



SAFETY OF MEDICINES IN SIERRA LEONE

**A GUIDE FOR DETECTING AND REPORTING
ADVERSE DRUG REACTIONS**

Why Health Professionals Need to Act?

**Designed By: Pharmacy Board
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***Drug Safety Monitoring Programme
Pharmacy Board of Sierra Leone
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We thank God and pray that the Safety Monitoring in Sierra Leone will be a success.

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This guide was prepared using the WHO, Eritrean, Nigerian and South African guidelines on detecting and reporting ADR's from the National Malaria Control Ministry of Health and Sanitation and the Global Fund Malaria Project. The Registrar of PBSL Mr. M. J. Lansana supervised the development of this guide and the pioneer staff of the DIPD developed the draft and put together the document.

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References

1. Lazarou J. et al., 1998 Incidence of ADR in hospitalization patients: A meta-analysis of prospective studies. JAMA, 1998, 279 (15) 1000-5.

2. Moore N. et al., 1998, Frequency and cost of serious adverse drug reaction in a department of general medicine. Br J Clin Pharmacol 1998, 45 (3) 301 308.

3. Imbs J. L et al, Iatrogenic medication: estimation of its prevalence in French public hospitals, Therapie, 1999, 54)1) 21-27.

4. Griffin G. P., The evaluation of human medicines control from a national to an international perspective. AD Drug React Toxicol rev., 1998, 17 (1), 19-50.

5. White T. et al, counting the cost of drug-related adverse events Pharmacovigilance, 1999, 15 (5), 455-458.

6. Venulet J., The Drug Monitoring programme. In: drug Surveillance, geneva, 1994, 13-21.

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Forward

The introduction of the Drug Safety Monitoring Programme in the Ministry of Health and Sanitation could have been timelier, especially at a time when the ministry is undergoing a process of rehabilitation and devolution in the management of health care delivery in Sierra Leone.

The realization that an efficient and effective pharmaceutical sector is the backbone of health care delivery that meets the needs of the majority of our citizenry, underscores the need for an apparatus to guarantee the quality and safety of pharmaceutical products.

In the world we live today, the propensity of counterfeiting, distribution of substandard pharmaceuticals, availability of products with quality defects and the uncertainty of the safety of medicines being used in the treatment of disease, have impacted negatively on our health care delivery machinery, resulting in the immensurable loss of much needed human and financial resources. As a consequence, this trend has had a direct influence on the socio-economic development of our nation.

It is in this context that the ministry has supported the development of a Drug Monitoring Programme, with the aspiration of improving the quality of health delivery in Sierra Leone, thereby strengthening the foundation of national development.

*Ms. Abator Thomas
Ministry of Health and Sanitation
December 2005*

ADR Forms are available at all tertiary, secondary and primary health care 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 Contact Person (s) (ICP) for Pharmacovigilance. If you are unable to send your filled ADR form directly to the DIPD, PBSL headquarters, please give your ICP for onward transmission 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.

The reporting form can also be accessed on the home page on the PBSL website as follows:

Website at www.pharmbdsi.org or requested from the DIPD by email:

infopharm_pbsl@yahoo.com, by Fax: 224526, Tel:225983/228497.

ADR Forms can also be obtained by contacting.

The Coordinator,

Drug Safety Monitoring Programme,

Drug Information and Pharmacovigilance Department (DIPD)

Pharmacy Board of Sierra Leone

P.M.B. 322

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

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

Introduction

Modern medicines/drugs 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 (additives 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 fake and substandard pharmaceuticals and is leading the fight against counterfeiting of all regulated products.

The risk of Adverse Drug Reactions (ADR's) 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 are not predictable, the chance or occurrence of several adverse drugs reactions can often be reduced by sufficient knowledge of the conditions under and disseminated through an efficient and effective Pharmacovigilance system. Never the less, the possibility of preventing ADR's underscores the need for a Pharmacovigilance system to monitor ADR's and other drug-induced problems.

Report of an alleged adverse drug reaction without any other details concerning the patient or the drug (s) should be sent to the DIP Unit .

PLEASE WRITE LEGIBLY

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

The Sierra Leone Drug Safety Programme is coordinated by the DIP which is located in PBSL and collaboration with the UMC and other national centres worldwide.

It is responsible for monitoring the safety of all medicines in Sierra Leone. The DIPD will be assisted, as the case requires by an Advisory Expert Committee comprising of expert from various fields of health care.

The Unit is responsible for providing reporting forms, collecting, evaluating and communicating the findings from ADR reports for making regulatory decisions on how to prevent or minimize the risk of ADR's in Sierra Leone. PBSL, through the DIPD 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 within the Ministry of Health and Sanitation, other public and private health institutions, the media and the public.

8.4 How do I report an ADR to the DIPD in PBSL?

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

SECTION 8

SOME BASIC PRINCIPLES OF EFFICIENT REPORTING

This Pharmacovigilance guide is intended to inform health professionals on the operations of the Drug safety Monitoring programme (DSMP) in Sierra Leone. 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 Drug Information and Pharmacovigilance department (DIPD), Pharmacy Board of Sierra Leone. It describes who can report suspected cases of ADR's to the DIP, 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 professional will take an active interest in Pharmacovigilance and report any suspicion of adverse drug reactions to the DIP. This way, we will make Sierra Leone and the world a safer place as far as the use of medicines and other relevant PBSL regulated products are life saving, if the suspicion for the drug causing the ADR is acted upon. As such, any report may give an early warning to us all.

8.0 Time of reporting

- 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. Send in the report to the DIP UNIT quickly, preferably within one week.
- If possible, take the decision to report whilst the patient is still with you, so that he/she can be easily questioned (by you) about the event and all the details filled in at once on the reporting form.
-

8.1 Integrity/reliability of Suspect Judgement

- 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 the reaction, please send in a supplementary note immediately.

8.2 Completeness/Eligibility of Report

Only report with some minimal standards of adequacy of information should be submitted to the DIP Unit. 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 identifiable suspect reaction

If any of these essential elements is missing, then such a report is unreliable and may not be useful.

OBJECTIVES

7.9 How can I prevent ADR's form occurring in patients?

Some ADR's are unavoidable and cannot be prevented. However, following the basic principles of rational use of medicines described as follows can prevent most ADR's:

1. Use few drugs, whenever possible
2. Use drugs that you know well.
3. Do not change therapy from known drugs to unfamiliar ones without good reasons.
4. Use textbooks and other reference material providing information on drug reactions and interactions.
5. Take extra care when you prescribe drugs known to exhibit a large variety of interactions and adverse reactions (anticoagulants, hypoglycemic, and centrally acting drugs) with careful monitoring of patients for such reactions.
6. Beware of the interaction of drugs, with certain foods, alcohol and house hold chemicals.
7. Review all drugs 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 patients with hepatic and renal diseases. 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 drug or reduce the dosage as soon as possible and please notify the adverse drug reaction to the DIPD, PBSL.

The objectives of the Guide are to:

- Raise awareness on the magnitude of drug problems.
- Convince health professionals that reporting of Adverse Drug Reactions (ADR's) is their professional and moral obligation.
- Aid health professionals in becoming vigilant in the detection and reporting of ADR's and other drug induced problems.

The ultimate goals of the Guide are to:

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

The DIP Department and PBSL 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 DIPD, PBSL with comments at the address below or your nearest pbsl office nationwide:

The coordinator
Drug Safety Monitoring Programme
Drug Information and Pharmacovigilance Department (DIPD)
Pharmacy Board of Sierra Leone (PBSL)
64 Siaka Stevens Street, Freetown Sierra Leone
Telephone: 225983, 228497, and 228351
Fax: (00 232 22) 224526
Email: infopharmpbsl@yahoo.com
Website: www.pharmbdsl.org

Definition of Pharmacovigilance (PVG)

Pharmacovigilance is the science and activities related to the knowledge, detection, assessment and prevention of adverse effects or any related problem.

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 quantities aspects of risk benefits analysis and dissemination of information needed to improve drug prescribing, drug dispensing and drug regulation.

The ultimate goals of Pharmacovigilance are to:

- Assess and communicate risk and benefits of medicines on the market.
- Promotes rational and safe use of medicines
- Educate and inform the patient.

This is because there is currently no monitoring system for those events that fall outside of the internationally accepted scope covering only normal dose of drugs.

- For ‘new’ drugs all suspected reactions, including minor ones.
- For established or well-known drugs—report all serious or unexpected (unusual) suspected ADRR’s.
- Report all suspected ADR’s associated with drug-drug, drug-food supplement interactions.
- Report ADR’s special fields of interest such as drug abuse and drug use in pregnancy and during lactation.
- Report when suspected ADR’s are associated with drug withdrawals.
- Report ADR’s occurring from overdose or medication error.
- Report when there is a lack of efficacy or when suspected pharmaceutical defects are observed.
- Report reactions suspected of causing death, danger to life, admission to hospital, prolongation of hospitalization, birth defects etc.

7.8 What product Quality Problem should I Report?

Report Product Quality problems such as:

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

Report ADR’s that are experienced in all health care institutions and public health programmes such as malaria, HIV/AIDS, Leprosy/Tuberculosis, EPI, ONCO, Reproductive Health, school Health programme, Nutrition etc, etc.

Thus, report all suspected adverse reactions that you consider of clinical importance as soon as you detect them!

Possible:

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

Unlikely:

- Clinical event, lab test with improbable time relationship to drug intake.
- Other drugs, chemical 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 DIPD.

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.

7.7 What should be reported?

For our monitoring purposes in Sierra Leone, reactions to be reported shall include all responses to medicines used in humans which are noxious (harmful) and unintended, including lack of efficacy or product quality suspicions which occur at any dose including the normal, overdose, misuse or abuse of a medicine.

Section 1**1.0 Rationale for Pharmacovigilance**

Drug safety monitoring gained worldwide attention following the thalidomide incident in the 1960s. Thalidomide was a drug given to pregnant 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 for close monitoring of the adverse effects of all of drugs used in Sierra Leone, it is possible to detect drugs causing unwanted ADR's and to control them. This can only be done effectively if health care professionals report all suspected ADR's to the DIPD.

The effectiveness of any Pharmacovigilance activity is dependent on the active participation of all health professionals. Health professionals are in the best position to report suspected ADR's observed in their every day practice. All health care professional should report suspected ADR's 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. There is therefore need for continuous monitoring for further safety assurance.

1.1 Definition of Terms

1. A Drug or medicine is:

A pharmaceutical product, used in or on the human body for the prevention (prophylaxis), mitigation, diagnosis and/or treatment of disease, or for modification of physiological function.

This definition includes prescribed medicines, over-the-counter medicines, vaccines, herbal medicines, traditional medicines and Biological (including blood and blood-related e.g. sera, plasma) and Cosmetics and Nutritional Agents.

2. The World Health Organization's definition for Adverse Drug Reaction (ADR) is:

“a response to a medicine which is noxious and unintended and which occurs at does normally used in man for the prophylaxis, diagnosis of disease or for the modification of physiological function”.

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 of the drug and may be “good” or “bad”.

3. An 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’.

4. An adverse Event/experience is:

“Any unwanted medical occurrence that may present treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment”.

E Check the known pharmacology of the medicine

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

7.6 Causality Classification

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

These criteria are defined as follows:

Certain

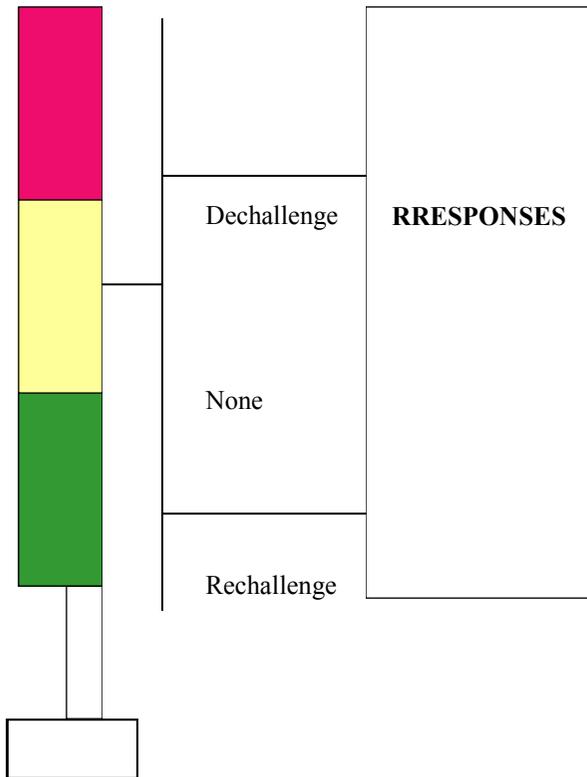
- Clinical event, lab test abnormality with plausible time relationship to drug intake.
- Cannot be explained by concurrent disease or other drugs/chemicals.
- Response to dechallenge = positive?
- Event must be definitive pharmacologically/immunologically.
- Positive rechallenge (if performed).

Probable/Likely:

- Clinical event, lab abnormally with reasonable time relationship to drug intake.
- Unlikely to be explained by concurrent disease, drugs/chemicals.
- Clinically reasonable response to withdrawal (Dechallenge).
- Rechallenges not required.

Effect of Dechallenge and Rechallenge should determined

(When necessary)



Yellow = No Action Taken
Red =dechallenge = withdraw of drug
Green =Rechallenge

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

Rechallenge = reintroducing the drug after 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 require serous ethical considerations.

The basic point here is that unwanted event occurs during or after the use of a drug. The term “adverse event” caused by the one encompassing ‘adverse drug reaction’. 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.

5. A 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 persistence or significant disability/incapacity,
- Causes a congenital anomaly or birth defect.
- Require an intervention to prevent permanent impairment or damage”.

6. A Side Effect is

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

Such effects may not be beneficial. Side effects are related to the known properties of the drug and we 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.

Health professionals must report all drug related problems to the DIPD.

7. An 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 ADR's even if they do not have all the information required.

8. A 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.

7.5 How to Recognize ADR's in My Patient?

ADR's are difficult and sometimes impossible to distinguish from the disease being treated since they may act through the same physiological and pathological pathway. However, the following step-wise approach may be helpful in assessing possible drug-related ADR's:

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

- A full drug 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 investigate to decide what the actual cause of any new medical problem is. A drug-related cause should be considered, especially when other causes do not explain the patient's condition.

B) Establish time relationship by asking and answering the following questions:

- Did the ADR immediately follow the drug administration?
- Some reactions occur immediately after the medication has 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 through physical examination with appropriate laboratory investigation (if necessary).

- Few drugs produce distinctive physical signs.
- Exceptions include fixed drug eruption, steroid-induced dermal atrophy, and acute extra-pyramidal reactions.
- Laboratory test are especially important if the drug is considered essential in improving patient care or if the laboratory test results will improve management of the patient.
- Try to describe the reaction as clearly as possible and where possible provide an accurate diagnosis.

7.3 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 relation 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) the WHO Collaborating Centre for international drug Monitoring. The names of the reporters or any other health professional and the patient will be removed before any details about a specific adverse drug reaction are used or communicated to others.

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

7.4 Why health professionals are in the best positions to detect and report on ADR's?

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 ADR's observed in their every day practice, because they are the people who diagnose, prescribe, dispense and monitor patients response medicines.

All health care 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 Drug Reactions including lack of effect.

SECTION 2

2.0 How Drug Safety is assured

All drugs undergo a significant amount of testing and evaluation before marketing to ensure their effectiveness as well as safety.

Marketed drugs undergo trials in animals (pre-clinical testing) and humans (clinical trials) to establish their efficacy, safety and quality.

2.1 Pre-marketing Evaluation

Pre-marketing involves animal studies and clinical trial in humans. 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 malfunctions 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 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 clinical trial is given below:

- Phase I—Single dose studies in healthy volunteers, using low doses of the drug. Subsequently, large doses and multiple sequences 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 evaluations have two significant drawbacks.

A Under-identification of adverse drug reactions

ADR's which occur infrequently, are difficult to identify. Statically, reactions with an incidence of less than 1% are frequently not identified.

B. Over-identification of ADR's

Many adverse drug reactions that are identified in pre-clinical studies are not proven to be related to the drug, but are nevertheless listed in the products literature as potentially causing the ADR's. This provides 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.

- 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 Leone.

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 risks associated with drug prescribing and administration and to ultimately improve patient care safety and treatment outcome.

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

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

Improvement on the quality of care offered to patients.

Reduction of drug related problems leading to better treatment outcome.

Improved patient confidence in the professional practice and consequently professional growth.

Improved knowledge access to feedback information on drug related problems reported within the country and internationally.

Satisfaction for the fulfilment of a moral and professional obligation.

Section 7

GUIDE TO REPORTING

7.0 Who should report Adverse Drug Reaction?

All health care professionals/ workers, including doctors, dentists, pharmacists, nurses, traditional medicine practitioners and other health professionals are requested to report all suspected adverse reactions to drugs including orthodox medicines, vaccines, X-ray contrast media, medical devices, cosmetics, traditional and herbal remedies, Nutritional Agents etc.

It is a vital to report an ADR to the DIP, PBSL even if you do not have all the facts or are uncertain that the medicine is definitely responsible for 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 drug. However, collection of reports from several health workers in different and parts of the country assists in making associations between drugs and particular adverse reactions.

7.1 What will happen to my Adverse 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 following:

2.2 Post-Market 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 manufacturers and health care professionals are responsible for post-market surveillance of these products. Drugs released to the market will be used not only more people, but also by different categories of people other than those in whom the drug was tested. The marketed drug will be used by those in whom 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 require long-term surveillance after marketing.

One of the most common methods of PMS is Spontaneous reporting using approved forms. In Sierra Leone, the DIPD issues Spontaneous reporting Forms, which health care professionals should use to report any suspected adverse drug reaction. Copies of the form can be obtained directly from the Drug Information and Pharmacovigilance Department PBSL Headquarters, Freetown.

SECTION 3

3.0 The Magnitude of the Problem

It has been demonstrated by a number of studies that medicine induced morbidity and mortality is a major to which health care professionals and the general public are becoming increasingly aware.

It has been estimated that DR's are the 4th to 6th largest cause of death in the USA (100,000 deaths per annum). Studies conducted in developed countries have consistently shown that approximately 5% of hospitalized patients will experience a serious ADR'S cause the death of several thousand patients each year.

The percentage of hospital admissions due to ADR's in some countries is about or more than 10%.

Norway	11.5%
France	13.0%
UK	16.0%

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

In addition, treatment of DR's imposes a high financial burden on health care. Some countries spend up to 15-20% of their hospital budget dealing with drug complication. A socioeconomic motive that needs to be urgently addressed.

Encainide (Enkaid)	Excessive Mortality	1987	1991
Flosequinan	Excessive Mortality	1992/1993	
Temafloxacin (Omniflox)	Hemolytic Anemia	1992	1992
Benoxaprofin (Oraflex)	Liver Necrosis	1982	1982
Mibefradil (posicor)	Fatal Cardiac arrhythmias	1985	1998
Terfendine (Seldane)	Fatal Cardiac Arrhythmias	1985	1998
Terfendine (Seldane)	Fatal Cardiac Arrhythmias	1985	1988
153 drug products withdrawn from the Sierra Leone Market	Substandard/Poor quality	1998	2004
Refacoxcib (Vioox)	Severe Cardiovascular Events	1999	2004

SECTION 6

6.0 How voluntary reporting of ADR's can new medicines tragedies from developing?

It took many before the deleterious effects of aspirin on the gastro-intestinal tract 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 of Spontaneous reporting and Testing

Generic Name (Brand Name)	Reason for with- drawal	Year of marketing	Year of withdrawal
Bromfenac (Duract)	Serious hapatotoxic effect	1997	1998

SECTION 4

4.0 What is the size and Severity of the ADR problem in sierra Leone?

While no studies comprehensively assessed the burden of adverse drug reactions on health care, it is likely that the problem is considerable in sierra Leone. There is very limited information available on DRS's. However, the National medicines Policy recognize 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 drugs, 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 drugs other than that from the pharmaceutical industry and the irrational use of drugs, compound the likelihood of a higher incidence of ADR's.

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

5.0 Why is Pharmacovigilance (PVG) needed in Sierra Leone?

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

- Diseases and prescribing practices
- Treatment seeking behavior e.g. self medication,
- Genetics, diet, traditional of the people e.g. high carbohydrate and fat diet, kola nut consumption etc,
- Drug 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 drugs (e.g. herbal remedies) which may pose specific toxicological problems, when used alone or in combination with other drugs, and
- Racial differences

Data derived from within the country have greater relevance and educational value and can assist PBSL to make evidence-based decisions. Information obtained in one country (e.g. the country of origin of the drug) 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 ADR's 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 drug safety through adverse drug reaction monitoring in Sierra Leone. The Drug Information and Pharmacovigilance Department in PBSL shall make the spontaneous reporting form available at all times. Health professionals are expected to report adverse reactions, lack of effects and other problems on a daily basis as a professional and moral obligation.