market, from WHO Rapid alert system, reports from other Authorities, market intelligence such as tip offs of possible SFs or any other deemed suiting by the Authority.

4.6.2.1 Quality Complaints

The following classification criterion is recommended for all quality complaints or defects. Defects are classified regarding the relative health hazard associated with the use of or exposure to the product. There are three possible classifications:

Class I	Class II	Class III
Defects that are potentially life threatening or could cause a serious risk to one's health.	Defects that could cause illness or mistreatment, but are not Class I.	Defects that may not pose a significant hazard to health, but withdrawal may have been initiated for other reasons.
a) Wrong product (label and contents are different products) b) Correct product but wrong strength, with serious medical consequences c) Microbial contamination of sterile injectable or ophthalmic product d) Chemical contamination with serious medical consequences e) Mix-up of some products (rogues) with more than one container involved. f) Wrong active ingredient in a multi-component product, with serious medical consequences.	a) Mislabelling, e.g. wrong or missing text or figures b) Missing or incorrect information (leaflets or inserts) c) Microbial contamination of non-injectable, non-ophthalmic sterile product with medical consequences d) Chemical/physical contamination (significant impurities, cross-contamination, particulates) e) Mix up of products in containers (rogues) f) Non-compliance with specification (e.g. assay, stability, fill/weight) g) Insecure closure with serious medical consequences (e.g. cytotoxins, child- resistant containers, potent products).	a) Faulty packaging, e.g. wrong or missing batch number or expiry date b) Faulty closure c) Contamination, e.g. microbial spoilage, dirt or detritus, particulate matter

a. Stakeholders shall be expected to report all quality complaints and/or rapid alerts associated with their products authorized and marketed in Botswana. By nature of their type as prescribed in this guideline, Class I and Class II medicine quality complaints should always be treated as urgent and reported within ***5 working days*** whilst for Class III medicine quality complaints should be reported within ***30 days***, **ALL** from the date of knowing.

b. The public is encouraged to report and inform the Authority on any quality issues using the latest BoMRA **Quality Complaints Reporting Form (BOMRA/PCT/PMS/P05/F01)** or any other convene means, whereby the complaint shall be transferred into this form to allow capturing of full details of the complaint. This could be with health care professionals and institutions where the product was issued. BoMRA may share received reports of these quality complaints with stakeholders for any further investigations deemed necessary, and once these are done, they shall be expected to share findings with the Authority.

c. Quality Complaints may also be identified by the Authority through several good practices inspections such as Good Vigilance Practices, Good Distribution Practices, Good Manufacturing Practices etc.

d. If the quality complaint is associated with an adverse event, the reporter shall ensure that they also report the adverse event to the Authority as guided by the latest issues of the following guidelines;
   - **Pharmacovigilance Guidance Document for Market Authorisation Holders (BOMRA/PCT/PV/P01/G02)**,
   - **National Pharmacovigilance Guidelines for ADR Reporting by Healthcare Professionals (HCPs) (BOMRA/PCT/PV/P01/G01)**,
   - **National Guidelines for Adverse Events Following Immunisations, (BOMRA/PCT/PV/P07/G01)**,
   - **National Guidelines for Medical Devices Adverse Event Reporting (BOMRA/PCT/PV/P10/G01)**,
   - **Reporting Veterinary Adverse Events for Animal Health Practitioners (BOMRA/PCT/PV/P05/G01**).

e. All reported quality complaints should be investigated and closed within **15 calendar days**. Conclusive decisions, either voluntary or statutory could entail actions such as recall of the product from the market. This shall be done following BoMRA guideline on **Product Recall and Withdrawal – (BOMRA/PCT/PMS/P01/G01)** and/or the destructions as per the **Guideline on the Safe Disposal of Unwanted Pharmaceuticals (BOMRA/IL/EN/P04/G01).**

f. Findings from quality complaints reports and investigations could be shared with the public and healthcare practitioners also for the purposes of knowledge dissemination, risk mitigation and enforcement of regulatory decisions.

4.6.2.2 Spot Checks

These are risk-based and unannounced spot checks that may entail picking and testing of samples for compliance from the market across the supply chain. This shall be done through the Authority's prescribed processes.

4.6.3 Traceability

This shall entail collaboration with key stakeholders to monitor and follow medicines of interest across the supply chain in detecting possible SFs. The program uses technologies like bar code scanning/data matrices and global standards for traceability. This shall be done through a Track and Trace (TT) program and the ***latest*** TT guideline; MRSA and Regulations shall be applicable in guiding the market.

4.6.4 Adjudication of Promotional Material and Adverts

These are assessed and adjudicated through the assigned Authority structures e.g., Pharmacovigilance and Advisory Committee (PVAC), to assure compliance with regulations i.e., for example, prevent misleading claims and false advertising. Outcomes of the adjudication are therefore shared with the applicants and the enforcement is done to assure market compliance once the promotional material/adverts are floated in the market. Further details shall be provided on the latest issue of the **Guideline Advertisement and Promotion of Medical Products (BOMRA/PCT/PMS/P02/G01)**.