	Title: GUIDELINE FOR DETECTING AND REPORTING ADVERSE DRUG REACTIONS	
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Pharmacy Board of Sierra Leone,

PMB 322

Central medical stores compound

New England Ville

Freetown

CONTENT

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SECTION 1

1.1. Introduction

Modern medicines have brought significant benefits to our lives offering reduction in morbidity and mortality due to disease. It is also apparent that the improving health status of an increasing number of the Sierra Leonean population can be attributed to medicines. However, even though medicines are generally seen as beneficial, all medications including the excipients (e.g. preservatives, coloring agents, lubricants etc.) in medicines are capable of producing adverse or unwanted effects.

In order to effectively safeguard the health of Sierra Leoneans, The Pharmacy Board of Sierra Leone (PBSL) is at the forefront of activities designed to ensure that all medicines used in Sierra Leone are safe, efficacious and of good quality. Furthermore, the Board has been crusading against substandard and falsified pharmaceuticals and is leading the fight against counterfeiting of all regulated products.

The risk of Adverse Drug Reactions (ADRs) is one probable consequence of the use of medicines. Almost all drugs, no matter how skillfully used, may cause adverse reactions. Although the occurrence of some adverse drug reactions is not predictable, the chance of occurrence of several adverse drugs reactions can often be reduced by sufficient knowledge of the conditions under which they are most likely to occur. Such knowledge is collated and disseminated through an efficient and effective pharmacovigilance system. Nevertheless, the possibility of preventing ADRs underscores the need for a pharmacovigilance system to monitor ADRs and other drug-induce problems.

This guideline is intended for information, guidance for patients, Healthcare Professionals, Marketing Authorization Holders, Manufacturers and the National Medicines Regulatory Authority to help in the continuous monitoring of the safety, efficacy, and benefit to risk balance of medicinal products granted marketing authorization in Sierra Leone and should be strictly adhered to.

It provides definitions of the main terms used in pharmacovigilance, gives a broad educational overview of pharmacovigilance in general and the organization of the Drug Safety Monitoring Programme, situated in the National Pharmacovigilance Centre (NPC) of the Pharmacy Board of Sierra Leone. It describes who can report suspected cases of ADRs to the NPC, how to report and

what to report. It also explains what happens after reports are sent and the benefits of a strong pharmacovigilance system to the reporting practitioner, the patient and the nation.

The PBSL through the Drug Safety Monitoring Programme, aims to ensure optimal safety of medicines and other regulated products by detecting, assessing and preventing drug related adverse events/reactions. Pharmacovigilance will also be another tool for aiding the fight against counterfeiting.

It is hoped that all health care professionals will take an active interest in pharmacovigilance and report any suspicion of adverse drug reactions to the NPC. This way, we will make Sierra Leone and the world a safer place as far as the use of medicines and other regulated products are concerned. Remember, even one seemingly inconsequential report may be lifesaving, if the suspicion for the drug causing the ADR is acted upon. As such, any report may give an early warning to us all.

1.2. **Objectives**

The objectives of the Guide are to:

- Raise awareness on the magnitude of drug safety problems
- Convince health professionals that the reporting of ADRs is their professional and moral obligation.
- Aid health professionals in becoming vigilant in the detection and reporting ADRs and other drug induced problems

The ultimate goals of the Guide are to:

- Promote early detection of drug safety problems in patients
- Improve selection and rational use of drugs by health professionals
- Reduce medicine induced morbidity and mortality

1.3. Definition of pharmacovigilance (PVG)

Pharmacovigilance is the science and activities related to the knowledge, detection, assessment and prevention of adverse effects or any drug related problem. Pharmacovigilance and Safety Monitoring are used interchangeably in this guideline.

1.4. The Major aims of pharmacovigilance are:

- Early detection of increases in frequency of previously unknown adverse reactions and interactions and other noxious drug induced problems
- Detection of an increase in known adverse reactions
- Identification of predisposing risk factors and possible mechanisms underlying adverse reactions
- Estimation of quantitative aspects of risk benefits analysis and dissemination of information needed to improve drug prescribing, drug dispensing and drug regulation.
- Promote rational and safe use of medicines.
- Educate and inform the patients.
- Contributing to the protection of patients' and public health.

1.5. Rationale for Pharmacovigilance

Drug safety monitoring gained worldwide attention following the thalidomide incident in the 1960s. Thalidomide was a drug given to pregnant women to prevent "morning sickness". The babies born to some of these women were badly deformed and it took a while before the link between the deformed babies and the drug was made. Once this link was established the drug was banned and regulatory authorities all over the world became aware of the fact that seemingly safe drugs could have potentially serious adverse effects. The World Health Organisation (WHO) therefore called for close monitoring of the adverse effects of all drugs. By continuous monitoring of all drugs used in Sierra Leone, it is possible to detect drugs causing unwanted ADRs and to control them. This can only be done effectively if healthcare professionals and patients report all suspected ADRs to the NPC.

The effectiveness of any pharmacovigilance activity is dependent on the active participation of all health professionals. Heath professionals are in the best position to report suspected ADRs observed in their everyday practice. All healthcare professionals should report suspected ADRs as part of their professional responsibility, even if they are doubtful about the precise relationship between the reaction and the given medication. The PBSL on its part assures the safety and quality

of all products before registration. However, some safety issues only come up after registration when the product is in use. Before a medicine is authorized for use, evidence of its safety and efficacy is only limited to the results obtained from clinical trials, which is not extensive. This is because up to the time of authorization, the medicine will only have been tested in a relatively small number of patients for a limited length of time (i.e. during clinical trials). As a result, some side effects may not be seen until a very large number of people have received the medicine and used it over longer time periods. There is therefore need for continuous motoring for further safety assurance.

1.6. Definition of Terms

A drug or medicines is:

A pharmaceutical product, used in or on the human body for the prevention (prophylaxis) mitigation, diagnosis and or treatment of disease, or for the modification of physiological function. This definition includes prescribed medicines, over-the counter medicines, vaccines, herbal medicines, traditional medicines and biologicals (including blood and blood-related products e.g. sera, plasma) and cosmetics, medical devices and nutritional agents.

Abuse

The persistent or sporadic, intentional excessive use of a medicinal product, which is accompanied by harmful physical or psychological effects

Adverse Drug Reaction (ADR) is:

"a response to a medicine which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis of disease, or for the modification of physiological function" (WHO).

What is important in this definition is that a patient experiences an unwanted and/or harmful (noxious) reaction following drug therapy. Individual factors may play an important role but the key point is that the phenomenon experienced is noxious. An ADR is essentially a "bad" reaction suffered by the patient and differs from "side effect' which is essentially an unexpected therapeutic response, which is related to the pharmacological properties of the drug and may be "good' or "bad"

Adverse Event/experiences is:

'Any unwanted medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment"

The basic point here is that an unwanted event occurs during or after the use of a drug. The term "adverse event" caused by the one encompassing "adverse drug reactions" caused by the drug, and other unwanted reactions, the time of occurrence of which may be related to the use of the drug but are not caused by the drug.

Adverse Drug Reaction (ADR) Case Report

A case report in pharmacovigilance is a notification related to a patient who has experienced an adverse medical event or laboratory test abnormality suspected to be induced by a medicine.

It is important to stress that healthcare workers should send reports of ADRs even if they do not have all the information required.

Board

Means Pharmacy Board of Sierra Leone

Consumer

A person who is not a healthcare professional such as a patient, friend or relative of the patient.

Drug Abuse

Drug abuse is a persistent or sporadic, intentional excessive use of medicines, which is accompani ed by a harmful physical or psychological effect.

Expedited Reporting

This is the immediate reporting and in not more than 7 calendar days, of a serious adverse reaction to the Board.

Healthcare professional

A person who is a medically qualified person such as a physician, dentist, pharmacist, nurse or community health officer.

Marketing Authorisation Holder

An organisation that has been issued licence by the competent authority to market a medicinal product, medical equipment, or cosmetics within Sierra Leone or any other country and may or may not be the manufacturer of the particular product.

Medication Errors

Any preventable medication related event occurring as a result of actions by a healthcare professional that may cause or lead to patient harm while the patient is in the care of the healthcare professional.

New Drug

A chemical or biologically active pharmaceutical ingredient that has not previously been issued with a marketing authorization as an ingredient in any pharmaceutical product in Sierra Leone.

Misuse

Situations where the medicinal product is intentionally and inappropriately used not in accordance with the authorized product information.

NPC

Means National Pharmacovigulance Centre

Occupational exposure

Exposure to a medicinal product as a result of one's professional or non-professional occupation

Off-label use

Situations where the medicinal product is intentionally used for a medical purpose not in accordance with the authorized product information.

Overdose

Administration of a quantity of a medicinal product given per administration or cumulatively, which is above the maximum recommended dose according to the authorized product information.

Periodic Benefit Risk Evaluation Report (PBRER)

An update of the world-wide marketing experience of a product at defined times with focus on formal evaluation of benefit in special population at defined times during post-registration period.

Periodic Safety Update Report (PSUR)

A regular update of the world-wide safety experience of a product at defined times during post registration period.

Post Authorization Safety Study (PASS)

Any study relating to an authorized product conducted with the aim of identifying, characterizing or quantifying a safety hazard, confirming the safety profile of the product, or of measuring the effectiveness of risk management measures.

Qualified Person for Pharmacovigilance (QPPV)

An individual named by a Marketing Authorization Holder (MAH) and approved by the Board as the person responsible for ensuring that the company (the MAH) meets its legal obligations in the for monitoring of the safety of the product marketed in Sierra Leone.

Risk Benefit Balance

This is an evaluation of the positive therapeutic effects of the medical product in relation to the risks (any risk relating to the quality, safety or efficacy of the medical product as regards patients' health or public health).

Risk Management Plan

A systematic approach and set of pharmacovigilance activities and interventions designed to identify, characterize, prevent or minimize risks relating to medical products, and the assessment of effectiveness of those interventions and how these risks will be communicated to the Board and the general population.

Serious Adverse Event (Experience) or Reaction is:

Any untoward medical occurrence that at any dose:

- Results in death,

- Is life-threatening
- Requires patient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity,
- Causes a congenital anomaly or birth defect
- Requires an intervention to prevent permanent impairment or damage

Side Effect is

"Any unintended effect of a pharmaceutical product occurring at doses normally used in human, which is related to the pharmaceutical properties of the drug."

Such effects may or may not be beneficial. Side effects are related to the known properties of the drug and can often be predicted. It must be stressed that in pharmacovigilance, we are interested in all drug related reactions, this includes side effects and suspected adverse drug reactions. Healthcare professionals must therefore report all drug related problems to the NPC.

Signal

A Signal refers to "Reported information on a possible causal relationship between an adverse event and a drug; the relationship being known or incompletely documented previously" Usually more than a single report is required to generate a signal depending upon the seriousness of the event and the quality of the information.

Spontaneous Report or Spontaneous Notification

Unsolicited communication by a patient, a consumer or healthcare professional to the Board, marketing authorization holder or local representative or an organization that describes a suspected adverse reaction in a patient, a consumer who is given one or more medicines and which is not derived from a study or any organized data collection systems where adverse event reporting is actively sought.

Unexpected adverse reaction is "an adverse reaction, the nature or severity of which is not consistent with domestic labeling or market authorization, or expected from the characteristic of the drug"

The National Pharmacovigilance Centre will be grateful to receive your comments on experiences gained from the practical use of this guide, which may help in developing it further.
Please contact the National Pharmacovigilance of PBSL with your comments at the address below or your nearest PBSL office nationwide.

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SECTION 2

2.1. How Medicine Safety is assured

All drugs undergo a significant amount of testing and evaluation before marketing to ensure their effectiveness as well as safety. Marketed medicines undergo trials in animals (pre-clinical testing) and humans (clinical trials) to establish their efficacy, safety, and quality

2.2. Pre-marketing Evaluation

Pre-marketing evaluation involves animal studies and clinical trials in human. Studies in two or more animal species are conducted to test whether the drugs are harmful and whether they may for instance induce cancer, damage and malformations in the unborn child etc. Once scientists are sure that a drug is safe, they start studies in human beings and these studies are known as clinical trials. Pre-marketing clinical trials take place in three phases (I, II and III). These trials are studies on the effects of drug on humans under rigorously controlled conditions. All clinical trials will assess safety of the drug in question. A brief description of each phase of clinical trial is given below:

- **Phase I** –Single or multiple dose studies in healthy volunteers, using low doses of the drug. Subsequently, large doses and multiple sequence are evaluated.
- **Phase II** –Efficacy is the primary objective of phase II trials, but safety is also continuously monitored and evaluated.
- **Phase III**- Evaluations of safety in groups of patients with the disease. Each phase involves increasing number of patients and by the end of full pre-marketing clinical trials about 5000 patients would have taken the medicine. However, when the drug is marketed millions of people will take the medicine. There is therefore the question of whether clinical trials involving just about 5000 people provided enough information to extrapolate the safety of a new medicine to millions of people through pre-marketing safety. Pre-marketing safety evaluation have two significant drawbacks:

a. Under-identification of ADRs

ADRs which occur infrequently are difficult to identify. Statistically, reactions with an incidence of less than 1% are frequently not identified.

b. Over –identification of ADRs

Many ADRs that are identified in pre-clinical studies are not proven to be related to the drug, but are nevertheless listed in the product literature as potentially associated to the drug. This provide some measure of legal protection for the pharmaceutical company but is misleading to practitioners and patients, as any of these reactions are not definitely proven.

2.3. Post-Marketing Surveillance (PMS)

It is not possible to identify all of the safety –related problems that may exist with a new drug during pre-market testing and evaluation. After drugs have been released on the market, the PBSL, the manufacturer/importers and health care professionals are responsible for post-marketing surveillance of these products. Medicines released to the market will be used not only by more people, but also by different categories of people other than those in whom the medicine was tested. The marketed medicine will be used by those with more serious illness, those from different ethnic groups, pregnant women and also by children in whom drugs are rarely tested. The medicines may also be used under many different dose regimens (not necessarily the correct and approved dose) and they could also be deliberately misused. These circumstances inevitably increase the potential for more adverse drug reactions. For these reasons, it is obvious that the safety of a drug requires long-term surveillance after marketing.

PMS activity is the responsibility of regulators, pharmaceutical companies, marketing authorization holders (MAHs) and healthcare professionals in Sierra Leone and they must work together to continuously monitor the safety and quality of medicines after they have been licensed and when necessary swift and appropriate actions should be taken to protect patients.

One of the most common methods of PMS is spontaneous reporting using approved ADR reporting forms. In Sierra Leone, the NPC issues spontaneous reporting forms, which health care professionals should use to report any suspected ADRs. Copies of the form can be obtained directly from any health institution, PBSL offices in the districts or directly from the NPC at PBSL Headquarter, New England Ville, Freetown.

Potential problems can be detected from reports on side effects of medicine, research(retrospective) carried out using patient records (patient personal details must be protected), quality checks on products, including labelling and packaging carried out by regulatory authorities, information from manufacturers and MAHs, Alerts raised by healthcare professionals on newly marketed drugs.

Regulators should be committed to acting promptly and responsibly to protect patients from potential harm by alerting, healthcare professionals, manufacturers/MAH about quality and safety concerns about medicinal products marketed in Sierra Leone, which should be graded according to the seriousness of their threat to the public's health. Healthcare professionals will in turn pass on this information to their patients in cases where continuing to take the medicine poses a serious risk.

2.4 Classification of ADR risk

Class 1: life threatening: immediate recall required

Class 2: harmful: recall is required within 48 hours

Class 3: unlikely to harm patients: action required within 5 days

Class 4: no threat to patient safety: caution advised

SECTION 3

3.1. The Magnitude of the Problem.

It has been demonstrated by a number of studies that medicine-induced morbidity and mortality is a major problem to which health care professionals and the general public are becoming increasingly aware. It has been estimated that ADRs are the 4th to 6th largest cause of death in the USA (1). Studies conducted in developed countries have consistently shown that approximately 5% of hospitalized patients are admitted into hospital as a result of an ADR, while 6-10% of in –patients will experience a serious ADR during hospitalization. ADRs cause the death of several thousand patients each year (2).

The percentage of hospital admissions due to ADRs in some countries is about or more than 10% (3).

Norway	11.5%
France	13.0%
UK	16.0%

Even these startling figures do not represent the whole picture. These studies generally excluded ADRs caused by other drug related problems such as overdose, drug abuse, misuse, poisoning, medication errors and therapeutic failures.

In addition, treatment of ADRs imposes a high financial burden on health care. Some countries spend up to 15-20% of their hospital budget dealings with drug complications (4). A socio-economic motive that needs to be urgently addressed.

SECTION 4

4.1. What is the size and severity of the ADR problem in Sierra Leone?

While no studies have comprehensively assessed the burden of ADRs on health care, it is likely that the problem is considerable in Sierra Leone. There is very limited information available on ADRs. However, the National Medicines Policy recognizes the need for a Drug Safety Monitoring Programme in Sierra Leone to deal with widespread irrational medicines use, including, preference for injections, misuse of antibiotics and other prescription medicines, unstandardized use of orthodox and traditional/herbal medicines and extensive self-medication.

The circulation of substandard and counterfeit medicines in Sierra Leone, lack of independent information on medicines other than that from the pharmaceutical industry and the irrational use of medicines, compound the likelihood of a higher incidence of ADRs.

Effective pharmacovigilance activity will enable Sierra Leone to develop a good record keeping habit and build a useful safety information database that will improve the quality of health care offered to the patient.

SECTION 5

5.1. Why is Pharmacovigilance (PVG) needed in Sierra Leone?

The information which we receive on adverse effects of medicines in other countries may not be relevant or applicable to Sierra Leone due to various differences that may influence patient response including;

- Diseases and prescribing practices;
- Treatment seeking behavior e.g. self-medication;
- Genetics, diet, traditions of the people e.g. high carbohydrate and fat diet, kola nut consumption etc.;
- Dug manufacturing processes which influence the quality and composition;
- Drug distribution and use, including indications, dose, storage and availability of pharmaceuticals.
- The use of traditional and complementary medicines (e.g. herbal remedies) which may pose specific toxicological problems, when used alone or in combination with other medicines; and
- Racial differences.

Data derived from within the country may have greater relevance and educational value and can assist PBSL to make evidence-based decisions. Information obtained in one county (e.g. the country of origin of the medicine) may not be relevant to other parts of the world, where circumstances may differ.

It is essential that doctors, pharmacists, nurses and other health professionals support a monitoring system for the safety of medicines in Sierra Leone in order to prevent unnecessary suffering and decrease the financial loss sustained by the patient due to ADRs and the inappropriate or unsafe use of medicines and the overall burden on the health care system and national economy.

The PBSL is committed to improving medicine safety through adverse drug reaction monitoring in Sierra Leone. The national pharmacovigilance centre of PBSL shall make the spontaneous reporting forms available at all times. Health professionals are expected to report adverse reactions, lack of effect and other medicines problems on a daily basis as a professional moral obligation

SECTION 6

6.1. *Specific responsibilities*

6.1.1. Pharmaceutical companies and MAH

- Shall employ and have continuously at its disposal an appropriately qualified person responsible for pharmacovigilance in Sierra Leone (QPPV).
- Submit the name and contact details of the QPPV to the PBSL
- The duties of the QPPV shall be defined in a job description
- The hierarchical relationship of the QPPV shall be defined in an organisational chart together with those of other managerial and supervisory staff
- Pharmaceutical companies and marketing authorisation holders shall ensure that the QPPV has sufficient authority to influence the performance of the quality system and the pharmacovigilance activities of the MAH.
- The authority over the pharmacovigilance system should allow the QPPV to implement changes to the system and to provide input into risk management plans as well as into the preparation of regulatory action in response to emerging safety concerns.
- MAH shall ensure that the QPPV has acquired adequate theoretical and practical knowledge for the performance of pharmacovigilance activities.
- Ensure it has an appropriate PV system and risk management system.
- Assume responsibility and liability for its products on the market.
- Ensure appropriate action can be taken when necessary.
- Ensure all information relevant to the risk-benefit balance of a medicinal product is reported to the PBSL fully and promptly in accordance with legislation.
- Submit regularly PSUR/PBRER within deadline limit.
- See PBSL QPPV guideline for more details.

6.1.2. Pharmacy Board of Sierra Leone

- Should establish a pharmacovigilance system for the collection and evaluation of information relevant to the risk-benefit balance of medicinal products authorised.
- Continually monitors the safety profile of the products available in Sierra Leone.
- Takes appropriate action where necessary.

- Monitors the compliance of Manufacturers and Marketing Authorisation Holders with their obligations with respect to pharmacovigilance.
- Ensures that Marketing Authorisation Holders implement, when appropriate, Risk Management Plans to effectively monitor and manage risks associated with the safety of their products
- Ensures that pharmacovigilance data are shared between stakeholders, health programmes and internationally.
- Collect and evaluate risk-benefit balance on medicinal products, monitor safety profile, take appropriate actions, monitor health care professional (HCP) and MAH.
- Have an established pharmacovigilance system for the collection and evaluation of information relevant to the risk-benefit balance of medicinal products.

6.1.3. Patient/consumers

Patients/consumers should report any suspected ADR to PBSL, Pharmaceutical Companies, MAH, HCP as soon as possible even if they are not sure of a causal relationship. If PBSL, pharmaceutical companies and MAH receives any ADR report from a consumer, the consumer should be advised to seek medical attention from their healthcare provider. All consumer reports should however be documented as for any other type of report and should be taken into account when overall safety assessments are made. Consumers should be encouraged to report any suspected adverse reaction within 7 days.

6.1.4. Healthcare professionals

Healthcare professionals are encouraged to report all adverse reactions received from consumers / patients. Spontaneous reports must be submitted within seven days to PBSL. Reports can also be sent directly to the manufacturers or MAH. During contacts with patients, attempts should be made to obtain information sufficient to ascertain the nature and seriousness of the event. Additional follow-up or medical confirmation may not be necessary for apparently non-serious and expected adverse reactions. On the other hand, if the event is serious / or unexpected, reasonable additional efforts should be made to contact the treating doctor or have the consumer provide the relevant medical documentation to allow for risk assessment and signal detection.

Health care professionals should be encouraged to be involved in active surveillance activities such as prescription event monitoring as PV is one of their key responsibilities

SECTION 7

7.0 How voluntary reporting of ADRs can prevent new medicines tragedies from developing

It took many decades before the deleterious effects of **aspirin** on the gastro-intestinal tract became apparent and almost as long before it was recognized that the protracted abuse of **phenacetin** could produce renal papillary necrosis, 35 years elapsed before it became clear that **amydopyrine** could cause agranulocytosis, and several years before the association of phocomelia with **thalidomide** became obvious.

Withdrawals from the Market as a result spontaneous reporting.

Generic Name (Brand Name)	**Reason for withdrawal**	**Year of marketing**	**Year of withdrawal**
Bromfenac (Duract)	Serious hepatotoxic effect	1997	1998
Encainide (Enkaid)	Excessive Mortality	1992	1991
Temafloxacin (Omniflox)	Hemolytic Anaemia	1992	1992
Benoxaprofen (Oraflex)	Liver Necrosis	1982	1992
Mibefradil (Posicor)	Multiple Drug Interaction	1997	1998
Terfenadine (Seldane)	Fatal Cardiac Arrhythmias	1985	1998
Over 153 Drug Products withdrawn from the Sierra Leone Market	Substandard/Poor Quality	1998	2017
Rofecoxib (Vioox)	Severe cardiovascular Events	1999	2004

SECTION 8

GUIDE TO REPORTING

8.1. Who should report Adverse Drug Reaction?

All health care professionals/workers, including doctors, dentists, pharmacists, Pharmacy technicians, nurses, community health officers, traditional medicine practitioners and other health professional are requested to report all suspected adverse reaction to medicines including orthodox medicines, vaccines, biotherapeutics, X-ray contrast media, medical devices, cosmetics, traditional and herbal remedies, chemical agents, nutritional agents etc. This includes all health care institutions such as primary, secondary and tertiary healthcare facilities and public health programmes, patients/consumers, MAH and Manufacturers.

It is vital to report an ADR to the national pharmacovigilance centre of PBSL even if you do not have all the facts or are uncertain that the medicine is definitely responsible or causing the reaction. What is required is to report all SUSPECTED adverse drug reactions. In many cases it will be impossible for an individual health worker to prove that the reaction was indeed caused by a medicine. However, collection of reports from several health workers in different parts of the country will assist in making an association between the medicine and a particular adverse reaction.

8.2. What to report

For all medicinal products the following should be reported:

- Suspected Adverse Drug Reactions (ADRs) resulting from non-prescription and prescription medicines (including biological products and radiopharmaceutical products).
- Adverse reactions resulting from herbal medicinal products and food supplements, medical devices, cosmetics and household chemical substances.

- For “new” medicines - report all suspected reactions, including minor ones
- For established or well-known medicines - report all serious or unexpected (unusual) suspected ADRs and minor ones.
- Drug abuse, drug overdose, drug interactions, quality defects, poor packaging, questionable stability, suspected contamination, suspected counterfeit and lack of therapeutic efficacy.

- Adverse reactions occurring in a recipient of blood or blood components
- Suspected ADRs associated with drug withdrawals.
- Reactions suspected of causing death, danger to life, admission to hospital, prolongation of hospitalization, birth defects.

All suspected ADRs should be reported even if the reporter thinks there is no causal relationship between the medicinal product and the reaction, except when the reporter is absolutely sure. All ADRs that occur in all health care institutions and public health programmes such as Malaria, HIV/AIDS, Leprosy/Tuberculosis, EPI, Neglected Tropical Diseases, Reproductive and Child Health, School Health Programme, Nutrition should be reported. Thus, all suspected adverse reactions of clinical importance should be reported.

8.3. What product quality problems should I report?

Report Product Quality problems such as:

- Suspected contamination
- Questionable stability
- Defective component
- Poor packaging or labeling
- Therapeutic failures
- Expired batches

8.4. What will happen to my Adverse Drug Reaction Report?

The information obtained from your report shall be used to promote the safe use of medicines on a local, national and international level. Your reported case will be entered into the national adverse drug reaction database and analyzed by expert reviewers. A well-completed adverse drug reaction reporting form submitted by you could result in one or more of the followings;

- ❖ Additional investigations into the use of the medication in Sierra Leone
- ❖ Educational initiatives to improve the safe use of the medication
- ❖ Appropriate package insert changes to include the potential for the reaction reported by Sierra Leonean health professional and workers
- ❖ Changes in the scheduling or manufacture of the medicine to make the medicine safer

- Other regulatory and health promotion interventions as the situation may warrant including change in supply status or withdrawal

Therefore, the purpose of ADR reporting is to reduce the risk associated with drug prescribing and administration and to ultimately improve patient care, safety and treatment outcome.

8.5. What are the benefits of these reports for my patients and I?

The health care professional and patient stand to benefit as follows:

- Improvement on the quality of care offered to patients
- Reduction of medicines-related problems leading to better treatment outcome
- Improved patient confidence in the professional's practice and consequently professional growth
- Improved knowledge, access to feedback information on drug related problems reported within the country and internationally
- Satisfaction for the fulfillment of moral and professional obligation

8.6. Will Reporting have any negative consequences on the health worker or the patient?

The adverse drug reaction report does not constitute an admission that you or any other health professional or the drug contributed to or caused the event in any way. The outcome of the report, together with any important or relevant information relating to the reaction you have reported, will be communicated to you as appropriate. The details of your report will be stored in a confidential database in Sierra Leone and the analyzed report sent to the Uppsala Monitoring Centre (UMC)-World Health Organisation Global Database.

The information obtained from your report will not be used for commercial purposes. The information is only meant to improve our understanding and use of medicines in Sierra Leone. ADR reports cannot be used in a court of law under any circumstances.

8.7 Why Health Professionals are in the best position to detect and report ADRs?

The effectiveness of the Drug Safety Monitoring Programme is directly dependent on the active participation of health professionals. Health professionals are in the best position to report suspected ADRs observed in their everyday practice, because they are the people who diagnose, prescribe, dispense and monitor patients' response to medicines.

All health care providers should report ADRs as part of their professional responsibility, even if they are doubtful about the precise relationship with the given medication.

You can reduce suffering and save thousands of patients' lives by doing just one thing:

REPORT SUSPECTED ADVERSE DRUG REACTIONS INCLUDING LACK OF EFFECT.

8.8. How do I Recognize ADRs in my Patient?

ADRs are difficult and sometimes impossible to distinguish from the disease being treated since they may act through the same physiological and pathological pathways. However, the following step-wise approach may be helpful in assessing possible medicine –related ADRs:

A) Take a proper history and do a proper examination of the patient:

- A full medicine and medical history should be taken
- Can this adverse reaction be explained by any other cause e.g. patients underlying disease, other drugs including over-the counter medicines or traditional medicines, toxins or foods?
- It is essential that the patient be thoroughly investigated to decide what the actual cause of any new medical problem is. A medicine-related cause should be considered, especially when other causes do not explain the patient's condition

B) Established time relationship by asking and answering the following question:

- Did the ADR immediately follow the medicine administration?
- Some reactions occur immediately after the medication has been given, while others take time to develop. The time from the start of therapy to the time of onset of the suspected reaction must be logical

C) Carry out a thorough physical examination with appropriate laboratory investigation (if necessary).

- Few medicines produce distinctive physical signs
- Exceptions include fixed medicine eruptions, steroid-induced dermal atrophy, and acute extra-pyramidal reactions

- Laboratory tests are especially important if the medicine is considered essential in improving patient care or if the laboratory test result will improve management of the patient.
- Try to describe the reaction as clearly as possible and where possible provide an accurate diagnosis.

D. Effect of Dechallenge and Rechallenge should be determined

(When necessary)

Yellow =No Action Taken

Red = Dechallenge = Withdrawal of drug

Green = Rechallenge

"A Positive Dechallenge implies improvement of reaction when Dechallenge occurs. Resolution of suspected ADR when the medicine is withdrawn is a strong, although not conclusive indication of medicine-induced reaction

Rechallenge = reintroducing the medicine after a Dechallenge

- Rechallenge is only justifiable when the benefit of reintroducing the drug to the patient outweighs the risk of recurrence of the reaction. This is rare. In some cases, the reaction may be more severe on repeated exposure.

  Rechallenge therefore requires serious ethical consideration.

E. Check the known pharmacology of the medicine.

- Is the reaction known to occur with the particular medicine as stated in the package insert or other references?
- If the reaction is not documented in the package insert, it does not mean that the reaction cannot occur with the particular medicine.

8.9. Causality Classification

In order to assess the likelihood that the suspected adverse reaction is actually due to the medicine, the WHO-UMC has provided a list of causality assessment criteria for deciding the association of the medicine towards the adverse event.

These criteria are defined as follows:

Certain

- Clinical event, lab test abnormality with plausible time relationship to medicine intake
- Cannot be explained by concurrent disease or other medicines/ chemicals
- Response to dechallenge – positive?
- Event must be definitive pharmacologically/immunologically
- Positive rechallenge (if performed).

Probable/Likely:

- Clinical event, lab test abnormality with reasonable time relationship to medicine intake
- Unlikely to be explained by concurrent disease, medicines/chemicals
- Clinically reasonable response to withdrawal (Dechallenge)
- Rechallenge not required

Possible

- Clinical event, lab test abnormality with reasonable time relationship to medicine intake
- Could also be explained by concurrent disease or other medicines or chemicals
- Information on drug withdrawal may be lacking or unclear

Unlikely:

- Clinical event, lab test with improbable time relationship to medicine intake
- Other medicines, chemicals and underlying disease provide plausible explanations

Inaccessible/Unclassifiable:

- Insufficient/contradictory evidence, which cannot be supplemented or verified

Conditional/Unclassified:

- More data is essential for proper assessment or additional data are under examination.

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;

however, this should not dissuade you from reporting the reaction to the national pharmacovigilance centre of the PBSL.

A well-documented report, which includes information about all the above-mentioned questions, can provide us with the first signal of a previously unknown problem.

8.10. How can I prevent ADRs from occurring in patients?

Some ADRs are unavoidable and cannot be prevented. However, following the basic principles of relational use of medicines described as follows can prevent most ADRs.

1. Use few medicines, wherever possible
2. Use medicines that you know well
3. Do not change therapy from known medicines to unfamiliar ones without good reasons.
4. Use textbooks and other reference materials providing information on medicines reactions and interactions.
5. Take extra care when you prescribe medicines known to exhibit a large variety of interactions and adverse reaction (anticoagulants, hypoglycemics, and centrally acting medicines) with careful monitoring of patients for such reaction.
6. Beware of the interaction of medicines, with certain foods, alcohol and house hold chemicals.
7. Review all medicines used by patients regularly, taking special notice of those bought without prescription, (over the counter, herbal preparations cosmetics etc.)
8. Be particularly careful when prescribing for children, the elderly, pregnant and nursing women, the seriously ill and patient with hepatic and renal disease. Careful continuous monitoring is essential in these patients.
9. If patients show signs or symptoms not clearly explained by the course of their illness, think adverse drug reaction.
10. If you suspect an adverse reaction, consider stopping the medicine or reduce the dosage as soon as possible and please notify PBSL of the adverse drug reaction.

SECTION 9

RISK MANAGEMENT PLAN

At the time of marketing authorisation of a medicinal product, information on the safety profile is relatively limited as a result of many factors. These includes the comparatively small numbers of subjects in clinical trials with the intended treatment population, restricted population in terms of age, gender and ethnicity, restricted co-morbidity, restricted co-medication, restricted conditions of use, relatively short duration of exposure and follow up, and the statistical problems associated with looking at multiple outcomes. The medicinal product is authorised based on the specified indication(s), at the time of authorisation and the benefit to risk balance is usually judged to be positive. Therefore, not all actual or potential risk will be identified, as a typical medicinal product will have multiple risks attached to it and individual risks will vary in terms of severity, effect on individual patients and public health impact. These risks will only be identified post authorisation thus the reason why it is important that a very good risk management system is put in place by the manufacturer and MAH.

9.1. **Objectives of RMP**

- Identify or characterise the safety profile of the medicinal product(s) concerned
- Indicate how to characterise further the safety profile of the medicinal product(s) concerned
- Document measures to prevent or minimise the risks associated with the medicinal product including an assessment of the effectiveness of those interventions.
- Document post-authorisation obligations that have been imposed as a condition of the marketing authorisation.

In order to fulfil these objectives, a RMP must:

- Describe what is known and not known about the safety profile of the concerned medicinal product(s).
- Indicate the level of certainty that efficacy shown in clinical trial populations will be seen when the medicine is used in the wider target populations seen in everyday medical practice and document the need for studies on efficacy in the post-authorisation phase (also known as effectiveness studies).

- Include a description of how the effectiveness of risk minimisation measures will be assessed.
- Plan pharmacovigilance activities to characterise risks and identify new risks and increase the knowledge in general about the safety profile of the medicinal product.
- Plan and implement risk minimisation, mitigation and assessment of the effectiveness of these activities.

The overall aim of risk management is to ensure that the benefits of a particular medicinal product (or a series of medicinal products) exceed the risks by the greatest achievable margin for the individual patient and for the target population as a whole. This can be done either by increasing the benefits or by reducing the risks

9.2. **Responsibilities for risk management within an organisation**

The principle organisations directly involved in medicinal products' risk management planning are manufacturers/marketing authorisation holders and the competent authorities like PBSL who regulate them.

9.2.1 Marketing authorisation holders/Manufacturerers

In relation to risk management of its medicinal products, an applicant/marketing holder is responsible for:

- ensuring that it constantly monitors the risks of its medicinal products in compliance with relevant legislation and reports the results of this, as required, to the appropriate competent authorities;
- taking all appropriate actions to minimise the risks of the medicinal product and maximise the benefits including ensuring the accuracy of all information produced by the company in relation to its medicinal products, and actively updating and promptly communicating it when new information becomes available

9.2.2. The medicines regulatory authority-PBSL

The principal responsibilities of PBSL in relation to risk management are:

- constantly monitoring the benefits and risks of medicinal products including assessing the reports submitted by pharmaceutical companies, healthcare professionals, patients and, where appropriate, other sources of information;
- taking appropriate regulatory actions to minimise the risks of the medicinal product and maximise the benefits including ensuring the accuracy and completeness of all information produced by the company in relation to its medicinal products;
- ensuring the implementation of risk minimisation activities at a national level;
- effectively communicate with stakeholders when new information becomes available. This includes providing information in an appropriate format to patients, healthcare professionals, patient groups, learned societies and so on.
- when necessary, ensuring that marketing authorisation holders of generic and/or similar biological medicinal products make similar changes to their risk minimisation measures when changes are made to those of the reference medicinal product;
- providing information to other regulatory authorities, this includes notification of any safety activities in relation to a product, including changes to the product information of originator and/or reference medicinal products.

9.3. Assessment of benefits

Manufacturers and MAH should regularly re-evaluate the benefits of their products marketed in Sierra Leone**.** Benefit should be seen as:

- a decrease in disease burden,
- cures,
- improvement in underlying conditions and symptoms,
- improved response rate,
- improved quality and duration of life,
- reduction of expected severity.

SECTION 10

10.1Some Basic Principles of Efficient Reporting

10.1.1 Time of reporting (Timelines)

Report the event soon after it occurs. A recent event is easier to report upon (i.e. less work is involved) and the report is more likely to be accurate. If possible, take the decision to report whilst the patient is still with you, so that he/she can easily be questioned (by you) about the event and all the details filled in at once on the reporting form.

Reporting by Healthcare Professionals

All serious suspected and serious unexpected adverse drug reactions associated with the use of any product in Sierra Leone should be reported to the Board within 7 calendar days. All other adverse drug reactions will be reported to the Board within a period of 28 days.

Reporting by the Local Representatives or Marketing Authorization Holders

Serious adverse reaction reports received by Marketing Authorization Holders shall be submitted to the Board within 7 calendar days. In case all the information needed is not available within 7 days, the Marketing Authorization Holder should submit an initial report containing at least the minimum data required (i.e. patient details, suspected product details, reaction details and the reporter details) in order to meet the expedited reporting time frames. A follow-up report containing more detailed information should be submitted later as soon as it becomes available.

Summary of Timelines and Report Format

TYPE OF SAFETY REPORT

	TIME FRAME FOR REPORTING	**FORMAT**
Local Reports:		PBSL Adverse Drug Reaction Reporting form (Appendix I)
Serious unexpected adverse reaction	7 days	
Serious expected adverse reaction	7 days	PBSL Adverse Drug Reaction Reporting form (Appendix I)
Non-serious expected and unexpected adverse drug reactions	28 days	PBSL Adverse Drug Reaction Reporting form (Appendix I)

10.1.2. Integrity /reliability of Suspect Judgment.

If you obtain any supplementary data e.g. if the same patient develops the reaction again, or if something happens which increases your suspicion or seems to exclude their reaction, please send in a supplementary note immediately.

10.1.3 Completeness/ Eligibility of Report

Only reports with some minimal standards of adequacy of information should be submitted to the NPC. Four (4) pieces of information constitute the minimum information required. They are:

1- An identifiable source of information
2- An identifiable patient
3- An identifiable medicine
4- An indefinable suspect reaction

If any of these essential elements is missing, then such a report is unreliable and may not be useful. Reports of an alleged adverse drug reaction without any other details concerning the patient or the medicine(s) should not be sent to the NPC. *PLEASE WRITE LEGIBLY*

10.2. What should I know about the Drug Safety Monitoring Programme in Sierra Leone?

The Sierra Leone Drug Safety Monitoring Programme is coordinated by the Pharmacovigilance and Clinical Trials Department of the PBSL and collaborates with the UMC and other PV national centers worldwide.

It is responsible for monitoring the safety of all medicines in Sierra Leone. The NPC will be assisted, as the case required by an Technical Advisory Expert Committee on Drug Safety and Clinical Trials comprising of experts from various fields of health care. The NPC is responsible for providing reporting forms, collecting, evaluating and communicating the findings from ADR reports to the management of PBSL. PBSL uses the findings from the reports for making regulatory decisions on how to prevent or minimize the risk of ADRs in Sierra Leone. PBSL, through the NPC may communicate their findings, recommendations and directives to appropriate organizations or individuals. These include, but are not limited to health professionals, pharmaceutical manufacturers, public health programmes, other public and private health institutions, the media and the public.

10.3. How do I report an ADR to the NPC of PBSL?

You are to write your report on the ADR reporting form provided by the NPC.

ADR forms are available at all tertiary, secondary and primary healthcare facilities at central and district levels, private hospitals, surgeries, clinics, pharmacies and drug stores nationwide. Other institutions that may wish to receive reporting forms directly may indicate so.

All Health Facilities should have an Institutional Contract Person(s) (ICP) for Pharmacovigilance. If you are unable to send your filled ADR form directly to the NPC at PBSL headquarters or to our Regional Offices, please give your ICP for onward submission to the Pharmacy Board of Sierra Leone.

The Pharmacy Board of Sierra Leone receives ADR forms either directly from the health professional or from their regional offices in the Northern, Southern, and Eastern provinces.

You can download the adverse drug reaction form from our website www.pharmacyboard.gov.sl or report online by clicking the Report an ADR on the PBSL website.

The National Pharmacovigilance Centre can be contacted on mobile: 025282886 or e-mail: drugsafety@pharmacyboard.gov.sl

ADR forms can also be obtained by contacting.

The Coordinator,
Drug Safety Monitoring Programme,
National Pharmacovigilance Centre
Pharmacovigilance and Clinical Trials Department
Pharmacy Board of Sierra Leone (PBSL)
Central Medical Stores Compound,
New England Ville,
Freetown, Sierra Leone
PMB 322

The form should be completed in as much details possible and returned to the address above.

Thank you for supporting the Pharmacy Board of Sierra Leone in the Drug Safety Monitoring Programme. Information provided will contribute to the improvement of drug safety and therapy in Sierra Leone.

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