PHARMACY BOARD OF SIERRA LEONE

Guidelines for Pharmacovigilance Inspections

Guideline No.	**: PBSL/PVGCT/GDL/QPPV/04-2017**
Effective Date.	**:27th March, 2017**
Version No.	**: 01**

TABLE OF CONTENT

1.0 INTRODUCTION

In order to assure that manufacturer's representative and Marketing Authorization Holders comply with Pharmacovigilance obligations within Sierra Leone and to facilitate compliance, the Pharmacy Board of Sierra Leone (PBSL) shall conduct Pharmacovigilance inspections of companies. Inspections shall be carried out by inspectors mandated by PBSL to inspect the premises, records, documents and pharmacovigilance system master file (PSMF) of the marketing authorisation holder or any firm employed by the marketing authorisation holder to perform their pharmacovigilance activities. The result will be used to help the manufacturer representatives and Marketing Authorization Holders to improve compliance in relation to PV.

2.0 GLOSSARY

In this guideline, unless the context otherwise states

Board

Means the Pharmacy Board of Sierra Leone (PBSL)

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.

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 as stipulated by the Pharmacy and Drugs Act.

3.0 PHARMACOVIGILANCE INSPECTIONS

To ensure that manufacturer's representatives and Marketing Authorization Holders (MAH) comply with PBSL Pharmacovigilance requirements and to ensure compliance with these obligations, the Board shall conduct Pharmacovigilance inspections.

Pharmacovigilance inspection programmes will be implemented, which will include routine inspections scheduled according to a risk-based approach and will also incorporate "for cause" inspections, which have been triggered to examine suspected non-compliance or potential risk, usually with impact on a specific product(s).

The outcome of an inspection will be provided to the manufacturer's representative or marketing authorisation holder who will be given the opportunity to comment on any non-compliance identified. Any non-compliance should also be addressed by the manufacturer's representative or marketing authorisation holder in a timely manner through the implementation of a corrective and preventive action plan and submission of a compliance report.

Information on the conduct and outcome of Pharmacovigilance inspections and follow-up and evaluation of the consequence may be made publicly available as part of the overall transparency of Pharmacovigilance activities.

The inspection will be conducted where Pharmacovigilance activities of the Local representative of Marketing Authorization Holders is located.

3.1. Objectives of Pharmacovigilance inspections

- To assess that the manufacturer's representative or marketing authorisation holder has personnel, facilities and mechanism in place to comply with PBSL PV requirements.
- To detect and document non-compliance which may be risky to public health
- To use the inspection results to ensure that PV obligations are enforced

3.2. Types of Pharmacovigilance inspections

Pharmacovigilance inspections will be done, which will include system and product –related, routine and "for cause", pre-authorisation, post-authorisation, announced and unannounced and re-inspections.

3.2.1 System and product-related inspections

Pharmacovigilance system inspections are done to review personnel, procedures and facilities that are in place and to assess their compliance with PV regulatory obligations. Product specific examples maybe be utilized in the assessment to illustrate the proper functioning of the PV systems.

Product –related PV inspections focuses on Pharmacovigilance issue that are product-related taking into consideration documentation, product –related activities. However, some aspects of the system that's related to the product may be assessed.

3.2.2 Routine and 'for cause" Pharmacovigilance inspections

Routine Pharmacovigilance inspections are scheduled before hand as part of the Board's inspection plan and it involves no specific trigger though it is risk analysis based. The kind of inspection is mostly system-based although one or more products can be selected to demonstrate practically the proper functioning and compliance of the system.

For cause Pharmacovigilance inspection, there is a specific trigger and an inspection is necessary to examine the issue. This inspection will primarily focus on specific PV processes or assessment that identifies compliance issues and their impact on specific product. Full system inspection may also be conducted due to the trigger. For cause inspections may arise when, for example, one or more of the triggers listed below are identified:

- Risk-benefit balance of the product:
    - Suspension or product withdrawal without notifying PBSL
    - Delays or failure to identify or communicate a risk or a change in the risk-benefit ratio
    - Communication of information on PV concerns to the public without prior notification to PBSL.
- Reporting obligation (expedited or periodic)
    - Delays or omissions in reporting
    - Poor quality or incomplete report
    - Inconsistencies between reports and other source
- Requests from PBSL
    - Failure to provide the requested information or data within the deadline specified by PBSL
    - Poor quality or inadequate provision of data to fulfil request for information from PBSL
- Fulfilment of commitments:
    - Concerns about the status or fulfilment of risk management plan (RMP) commitments
    - Delays or failure to carry out specific obligation relating to the monitoring of product safety, identified at the time of the marketing authorisation.

3.2.3 Pre-authorisation PV inspections

These are inspections conducted prior to the granting of marketing authorisation (MA). This kind of inspection is done to assess existing or proposed PV system in support of the MA application. They are not mandatory but maybe requested in specific situations. Due to product –specific safety concerns, it may be prudent to examine the applicant's ability.

- To implement product specific risk-minimisation activities, or
- To manage the routine safety monitoring for the product concern (e.g.-anticipated significant increase in adverse reaction reports where compared to previous products).

3.2.4 Post-authorisation inspection

These are inspections conducted after a marketing authorisation has been granted and are intended to determine whether the manufacturer's representative or MAH has complied with its

regulatory obligations as stipulated by PBSL. This kind of inspection can be either 3.2.1 or 3.2.2 as mentioned above.

3.2.5. Announced and unannounced inspections

Usually inspections are done with prior notification to the MAH to ensure the availability of relevant documentation and personnel for the inspection. However, in some instance it may be prudent to do unannounced inspections or to announce an inspection at very short notice (e.g. when the announcement could potentially compromise the goal of the inspections or when the inspections is conducted in a short time frame due to urgent safety reasons.

3.2.6. Re-inspection

These inspections are conducted on a routine basis as part of a routine inspections programme. Risk factors will be assessed in order to prioritise re-inspections. Early re-inspection may take place where significant non-compliance has been identified and where it is necessary to verify actions taken to address findings and to evaluate on going compliance with PV obligations. Early re-inspections may also be warranted when the MAH filed to implement appropriate corrective and preventive actions in response to an earlier inspection.

3.3. The inspection Programme

The Board will perform Pharmacovigilance inspections for manufacturer's representatives and MAHs based on using a risk-based approach. This will help to focus resources to improve the protection of public health where there is a potential risk.

Factors which may affect inspection scheduling may include but not limited to the following:

3.2.1.1 number of products issued marketing authorization by the Board;

3.2.1.2 product portfolio;

3.2.1.3 failure to provide details of the Qualified Person for Pharmacovigilance to the Board;

3.2.1.4 number of product with known safety risks:

3.2.1.5 non-compliance with the Board's reporting requirements

3.4. Inspection process

Pharmacovigilance inspections should be well planned, coordinated, conducted and reported on, follow-up and documented in accordance with prescribed inspection procedure.

Planning: Pharmacovigilance inspections planning should be based on a systematic and risk-based approach to make the best use of surveillance and enforcement resources whilst maintaining a high level of public health protection. In order to ensure that the inspection resources are used in an efficient way, the scheduling and conduct of inspections will be driven by the preparation of an inspection programme.

A preliminary notification to the manufacturer's representative or the MAH about the scheduled inspections and pertinent documents to facilitate the inspection may be requested by the Board at least 21 days to the scheduled date of inspection. The date for the inspection will be agreed with the MAH.

The Board may request for the following documents prior to the inspection. This may include but

not limited to;

3.2.2.1. Curriculum vitae, job descriptions and training records for QPPV and any other employee the Board considers relevant.

3.2.2.2. Contract between the manufacturer's representative or the MAH and the QPPV

3.2.2.3. Organization charts/organograms (with names and job titles);

3.2.2.4. Procedural documents (e.g Standard Operating Procedures, working instructions, Job descriptions, terms of reference etc.);

3.2.2.5. Standard training material and presentations;

3.2.2.6. Minutes of meetings specific to Pharmacovigilance

3.2.2.7. Individual adverse reaction cases files and adverse event reports;

3.2.2.8. Recent PSURs/PBRERs for marketed products;

3.2.2.9. Contacts and agreements with third parties and list of distributors;

3.2.2.10. Sierra Leone specific RMPs for selected products when applicable;

3.2.2.11. Line listings of adverse reaction reports;

3.5. Conduct of inspection:

The inspection may be conducted at the MAHs location, and if a third party is involved in any Pharmacovigilance activity, their site may also be inspected by the Board. The inspection will normally commence with an opening meeting and end with a closing meeting. The MAH has the right to choose which members of staff participate in these meetings but shall include the QPPV. Reporting and follow-up Deficiencies found during the Board's Pharmacovigilance inspection are graded as follow.

Critical: A deficiency in Pharmacovigilance systems, practices or processes that could either adversely affect the rights, safety or well-being of patients or that poses a potential risk to public health or that represents a serious violation or regulatory offence of the pharmacy and Drugs Act and the applicable PBSL guidelines.

Major: A deficiency in Pharmacovigilance systems, practices or processes that could either potentially adversely affect the rights, safety or well-being of patients or that could potentially pose a risk to public health or that represents a violation of the Pharmacy and Drugs Act and the applicable PBSL guideline

Minor: A deficiency in Pharmacovigilance systems, practices or processes that would not be expected to adversely affect the rights, safety or well-being of patients. Lots of minor non-compliance may add up to a major non-compliance.

In general, preliminary findings will be communicated at the closing meeting. An inspection report is then prepared and reviewed internally to ensure consistency of classification of deficiencies prior to issue of the final report. The report is sent to the MAH, usually within 30 working days of the site visit or

the date of the provision of the last document requested. It should be noticed that the factual matter contained in the inspection report relates only to those things that the inspection team sees and hears during the inspection process.

3.6 Responding to Findings

Following the issue of the inspection report, the manufacturer's representative or MAH is requested to respond to any deficiencies identified and to provide the Board with an appropriate corrective action and preventative action plan (CAPA) within 14 working days or a deadline to be determined by the Board based on the magnitude of non-compliance identified and a compliance report within 28 working days on receipt of PV inspection report.

The manufacturer's representative or MAH may be required to provide report and where necessary evidence of the progress and completion of the action plan. There may be re-inspections at an appropriate time to verify the progress and success of these remedial actions.

Note that, in some circumstances, the manufacturer's representative of MAH may be required ot take immediate action to address a critical or major finding, for the protection of public health and safety.

4.0. RECORD MANAGEMENT AND ARCHIVING

All Pharmacovigilance data should be maintained in a secure area (dedicated for that purpose) and the data should be stored to ensure:

- Limited access to data
- Protection of Information
- Easy retrieval

Documents must be stored in secured cabinets that will protect them from hazards (rodents flood, fire). Pharmacovigilance data should be stored throughout the life cycle of the product.

5.0. REGULATORY ACTIONS AND SANCTIONS

The following regulatory sanctions shall be applied in the case of non-compliance;

5.1. Non-compliant manufacturer representative or Marketing Authorization Holder may be inspected to determine the extent of non-compliance and then re-inspected to ensure compliance is achieved.
5.2. The Board may issue a formal warning remaining manufacturer's representative or Marketing Authorization Holder of their Pharmacovigilance regulatory obligations.
5.3. The non-complaint manufacturer's Representative or Marketing Authorization Holder may be placed on high risk leading to additional monitoring and retraining.
5.4. Product recalls e.g. where important safety warnings have been omitted form product information;
5.5. Deferral of application for registration of product(s) or delays in approval of new products until corrective and preventive or actions have been implemented or the addition of safely conditions to new approvals.
5.6. The Board may consider making public a list of Manufacturers representative or Marketing Authorization Holder found to be seriously or persistently non-compliant
5.7. Urgent safety Restriction

5.8. Variation of the marketing Authorization
5.9. Suspension of the Marketing Authorization
5.10. Revocation of the Marketing Authorization
5.11. Amendment or suspension of clinical trials due to product-specific safety issue
5.12. Administrative penalties, usually in the forms of fines as stipulated in the fines schedule

6.0. PENALTIES

Non-adherence to the requirements of these guidelines by manufacturer Representatives and Marking Authorization Holders and will result in the Board imposing sanctions.

7.0. REFERENCES

1. European Medicine Agency 2012. Guidelines on Good Pharmacovigilance Practices (GVP)-Module III-Pharmacovigilance Inspection (Rev1).

2. Food and Drug Authority Ghana 2013. Guidelines for conducting Pharmacovigilance inspections.