

**THE UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH**



**GUIDELINES FOR MONITORING AND
REPORTING ADVERSE DRUG
REACTIONS (ADRs)**

(Made under section 5 (c) of the Tanzania Food, Drugs and Cosmetics Act, 2003)

**Prepared by
TFDA
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ABBREVIATIONS

| | | |
|---------|---|--|
| ADRs | - | Adverse Drug Reactions |
| ICD | - | International Classification of Diseases |
| TFDA | - | Tanzania Food and Drugs Authority |
| UMC | - | Uppsala Monitoring Centre |
| WHO | - | World Health Organisation |
| WHO-ART | - | WHO Adverse Reaction Terminology |

PREFACE

Adverse drug reactions (ADRs) are inevitable consequences of pharmacotherapy. It is well known that all drugs carry the potential to produce both desirable and undesirable effects. No drug is absolutely safe under all circumstances of use or in all patients and ADRs may occur even if a drug is correctly selected and dosed.

In Tanzania ADR monitoring and reporting system is still weak hence serious and mild ADRs tend to go unreported. Many drug effects are highly subjective and a fraction of the total ADR burden in the country has not been recognized.

Section 5(c) of the Tanzania Food, Drugs and Cosmetics Act, 2003 provides for monitoring and reporting of existing and new adverse events including ADRs associated with the use of medicinal products in Tanzania. Implementation of this law obligates the Authority to carry out effective ADR monitoring and reporting activities which essentially embraces detection, assessment, understanding and prevention of ADRs. This exercise necessitates cooperation among all healthcare providers, drug registrants and manufacturers in the country.

The intention of these guidelines is therefore to provide guidance to all stakeholders who deal with manufacturing, selling, distribution and provision of healthcare services on how to monitor and report ADRs to the Tanzania Food and Drugs Authority (TFDA).

It is my sincere belief that you will find these guidelines very useful and that you will commit yourselves and cooperate in this imperative undertaking in order to safe guard the health of the people of Tanzania. Your active involvement and immediate response will certainly enable the TFDA take

prompt regulatory actions to protect even more serious ADRs that might occur to drug users.

Finally, TFDA will be highly indebted to receive your comments and experience gained from the use of these guidelines for future improvements.

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GLOSSARY OF TERMINOLOGY

1. Adverse Drug Reactions (ADRs)

A response to a medicinal product that is noxious or potentially harmful and unintended and which occurs at doses normally used in human for prophylaxis, diagnosis or therapy of a disease or for the modification of physiological function in which individual factors may play an important role.

2. Adverse event or experience

Any unfavourable medical occurrence that in coincidence may present during treatment with a pharmaceutical product, but which does not necessarily have a causal relationship with the treatment.

3. An Adverse Drug Reaction (ADR) Case Report

A case report in ADR monitoring programme is a notification relating to a patient with an adverse effect or laboratory test abnormality suspected to be induced by a medicinal product

4. Benefit/risk analysis

Examination of the favourable (benefit) and unfavourable results of undertaking a specific course of action

5. A drug or a medicinal product

Any substance or mixture of substances manufactured, sold or presented for use in:

- i. the diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical or mental state, or the symptoms thereof, in human or animal.
- ii. restoring, correcting or beneficial modification of organic or mental functions in human or animal.

6. Health care professionals

For the purposes of reporting suspected ADRs, these include specialists, medical practitioners, pathologists, dentists, pharmacists, nurses, medical assistants, pharmaceutical technicians, pharmaceutical assistants, etc.

7. Herbal drugs

Any labeled preparation in pharmaceutical dosage form that contains one or more substances of natural origin that are derived from plants as active ingredients.

8. Life-threatening reaction

A reaction in which the patient was at risk of death at the time of the event and does not refer to an event, which hypothetically might have caused death if it was more severe.

9. Serious adverse drug reaction

A noxious and unintended response to a drug that at any dose, result in death, is life-threatening (such as Stevens-Johnson Syndrome), requires patient hospitalization or prolongation of existing hospitalisation, causes a congenital anomaly or birth defect, results in persistent or significantly disability or incapacity, or require intervention to prevent permanent impairment or damage.

10. Side effect

Any unintended effect of a pharmaceutical product occurring at doses used in man which is related to the pharmacological properties of the product and in which there is no deliberate overdose.

11. Signal

Reported information (at least 3 spontaneous case reports) on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously.

12. Unexpected adverse drug reaction

An adverse reaction, the nature or severity of which is not mentioned in the summary of product characteristic or market authorization, or expected from characteristics of the drug.

CHAPTER ONE

INTRODUCTION

Adverse Drug Reactions monitoring is a process of continuously monitoring of undesirable effect suspected to be associated with use of medicinal products. It facilitates collection of unbiased safety data observed during clinical practice in 'real life' circumstances.

The guidelines have been developed to assist health care professionals on understanding the importance of ADRs monitoring, procedures of reporting an ADR and the four essential components of an ADRs case report to improve drug safety. The essential components include information about the patient, description of the adverse drug reactions, the suspected drug(s) and the reporter.

The System of ADRs notification in Tanzania is a centralised reporting, whereby suspected case reports of ADR are reported by health care professionals and pharmaceutical manufacturers to TFDA.

Public health programmes, such as Malaria, Human Immuno Deficiency Virus/Acquired Immuno Deficiency Syndrome (HIV/AIDS), Tuberculosis (TB) and Leprosy, Parasitic infections and vaccines should introduce ADR reporting in their programmes. This should include sensitizing health workers during seminars and trainings to report adverse drug reactions. Close collaboration between TFDA and these programmes is necessary.

It is mandatory for pharmaceutical manufacturers or product registrants to monitor their products in the market and report any suspected undesirable effects to TFDA.

ADR reporting covers all pharmaceutical products, biologicals, herbal drugs, cosmetics and medical devices circulating in the Tanzanian market. For those

conducting clinical trials phase I – IV it is mandatory to report all adverse event encountered to the Authority.

The current Tanzanian system of ADR notification is a modified model of WHO. This system is a long established, cost effective and useful method for detecting signals by identifying previously unknown adverse reactions to medicinal products or changes in the patterns of known adverse effects which aim at ensuring that patient obtain safe and efficacious medicinal products and other pharmaceutical products. Where necessary, epidemiological studies may be conducted in collaboration with research institutions to substantiate generated signals.

In addition, drug monitoring is important in detection of lack of efficacy, detection and prevention of counterfeit and substandard products in clinical practice. It is essential that the ADR monitoring program for safety of medicinal product be supported by health care professionals

All adverse reactions should be considered reportable according to the requirements outlined in these guidelines and key players to this activity are all health care professionals, preferably those directly associated with the care of patients/consumers

Disadvantage of not reporting may result in deleterious effects of a medicinal product not being noticeable for a long time or the association became clear worldwide e.g. Aspirin in the Gastro-intestinal tract, amydopyrine in agranulocytosis, phocomelia with thalidomide. For the same reason it may take too long before it is recognised that prolonged abuse of a medicinal product can produce deliberate health effects e.g. Phenacetin in renal papillary necrosis

Therefore, proper implementation of these guidelines will help to reduce the harmful effects resulting from use of medicinal products by early detection of drug safety problems in patients, assessing the risk benefit in an individual and

the population, improving the selection, rational use of drugs through provision of timely warning to healthcare professionals.

The guidelines give brief definitions related to ADR monitoring and classification based on etiology. It highlights the importance of monitoring and reporting procedures. Principles of efficient reporting by healthcare providers, data handling and analysis have also been covered.

CHAPTER TWO

OBJECTIVES OF ADVERSE DRUG REACTIONS MONITORING

Rationale for ADRs Monitoring

Information on safety and efficacy of a pharmaceutical product once it is marketed is limited to premarketing evaluation, clinical trials (phase I, II and III), animal tests and other factors in the product development process.

1. Phase I trial – Single dose studies in healthy volunteers, using low doses of the drug. Subsequently, larger doses and multiple sequences, the pharmacological and pharmacokinetics properties of a drug are evaluated
2. Phase II trial – Efficacy is the primary objective of this phase, but safety is also continuously monitored and evaluated.
3. Phase III trial – Evaluation of safety in a group of patients with the disease.

Each phase involves increasing number of patients and by the end of full pre-marketing clinical trial about 5,000 patients would have taken the drug. However, there is a problem of whether clinical trial involving 5,000 people provides enough information to extrapolate the safety of new drug to millions of people.

Therefore, premarketing safety evaluation of pharmaceutical products at the time of registration is inherently limited due to the following three reasons:

1. The population in phase III clinical trials is very selective and limited. Many types of patients with different characteristics are often excluded from studies, such as patients in certain age groups and pregnant women, patients with diseases other than the one being treated and patients using other drugs concomitantly. This often prevents the identification of side

effects caused by interaction of more than one drug given at the same time. Statistically, reactions with an incidence of less than 1% are frequently not identified.

2. The duration of clinical trial is too short. Such studies do not allow the detection of adverse effects that appear after long periods of use or exposure, especially with chronic medication e.g. oral contraceptives.
3. **Differences between countries which lead to variation in patient factors, variation in drug utilisation among health care professionals, variation in drug manufacturing processes used which influence pharmaceutical quality and composition of locally produced products and those imported outside the country**

Post Marketing Surveillance

It is not possible to identify all safety-related problems that may exist with drug during premarketing test and evaluation.

For these reasons, it is obvious that safety monitoring of a drug is carried out through the life cycle of each medicinal product. TFDA, pharmaceutical product registrants and health care professionals are responsible for post-marketing surveillance of these products. One of the most common methods of Post Marketing Surveillance is ADRs monitoring

Objectives of ADRs Monitoring

1. To detect the nature and frequency of ADRs including periodic re-evaluation of the benefit-risk ratio of medicinal products in order to assist the drug regulatory authority, public health programs, scientists and consumer society take appropriate action to minimise risks of ADRs to consumers by:

- i. Providing updated drug safety information to health care professionals and other stakeholders including WHO ADRs Monitoring Centres
 - ii. Upgrading package insert, design appropriate package insert information and dissemination of information which may constitute institution of recall or withdrawal of the product in the market or restrictions for marketing
 - iii. Dissemination of information by designing proper education program to consumers and other users
 - iv. Initiation of further studies for education value. For example benefit of the drug especially in long term for prevention of relapse or study of new indication, overuse, possible mechanism underlying the adverse reaction observed or misuse (utilisation pattern)
2. To identify risk factors that may predispose, induce or influence the development, severity and incidence of adverse reactions in the population of Tanzania, examples;
- i. **Patient factors: genetics, racial differences, diets, diseases, prescribing practices, culture of drug use and traditions of the people e.g. high carbohydrate, fat diet etc.**
 - ii. **Drug interactions, drug distribution, storage and use including indications, dose, availability and other underlying conditions.**

CHAPTER THREE

THE PHARMACOLOGICAL BASIS OF ADVERSE DRUG REACTIONS AND INTERACTIONS

ADR is an unexpected consequence of drug usage and its risk of occurrence can not be predetermined. Almost all effective drugs, no matter how skilfully used, may cause adverse reactions. The fact that an adverse reaction has occurred does not reflect in any way discredibly on the health care professional who prescribed, dispensed or sold the drug.

1. Classification of ADRs (etiological basis)

In many cases no specific reason can be given as to why a particular patient develops an adverse drug reaction, while another patient does not. With some relatively toxic drugs, adverse reactions are the rule rather than the exception. Four special etiological factors can however be defined. They comprise of inherent anomalies in patient response (allergic or idiosyncratic), acquired patient anomalies, anomalies of drug presentation and administration, and interactions.

1.1 Inherent anomalies in patient response (allergic or idiosyncratic)

(a) Drug allergy (hypersensitivity):

Reactions are due to genetic factors and physiological variables such as age, sex and pregnancy. Drug allergy is mediated by immunological mechanisms. Characteristics of allergic reactions;

- i. are not correlated with the known pharmacological effects
- ii. can be precipitated by small amounts of drugs
- iii. repeated exposure will cause recurrence of reactions
- iv. often include skin rash, angioneurotic oedema, serum sickness and anaphylaxis or asthma.

Factors affecting the incidence of allergic reactions are the drug, the patient and the disease for which the drug is given.

(b) Genetically determined ADRs (idiosyncratic):

The major genetically determined ADRs can be divided into two types;

- i. Reactions due to altered pharmacokinetic handling of the drug in the body
- ii. Reactions due to altered tissue responsiveness.

1.2 Acquired patient anomalies

These reactions are due to the presence of intercurrent illness, which may unmask pharmacological effects that are not apparent in normal individuals. For examples, haemorrhage or perforation of the peptic ulcers due to aspirin or corticosteroids. Liver disease may impair drug detoxification and renal disease which impairs glomerular filtration leading to reduced elimination of drugs that undergo renal excretion.

1.3 Anomalies of drug presentation and administration

These reactions may be a consequence of excessive response, alterations in bioavailability or an inappropriate method of administration. There are three main potential sources of ADRs in this class. They include decomposition of active constituents, effects of by-products of the active constituents derived from chemical synthesis and effects of additives, solubilizing, stabilizing, colouring agents and excipients commonly incorporated in pharmaceutical preparations. Therefore, alteration in production methods may have marked adverse effects consequences.

1.4 Drug interactions

These are ADRs resulting from interactions of more than one drug given at the same time and are likely to be proportional to the number of drugs given. However, some drug interactions may have both unwanted consequences and certain benefits (e.g. potentiation). The frequency of adverse drug interactions in clinical practice makes it mandatory for health care professionals to know the principle drugs and mechanisms of interactions involved.

2. Predisposing factors of ADRs and the mechanisms of drug interaction

Many reactions occur early in the course of treatment (such as anaphylaxis after penicillin injection); some other reactions may develop over a prolonged period of treatment (such as osteoporosis with oral steroids); the other reactions may appear long after the drug is discontinued (such as vaginal adenocarcinoma due to diethylstilbestrol given to the mother).

The following are predisposing factors of ADRs:-

2.1 Age

The incidence of adverse drug reaction appears to be highest in the very young and very old people. In these two extreme periods of life, there is poorly developed and altered physiological function respectively. Therefore, metabolism and elimination of some drugs may be delayed.

2.2 Pathophysiological conditions

Intercurrent diseases may alter the pharmacokinetic handling of a drug, its tissue sensitivity or the response to a drug. That is, diseases can alter drug absorption, metabolism, elimination and the body's response to drugs.

2.3 Amount of drug administered

An excessive response to drug or prolonged therapy may be a predisposing factor for ADRs. Over dosage is often relative rather than absolute because the individual response to a drug varies.

2.4 Sex

Several studies have shown that for some drugs women are more likely to suffer from ADRs than men. This is due to pharmacokinetic and or pharmacodynamic sex-related factors.

2.5 Previous history of allergy

Patients who have previously suffered an allergic drug reaction appear to be more susceptible than others to allergic ADRs in general. Heredity may make some people more susceptible to the toxic effects of certain drugs.

2.6 Racial or Genetic Factors

There may be racial differences in the incidence of some type of ADRs or some individuals have a genetically determined response to development of ADRs. e. g. ethnopharmacological difference such as glucose 6-phosphate dehydrogenase deficiency, which predisposes to some drug induced haemolytic anaemia, is commoner amongst Africans, Kurdish and Iraqi Jews, some Mediterranean people and Filipinos and is relatively infrequent amongst other races.

2.7 Multiple Drug Therapy (Polypharmacy)

The incidence of ADRs increases with the number of drugs given due to risk of interactions. Interaction between prescribed drugs is therefore an area, which is of concern to every health care professional.

The following are the mechanisms of drug interactions: -

- (a) Direct physical or chemical interactions of more than one drug given concomitantly.
- (b) Altered gastrointestinal absorption, competition for protein binding sites or receptors.
- (c) Increased or decreased metabolism of a drug by induction, activation or inhibition of drug metabolizing enzymes.
- (d) Alteration of acid-base equilibrium thereby influencing drug distribution and renal clearance.
- (e)** Alteration of haemodynamics or renal function that influences rates of renal excretion.

CHAPTER FOUR

PROCEDURE FOR REPORTING ADVERSE DRUG REACTION

Health care professional should bear in mind when reporting an ADR that ADR reports are, for the most part, only suspected associations that a drug has caused a particular adverse event. Reporting an ADR does not imply a causal association between the drug and the adverse reaction. However, in a doubtful case it is better to report than not to report.

1. WHAT TO REPORT

Any undesirable adverse event suspected to be associated with use of drug, biological (including blood products), herbal drugs, cosmetics or medical devices should be reported. They should include;

1. All ADRs as a result of prescription and non-prescription
2. All suspected adverse drug reactions regardless of whether or not the product was used in accordance with the product information provided by the company marketing the product
3. Unexpected reaction, regardless of their nature or severity, whether not consistent with product information or labelling
4. An observed increase in frequency of a given reaction
5. A serious reaction, whether expected or not
6. All suspected ADRs associated with drug-drug, drug-food or drug-food supplements interactions
- 7. ADRs in special field of interest such as drug abuse and drug use in pregnancy and during lactation**
- 8. ADRs occurring from overdose or medication error**
- 9. Unusual lack of efficacy or when suspected pharmaceutical defects are observed**

What information is required for an ADR case report?

The minimal standard information to be provided for proper assessment of the ADR case report are;

- 1. Patient information**
- 2. Adverse reactions description (include laboratory results if available)**
- 3. Information related to the suspected drug(s)**
- 4. Information on management of the adverse reactions**
- 5. Information about the reporter**

Reporters are advised to study carefully and adhere to the guides on how to complete an ADR reporting form for proper interpretation. (See ADR reporting form annexed).

I. Patient information

1. *Patient identity*: indicate initials or record number of the patient in hospital, medical institution, dispensary, clinic or pharmacy.
2. *Birth dates or age*: indicate date, month and year
3. *Sex*: Male or Female
4. *Weight*: should be in Kilograms

II. Adverse reaction(s)

1. *Brief description of the ADR(s)*: indicate the adverse(s) reaction by marking X in the appropriate box. Preferably describe briefly the nature of the adverse reaction being reported but as clearly as possible, including the body site and severity.
2. *Time/date of onset of the adverse reactions*: State the time of onset or the occurrence of the adverse reaction in relation to the administration of the drug. Indicate the date of onset in the following order; day, month and year. For example, did the drug reaction appear immediately following drug administration or there was temporal or spatial correlation with administration.
3. *Other relevant information*:
 - i. Patient medical history or laboratory data including dates if available, considered relevant to the case or the adverse reaction being reported should be entered.
 - ii. Mention appropriate laboratory tests done to the patient and results to confirm the adverse reaction.
 - iii. State this concisely but clearly.

III. Suspected drug(s)

1. *Name of the suspected drug (s):* trade name should preferably be used, if trade name not available, generic name may be used. Strength of the drug (s) should be stated
2. *Dosage, frequency and route of administration* should be clearly notified.

For example;

- i. Dosage (specify dosage form; tablet, capsules, syrup, injection, cream, eye drops, etc. including total amount of drugs).
- ii. Frequency: specify unit first i.e. mg, ml, mg/kg and number of time given e.g. 4 times daily or q.i.d.
- iii. Route of administration by which the drug was administered. This should be entered in full term or abbreviated using the World Health Organisation (WHO) codes as follows: -

| ROUTES | CODES | ROUTES | CODES |
|-----------------|--------------|--------------------------------------|--------------|
| Buccal | BU | Intrathecal | IT |
| Conjunctival | CO | Intratracheal | TR |
| Dental | DE | Intrauterine | IU |
| Implant | MP | Intravenous | IV |
| Inhalation | IH | Intravesical | IB |
| Insufflation | IS | Per oral | PO |
| Intra-arterial | IA | Per rectal | PR |
| Intra-articular | IR | Subcutaneous | SC |
| Intra-cardiac | IC | Sublingual | SL |
| Intradermal | ID | Systemic (if route is not Specified) | SY |
| Intramuscular | IM | Topical (external) | TO |
| Intranasal | IN | Transmammary transfer | TM |

| | | | |
|-----------------|----|----------|----|
| Intraperitoneal | IP | Urethral | UR |
| Intrapleural | IL | Vaginal | VA |

3. *Therapy date*: the dates of beginning and termination of the administration of each drug should be stated, and preferably recorded as follows:- date, month and year. If dates are not available, record duration of treatment. If drug administration has not been terminated at the time of reporting, state 'Continuing'
4. *Batch number and expiry date*: provide these information if are available
5. *Reason for use*: state indication or condition for which the drug(s) was given for.
6. *Particular of concurrently drugs(or other treatment)*: state particulars of other drug (s) administered by the patient concurrently with the suspected drug, including drug administration for at least 1 month back with dosage, route of administration, duration of administration and indications.
7. *Provide relevant information on medical devices*

IV. Management of the adverse reaction

1. *Confirmation of the ADRs*: indicate what assisted in confirming the suspected adverse reactions. For example:
 - i. Drug reactions confirmed by disappearance of the reaction after stopping administration of the drug or reducing the doses.
 - ii. Recovery on withdrawal of suspected drug(s) if no other drug is withdrawn and no therapy given.
 - iii. Recovery follows treatment of the reaction in addition to withdrawal of drug.
2. *Mention the criteria* for regarding the reaction as serious
3. *Mention any treatment given* to the patient after experiencing the ADRs.
4. *Outcome*: indicate the outcome of the adverse reaction by marking X in the appropriate box with dates in case of fatal outcome.

V. Reporter information

Details on reporter of an ADR: mention your particulars:-name, address of the health facility (hospital, institution, dispensary, clinic, company, pharmacy or maternity home). E-mail address (optional), signature, telephone number and date of reporting the reaction (indicate date, month and year)

2. WHO SHOULD REPORT

Submission of a report does not constitute an admission that a health care professional or the drug or the product caused or contributed to the ADR in any way as all reports are termed as suspected.

Reporters should bear in mind that any information related to the reporter and patient identities shall be kept confidential.

The following should provide reports of any case of suspected ADRs when encountered to the patient as part of their professional responsibility:-

1. All health care professionals in Tanzania including specialists, doctors, dentists, pharmacists, nurses, assistant medical officers, clinical officers, pharmaceutical technicians, pharmaceutical assistants, traditional medicine practitioners and others health care providers
2. Manufacturers or Product registrants
They should develop system for ADR follow-up within their company and assessment of impact of notification of significant safety data on their products.
3. All government hospitals, private hospitals, health centres, dispensaries private clinics, private pharmacies and private nursing homes have obligation to report all ADR cases encountered or reported to them by the patients.

Incharge of the following facilities; government and private hospitals, health centres and dispensaries they are required to nominate a focal person who will coordinate the ADRs collection and reporting within the facility.

This person will be a link between the institution and TFDA

It is vital to report an ADR to TFDA even if you are doubtful about the precise relationship with the given medication or you do not have all the facts. What is required is to report all SUSPECTED ADRs.

Collection of reports from several healthcare providers in different parts of the country assists in making associations (strengthening of signal) between a particular drug and the adverse reaction.

Therefore, you must ensure that all necessary information for submission of ADR reports are obtained and reported through the reporting forms.

3. WHEN TO REPORT

Any suspected ADR should be reported as soon as possible. Delay in reporting will make reporting inaccurate and unreliable. If possible, report while the patient is still in the health facility this gives a chance to reporter to clear any ambiguity by re-questioning or examining the patient

4. HOW TO REPORT

Reporters should send accurate information to achieve a better and efficient program on ADRs monitoring in Tanzania.

1. Send your report in a standardised form for reporting ADRs. The reporting form is self adhesive postage paid “yellow form”
2. Dully fill in the ADRs reporting form (annexed) when encountering an ADR to the patient.
3. Use a separate form for each patient (refer to filling guides)
4. A completed ADRs case report form should immediately be sealed and mailed preferably directly to TFDA within three days or through other reporting centres for onward transmission to the TFDA
5. Reports can also be submitted online by going to the TFDA website <http://www.tfda.or.tz> and clicking on “adverse drug reaction reporting” on the bottom-right

6. Reports may be sent by e-mail through the following e-mail address; adr@tfda.or.tz
7. ADR reports may be faxed in cases of perceived urgency
8. Any follow-up information for an ADR case that has already been reported can be sent on another ADR form, or communicated by telephone, fax or e-mail. To enable this information be matched with the original report it is very important that follow-up reports are identified and the following should be indicated in the report;
 - i. that it is a follow-up information,
 - ii. the date of the original report and
 - iii. the patient identities.

Basic principles of efficient reporting

1. Report the adverse reaction immediately after it occurs.
2. If possible, take the decision to report whilst the patient is still with you, so that the details can be filled in at once on the reporting form.
3. Think about any other factors which may contribute in causing the event such as other prescribed drugs, self-medication, herbal products, food, chemicals, ask the patient particularly about other medicines taken.
4. If you get any supplementary data later, e.g. if the same patient develops the effect again or if something happens which increases your suspicion or seem to exclude the reaction, please send in a supplementary note immediately using ADRs reporting form with the patient identifiers.
5. All reports must have the following four data elements
 - i. An identifiable patient
 - ii. A suspected adverse effect
 - iii. A named suspected drug (s)
 - iv. An identifiable reporter
6. Always write legibly.

5. WHERE TO REPORT

Report any suspected ADRs for pharmaceutical products marketed in Tanzania to the appropriate channels as follows:-

1. Preferably directly to TFDA by post or online
2. Via Zonal Drug Information Centres at Muhimbili National Hospital (MNH), Mbeya Consultant Hospital, Bugando Medical Centre (BMC) and Kilimanjaro Christian Medical Centre (KCMC), for onward transmission to TFDA
3. Via a focal person in the following health facility; government hospitals, private hospitals, health centres, dispensaries for onward transmission to TFDA

How to obtain the reporting form?

The ADR reporting form is obtained free of charge from;

1. TFDA offices
2. The website of TFDA, downloaded at <http://www.tfda.or.tz>
3. Zonal Drug Information Centres.
4. Regional hospital, district hospitals and ADRs focal persons in hospitals, health centres, clinics and dispensaries.

CHAPTER FIVE

PROCESSING OF COLLECTED ADVERSE DRUG REACTION DATA

1. ASSESSMENT OF ADR CASE REPORTS

Assessment of case report aim at identifying national drug safety problems and respond to these through communication and or scientific risk/benefit assessment.

TFDA is responsible with continuous collection, assessment and storage of reports of, suspected adverse reaction to medicinal products marketed in the country.

Reports are initially separated according to their source. All case reports will be individually assessed and the following shall be considered: -

1. Quality of documentation in respect to completeness on the four elements of a case report as possible, integrity of data, quality of diagnosis and follow-up.
2. Analysis; this shall be based on the temporal relationship between the reaction and the drug, whether there was positive dechallenge/rechallenge, the seriousness of the reaction, whether the current labelling lists the reaction and whether the reaction is reported on the medical literature.
3. Clinical relevance in respect to detection of new reaction especially for new drugs, unknown reactions or serious. If similar cases are found, the report becomes a monitored adverse drug reaction.
4. Quality control in respect to identification of duplicate reports. Certain characteristics of a case report for example; sex, date of birth or age, name of the suspected drug, dates of drug exposure etc. shall be used to identify duplicate reporting or follow up report.
5. Causality assessment and transmission of the assessed reports in suitable format to the WHO database of International Drug Monitoring at Uppsala Monitoring Centre (UMC) shall be done monthly.

The causality assessment and ADR coding shall be based on WHO causality categories. The categories are based on four considerations:-

- i. The association in time between drug administration and event
- ii. Pharmacology (including current knowledge of nature and frequency of adverse reactions)
- iii. Medical or pharmacological plausibility (signs and symptoms, laboratory tests, pathological findings, mechanism)
- iv. Likelihood or exclusion of other causes

The Coding; drug names shall be entered in a systemic way by using the WHO Drug Dictionary and preferably the trade name of the suspected product shall be used. Diseases will be classified based on International Classification of Diseases (ICD) developed by WHO. The adverse events description shall be entered based on the WHO Adverse Reaction Terminology (WHO-ART).

6. Generation of hypotheses or the identification of signals. This activity shall be strengthened by a search from the cumulative data in the global WHO database for similar report.
7. Presentation of analysed case reports to the TFDA Drug Committee. This committee of experts shall be responsible for evaluation and interpretation of the compiled coded case reports and giving advice on appropriate interventions.
8. Receipt and communication of appropriate safety information resulting from analysis of local reports, from UMC, other national Centre, regulatory agencies and literature.

2. HANDLING OF ADR DATA

An acknowledgement letter or note will be sent to the reporter for every ADR report received with an additional reporting form.

The ADR reports shall be stored in a confidential database at TFDA and analysed report sent to the WHO database of International Programme on safety monitoring of drugs to which all case reports received by the National centres are sent.

The names of reporter and the patient will be removed before any details about a specific adverse drug reaction are used or communicated to others. Publications will not disclose trade name of products unless regulatory actions have been taken. In this regard information obtained from spontaneous ADR monitoring system will not be used for commercial purposes. The information is only meant to improve our understanding on use of medicinal products by reducing the risks associated with drug prescribing and administration and to ultimately improve patient care, safety and treatment outcome. In the same way suspected ADR reports cannot be used in a court of law under any circumstances.

TFDA is responsible for providing reporting forms, collecting, analysing and communicating the findings and evaluation reports. TFDA shall use the finding from the reporter for making regulatory decisions on how to prevent or minimise the risk of ADRs from the use of pharmaceutical products circulating in the country.

TFDA may communicate the findings, recommendations and directives to appropriate organisations or individuals. These include, healthcare professionals, pharmaceutical manufacturers, public health programmes within the country, other public and private health institutions, the media and the public.

Provision of feedback to reporters

The outcome of the report, together with any important or relevant information relating to the reaction reported, will be communicated to the reporters and other parties as appropriate.

After a significant ADR is detected and a decision on the course of action determined, the information shall be communicated rapidly and systematically to healthcare providers and product registrant.

In addition, healthcare professionals will have an increased advantage of access to feedback information on reaction to drug within the same pharmacological class reported within the country and internationally and availability of additional database for further investigation.

3. UTILISATION OF ADR DATA

Data collected will be used for provision of timely advice to health-care professionals and consumers on drug safety issues at facility level, national and international level. A well-documented adverse drug reaction case could result in one or more of the following;

1. Further investigation of signals. For example, identifying 'at risk' group, a dose range which might be more suspected, suggesting a pharmaceutical group effect, pharmacological mechanisms, lack of effect by a particular drug or investigation into the use of a drug in the country
2. Drug regulation and dissemination of information of current importance
3. Education and training initiatives to improve the safe use of the medication and other health promotion interventions as the situation may warrant including change in supply status or withdrawal

Report on drug problems from healthcare provider can prevent new drugs tragedies or can reduce suffering and save lives of thousands of patients.

REPORT OF SUSPECTED ADVERSE DRUG REACTION INCLUDING BIRTH DEFECTS

TANZANIA FOOD AND DRUGS AUTHORITY

Note: Identities of reporter, patient and institution will remain confidential

PARTICULARS OF PATIENT

Patient Initials or Record No.: _____ Sex: _____
 Date of Birth (DD-MM- YYYY) or age:- _____ Weight in kg:- _____

DETAIL OF ADVERSE DRUG REACTION

| | | | |
|---|--|------------------------------------|--|
| <input type="checkbox"/> Headache | <input type="checkbox"/> Shock / anaphylaxis | <input type="checkbox"/> Skin rash | Date Reaction Started → _____/_____/_____ Date Reaction Stopped (if known) → _____/_____/_____ _____ |
| <input type="checkbox"/> Diarrhoea | <input type="checkbox"/> Nausea or vomiting | <input type="checkbox"/> Others | |
| Description of reaction (if possible)..... | | | |

Other relevant information: e.g. medical history, allergies, pregnancy, smoking, alcohol use, etc. **Please enclose any relevant laboratory results including dates (if done)**

.....

.....

III. DETAILS OF SUSPECTED DRUG (S) AND ALL OTHER DRUGS USED

| Name of suspected drug(s) (Please specify brand name if known) | Dosage | Frequency | Route | Therapy Date | | Batch. No & Expiry date (If known) | Reason for use |
|---|--------|-----------|-------|--------------|------|---------------------------------------|----------------|
| | | | | Start | Stop | | |
| 1. | | | | | | | |
| 2. | | | | | | | |
| 3. | | | | | | | |
| Other drugs (including herbal medicines consumed at the same time and or 1 month before) | | | | | | | |
| 1. | | | | | | | |
| 2. | | | | | | | |
| 3. | | | | | | | |

IV. MANAGEMENT OF ADVERSE REACTION

Reaction subsided after stopping the suspected drug/reducing the dose: Yes No Unknown

Reaction reappeared after reintroducing drug: Yes No Not applicable

Do you consider the reaction to be serious? Yes No

If yes, please indicate why the reaction is considered to be serious **(please tick all that apply)**:

| | |
|---|---|
| <input type="checkbox"/> Patient Died due to reaction | <input type="checkbox"/> Required or prolonged hospitalization |
| <input type="checkbox"/> Is life threatening | <input type="checkbox"/> Causes irreversible disability or incapacity |
| <input type="checkbox"/> Causes a congenital anomaly | <input type="checkbox"/> Others, please give details..... |

Treatment of adverse reaction Yes No **(if yes please specify)**:.....

Outcome of the reaction Not yet recovered Recovered Fatal (Date of death): _____/_____/_____

| V. PARTICULARS OF REPORTER (HEALTH CARE PROVIDER) | | | | | | | | | | | | |
|---|---|--|--|--|--|--|--|--|--|--|--|--|
| Name: _____ | Profession: _____ | Name and Address of the health facility: _____ | | | | | | | | | | |
| Contact phone No: _____ | E-mail: _____ | _____ | | | | | | | | | | |
| Signature: _____ | Date of this report: ____/____/____ | _____ | | | | | | | | | | |
| <input type="checkbox"/> Please tick if you wish to receive information about other local reports associated with the suspected drug(s) | | | | | | | | | | | | |
| Thank you for your cooperation | Submission of an ADR case report does not discredit the competence of the reporter. | Ref No. (for official use) <table border="1"> <tr> <td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td> </tr> </table> | | | | | | | | | | |
| | | | | | | | | | | | | |

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Guide to filling the form

How to report?

- Dully fill in the form as required
- Use a separate form for each patient
- Report direct to TFDA through the following addresses:-



Mail : Tanzania Food and Drugs Authority,
P. O. Box 77150, Dar es Salaam



Fax:: 22- 2450793



Phone: 22-2450512 / 2450751



Internet; <http://www.tfda.or.tz>
E-mail: adr@tfda.or.tz

The ADR reporting form and the guidelines are also available for downloading at <http://www.tfda.or.tz>

An Adverse Drug Reaction (ADR) is defined as a reaction which is noxious and unintended, and which occurs at doses normally used in human for prophylaxis, diagnosis, or therapy of a disease, or for the modification of physiological function.

What to report?

Please report all undesirable patient effect suspected to be associated with drugs, cosmetics or medical devices use.

Report even if:

- You're not sure that the product caused the event
- You don't have all the details

When to report?

As soon as possible

Submission of follow-up reports:

Any follow-up information for an ADR that has already been reported can be sent on another ADR form or it can be communicated directly to TFDA by telephone, fax or e-mail. Please indicate that it is a follow-up report.. It is very important that follow-up reports are identified and linked to the original report.

Moisten gum and fold. For maximum adhesion, press down for few seconds

←····→ Second Fold ←····→

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TO: THE DIRECTOR GENERAL
TANZANIA FOOD AND DRUGS AUTHORITY
P. O. BOX 77150
DAR ES SALAAM