

TANZANIA

9. The pharmacovigilance system in Tanzania

1 E-learning objectives

At the end of this session, participants should be able to recognize the different roles of various parties in PV in Tanzania

2 The History

The **national PV system** in **Tanzania** was first established in 1989 as a drug information center known as the Tanzania Drug and Toxicology Information Services (TADATIS), in Muhimbili National Hospital. Among the key functions of TADATIS were promoting, reporting and analyzing ADRs.

In 1993 Tanzania officially became member of the WHO International Drug Monitoring and all Tanzanian ADR reports were submitted to the World Health Organization's global database. In 1998, TADATIS became the Tanzania Food & Drug Authority. In 2019 became TMDA (Tanzania Medicines and Medical Devices Authority)

3 What's TMDA?

TMDA is an Executive Agency under the Ministry of Health, Community Development, Gender, Elderly and Children (MOHCDEG) with headquarters in Dar Es Salaam. TMDA is responsible for regulating safety, quality and effectiveness of **medicines, medical devices and diagnostics**. TMDA main responsibility is stated in the Health policy, 2007, and its mandate is stipulated in the Tanzania food, drugs and cosmetics act (TFDCA) cap. 219.

In order to improve public service delivery, TMDA is managed as an Executive Agency in accordance with the Executive Agencies Act, cap. 245 as amended in 2009. (TMDA, web: <https://www.tmda.go.tz/>; e-mail address: info@tfda.go.tz).

4 Roles of various parties in pharmacovigilance

The National Pharmacovigilance Centre

The National PV centre, that oversees overall PV activities of the whole country, is where the TMDA headquarter is located (Dar Es Salaam).

. The centre is under custodian of TMDA and acts as the central coordination point for the Zone Pharmacovigilance centre. The main tasks of the National Pharmacovigilance Centres are:

- developing and reviewing ADR forms and collecting reports of suspected adverse reactions of medicines and other products on the market (medical devices and diagnostics);
- conducting causality assessment and analyzing adverse reactions reports;
- generating hypotheses or identifying signals of adverse drug reactions and communicating with the authority for action.

TMDA headquarter

TMDA **tasks** of the pharmacovigilance staff at the headquarter include:

- collecting and communicating relevant safety information to all stakeholders;
- providing feedback to reporters (e.g. issuing ADR Bulletins/Newsletters etc), including alerting prescribers, manufactures and the public to new risks of adverse reactions;

- monitoring and evaluating all pharmacovigilance activities in the country;
- uploading the Tanzanian ADR reports into the global pharmacovigilance database (VigiBase®);
- carrying out inspections to ensure company pharmacovigilance systems comply with good pharmacovigilance practice;
- each year the Authority shall make public a list of the medicinal products for which the market authorisation has been refused, revoked or suspended in the Union, whose supply has been prohibited or which have been withdrawn from the market, including the reasons for such action.

TMDA Zone Offices

Seven TMDA Zone Offices: these are located in Mwanza (for Lake Zone) Arusha (for Northern Zone), Mbeya (for Southern Highlands Zone), Mtwara (for Southern Zone), Dodoma (for Central Zone), Tabora (for Western Zone) and in Dar-es-Salaam (serving Eastern zone).

The TMDA Zone Officers shall:

- planning and budgeting for pharmacovigilance activities in the respective zones;
- working in collaboration with zonal pharmacovigilance centers in coordinating pharmacovigilance activities in the respective zones;
- receiving and distributing ADR forms to zonal pharmacovigilance centres;
- collecting, screening and entering ADR reports into Vigiflow where possible or send the reports directly to TMDA headquarter offices for further processing;
- responding to queries and providing feedback information related to pharmacovigilance to the council and regions in the respective zones;
- receiving safety alerts from TMDA and sharing them with health care providers and patients in the respective zones.

Zonal Pharmacovigilance Centres

The **Four Zonal Pharmacovigilance Centers** are located at Kilimanjaro Christian Medical Center (KCMC) – Kilimanjaro; Muhimbili National Hospital (MNH) - Dar-es-Salaam; Bugando Medical Center (BMC) and Mwanza and Mbeya Medical Center (MMC) - Mbeya. The following activities are coordinated by the four Zonal Pharmacovigilance Centers:

- working in collaboration with TMDA zone offices in coordinating pharmacovigilance activities in the respective Zones;
- receiving information, responding to queries and provide information related to pharmacovigilance to the council and regions within the respective zones;
- receiving and distributing reporting forms to health facilities;
- collecting reports and providing feedback to health facilities.

Other centres

Healthcare professionals and patients are assisted in their pharmacovigilance duties (filling in the form, retrieving the form, etc...) from some centers:

- Health Facilities

- Council Health Management Team (CHMT)
- Regional Health Management Team (RHMT)
- Regional PV System

5 Key-points

- ✓ TMDA is responsible for regulating safety, quality and effectiveness of food, medicines, cosmetics, medical devices and diagnostics.
- ✓ There is a National Pharmacovigilance Centre which is embedded with TMDA Headquarter Office in Dar es Salaam.
- ✓ There are seven TMDA Zone Offices.
- ✓ There are four Zonal Pharmacovigilance Centers.
- ✓ All centers work in collaboration.

6 Intermediate Questionnaire

Tanzania Medicines and Medical Devices Authority Zone Offices:

- collect, screen and enter ADR reports into Vigiflow or send the reports directly to TMDA headquarter offices**
- collect, screen and enter the Tanzanian ADR reports into Vigibase
- conduct causality assessment and analysis of ADR reports
- look for signals of adverse drug reactions

Teaching:

The TMDA Zone Officers shall:

- planning and budgeting for pharmacovigilance activities in the respective zones;
- working in collaboration with zonal pharmacovigilance centers in coordinating pharmacovigilance activities in the respective zones;
- receiving and distributing ADR forms to zonal pharmacovigilance centres;
- collecting, screening and entering ADR reports into Vigiflow where possible or send the reports directly to TMDA headquarter offices for further processing;
- responding to queries and providing feedback information related to pharmacovigilance to the council and regions in the respective zones;
- receiving safety alerts from TMDA and sharing them with health care providers and patients in the respective zones.

How many Zonal Pharmacovigilance centers are present in Tanzania?

- a. seven, located in seven different Zones
- b. only one, located in Dar-es-Salaam
- c. four, located in four different facilities**
- d. four, located in Dar-es-Salaam

Teaching:

The **Four Zonal Pharmacovigilance Centers** are located at Kilimanjaro Christian Medical Center (KCMC) – Kilimanjaro; Muhimbili National Hospital (MNH) - Dar-es-Salaam; Bugando Medical Center (BMC) and Mwanza and Mbeya Medical Center (MMC) - Mbeya.

10 The spontaneous reporting system in Tanzania

1 E-learning objectives

At the end of this session, participants should be able to:

- know how, what, to whom, when report a spontaneous reporting form
- know where to find the spontaneous reporting form

2 Introduction

When an adverse reaction to medicine is suspected, the first step to take consists in managing the patient and add the adverse reaction to his personal chart. Then, one has to complete the ADR reporting form. TMDA has established an Adverse Reaction Reporting Tool (ARRT) for Drugs, Medical Advices and Clinical Trials. For drugs we have:

- A patient form (Attachment_1). Patients who experienced serious adverse drug reaction should be given special cards (i.e. Patient ADR Alert Card appended as Attachment 4) by the health care provider who diagnosed and managed the reaction. The Alert Card will be prepared and distributed to health facilities/Zone Offices and Zonal Centres by TMDA.
- A healthcare providers form (Attachment 2).
- A form for reporting poor quality (Attachment 3).

Since there is one form for ADRs and one for poor quality, depending on if HCPs think the ADRs is due to poor quality or not he/she can choose one form or the other.

Suspected adverse reaction to herbal medicines should be reported using ADR reporting form (Attachment 2). With regards the reporting with a DSM for new MR-drugs TB please see TBC course.

3 How to report

Adverse drug reactions can be reported by:

- web-reporting: electronically using the electronic reporting form which is available online at www.tmda.go.tz;

- calling TMDA: ADRs can be reported by calling TMDA using numbers printed on the ADR form (22-2450512/22-2450751).;
- mail or e-mail;

Web-reporting

In 2016 TMDA has established an electronic system for reporting ADR. The tool is accessed through the link <http://www.tmda.go.tz>.

- You can access to the tool by using a computer connected to internet (preferred browser is Google Chrome), fill the form online and send/submit it. Three forms will be displayed appearing in green, yellow and blue.
 - GREEN: A form for consumer reporting of suspected ADRs.
 - YELLOW: A form for reporting suspected ADRs by healthcare providers.
 - BLUE: A form for reporting on poor quality.
- You can also access to the tool by using a mobile phone connected to the internet. An app can be downloaded on the smart phone (an android app in a Swahili version) from the Google 'play store' and be installed on the phone. For instructions on how to download the app, please see Figure 1 and Figure 2:

1	Go to 'Play Store' item on the phone	
2	Search for 'ADR Reporting Tool'	
3	Select and accept the 'TFDA Reporting'	

Figure 1 - How to download the TMDA ADR Reporting Tool on your device



4	Install the application	
5	Open the installed application	
6	Get onto the tool's displaying the three forms	<div>Reporting by Consumers</div> <div>Reporting by HealthCare Workers</div> <div>Reports of Product Quality Products</div>

Figure 2 - How to install the TMDA ADR Reporting Tool on your device

Calling TMDA

You can also use the Unstructured Supplementary Service Data (USSD) code by call *152*00# on your (mobile phone). Follow these steps:

- 1) call *152*00# to find the list of available menus;
- 2) choose TMDA;
- 3) in the list of menu select '7.TMDA';
- 4) select ADR to start reporting.

Mail or e-mail

- a) Mail: the reporting forms are provided free of charge by TMDA and as they are already pre- paid and self-adhesive; reporters will not be charged for postal mailing.

The mail address is: TMDA, P.O. Box 1253, Dodoma

The ADR reporting form can be obtained, completed and sent to the following offices:

- 1) TMDA Headquarter offices;
 - 2) TMDA Zonal offices;
 - 3) Zone Pharmacovigilance centres;
 - 4) Regional Medical Officer's office;
 - 5) District Medical Officer's office;
 - 6) In-charge of the regional and district hospitals;
 - 7) In-charge of the health centres;
 - 8) In-charge of the dispensaries;
 - 9) Superintendent of the community pharmacies; and
 - 10) Superintendent of the private health facilities.
- b) e-mail: the reports can be scanned and be sent to email adr@tfda.or.tz

4 What to report

All suspected adverse reactions should be reported whether known or unknown, serious or not, including minor ones.

The following should be reported:

- a) all adverse drugs reactions as a result of prescription and non-prescription drugs;
- b) 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;
- c) unexpected reactions, regardless of their nature or severity
- d) an observed increase in frequency of a given reaction;
- e) a serious reaction, whether expected or not;

- f) all suspected ADRs associated with drug-drug, drug-food or drug-food supplement interactions;
- g) ADRs in special field of interest such as drug abuse and drug use in pregnancy and during lactation;
- h) ADRs occurring from overdose or medication errors;
- i) unusual lack of efficacy or when suspected quality defects are observed.
- j) product quality problems include colour change, separating of composition, caking, change of odour, questionable stability, suspected contamination, poor packaging and labeling, mislabeling, incomplete pack, defective and expired product.

ADRs of special interest

- TMDA asks you to report through the Yellow Cards for all suspected ADRs to medicines and vaccines under additional monitoring (new drugs) (marked with an inverted black triangle symbol (▼) on the box.
- TMDA is also particularly interested in receiving, through the Yellow Card Scheme, reports of suspected ADRs that occurred:
 - 1) in children;
 - 2) in patients that are over 65;
 - 3) after the use of biological medicines (a medicine that contains one or more active substances made by or derived from a biological source);
 - 4) associated with delayed drug effects and interactions; and
 - 5) after the use of complimentary therapies such as homeopathic and traditional remedies.

5 Who should report

- All health care providers including specialists, doctors, dentists, pharmacists and nurses can report ADRs.
- All affected consumers are encouraged to report ADRs directly to their healthcare professionals and zonal Drug Information centers.
- Marketing Authorization Holders/manufactures.

6 When to report

Any suspected ADR should be reported as soon as possible. It is vital to report an ADR even if you are doubtful about the precise relationship with the given medication or when you do not have all the details. What is important is that you SUSPECT an ADRs.

Collection of reports from several health care providers in different parts of the country assists in identification of a relationship between a particular drug and the adverse reaction. A causal relationship does not have to be proved in order to report an ADR, a suspicion is enough.

By reporting a suspected ADR, the health care provider contributes to strengthen the spontaneous reporting system. In fact, even a single report may help to identify a potential causal relationship between a drug and an adverse reaction. This in turn might lead to the identification of a drug safety issue that must be properly addressed by the competent authority (example Thalidomide Story).

All serious reactions, which are defined as any untoward medical occurrence that, at any dose, results in death; is life threatening; requires patient hospitalization or prolongs current hospitalization; results in persistent or significant disability, incapacity, or congenital abnormality, must be reported on an **expedited basis** using the normal ADR reporting form (Attachment_2).

Expedited reports should be submitted to TMDA immediately and not later than 15 calendar days from receipt of the minimum information required for an ADR. Lack of efficacy of medicines used for the treatment of life-threatening diseases, vaccines and contraceptives should be considered as requiring expedited reporting. The health care provider should report cases of overdose (accidental or intentional) that lead to suspected serious adverse reactions on an expedited basis.

7 Guideline to complete the reporting form

A form contains the following elements:

- 1)** Patient information including Patient identifier, Age/Date of birth, Sex, Weight and relevant medical history.
- 2)** Description of the adverse reaction including date of onset.
- 3)** Suspected drug(s): name (including brand name, if known), dosage, route, start and stop dates, and reasons for use.
- 4)** Treatment given for the reaction(s).
- 5)** Outcome of reactions.
- 6)** Name, date, signature and address of the reporter.

This information is needed in order to get a full report. Above all, a patient, an ADR, a drug and a reporter must be present in the report. All submitted reports will be kept CONFIDENTIAL.

- a)** The patient's identity - Information about the patient's age, sex, weight, ethnicity and use of substance of abuse can be provided. The patient file number has to be stated as it is useful to get additional information when needed.
- b)** Information on the suspected drug - This information includes the name of the medicine, source, the dose, route of administration and the impact of withdrawal and re-administration of the suspected medicine on the adverse reaction.

For example, it could be useful to know whether or not the patient's condition improved after the drug withdrawal or after the drug re-administration. Resolution of suspected ADR when the drug is withdrawn is a strong, although not conclusive indication of drug-induced disease.

- 1)** Use brand name of suspected medicine(s). If generic name is used, specify the manufacturer of the medicine if known.
- 2)** Avoid non-standard abbreviations such as TCL (tetracycline), PCM (Paracetamol), CPZ (Chlorpromazine), etc. In TB that can sometimes be a problem as HCPs use a lot of abbreviations, that is also the case for HIV treatment.
- 3)** List any other prescription, non-prescription medicines and/or traditional medicine used concurrently with the suspected medicine with all descriptions i.e. brand name, route, dosage form, strength, frequency, indication, date started and date stopped.
- 4)** The dosage form such as tablet, capsule, syrup, suspension, elixir, emulsion, injection, eye drop/ointment, topical crème/ ointment, nasal drop, suppositories rectal/ vaginal etc. should be stated.
- 5)** The strength must also be expressed in metric system, e.g. 500mg tab, 250mg/5ml syrup, 1gm rectal suppository etc. Sometimes strength can be expressed in %, e.g. 2% hydrocortisone ointment.
- 6)** Frequency of drug administration should be clearly notified using standard abbreviations, e.g. 3 times a day as tid or 8hrly, 2 times a day as bid or 12hrly, 4 times a day as qid or 6 hrly etc.
- 7)** Route of administration expressed using standard abbreviations like IM (intramuscular), IV (intravenous), IU (intrauterine), etc... should be used.

- 8) The date medicine was started and discontinued (if applicable) is important data to assess the causal relationship between the medicine and adverse drug reaction. Therefore, it has to be stated clearly on the reporting form as date/ month/year. If the medicine has not been discontinued at the time of reporting, write continuing.
 - 9) Write the reason why the medicine was used or the diagnosis for which the medicine was prescribed for both suspected medicine and other medicines.
- c) Information on the adverse reaction - A clear and brief description about the nature of adverse reaction, the date of onset, duration, time course and laboratory test results including “negative” and normal results of any relevant test performed should be reported.

The seriousness of the reaction i.e. whether it has necessitated prolonged hospitalization or not, discontinuation of the medicine or not, etc. and the outcome of the de-challenge and re-challenge tests with the suspected medicines have to be reported.

- d) Additional information - Any reaction the patient may have experienced previously, particularly similar to the current adverse event, either caused by the same or different medicine has to be reported. Other relevant medical history, such as allergy, chronic disease, pregnancy and other factors, which may contribute including herbal products, foods and chemicals, should be reported under this heading. You may also add here why you think the adverse effect is due to the particular medicine.
- e) Follow-up report for an ADR that has already been reported - Any follow-up information for an ADR that has already been reported can be sent on another ADR form (the centre will understand to which initial report it belongs), or it can be communicated by telephone, fax or e-mail to TMDA indicating that it is a follow up information. The date of the original report and the report case number must be retrieved from the ADR register so that the follow up information can be matched with the original report. It is very important that follow-up reports are identified and linked to the original report.

8 Flow of ADR information

The flow of ADR information is summarized in Figure 3.

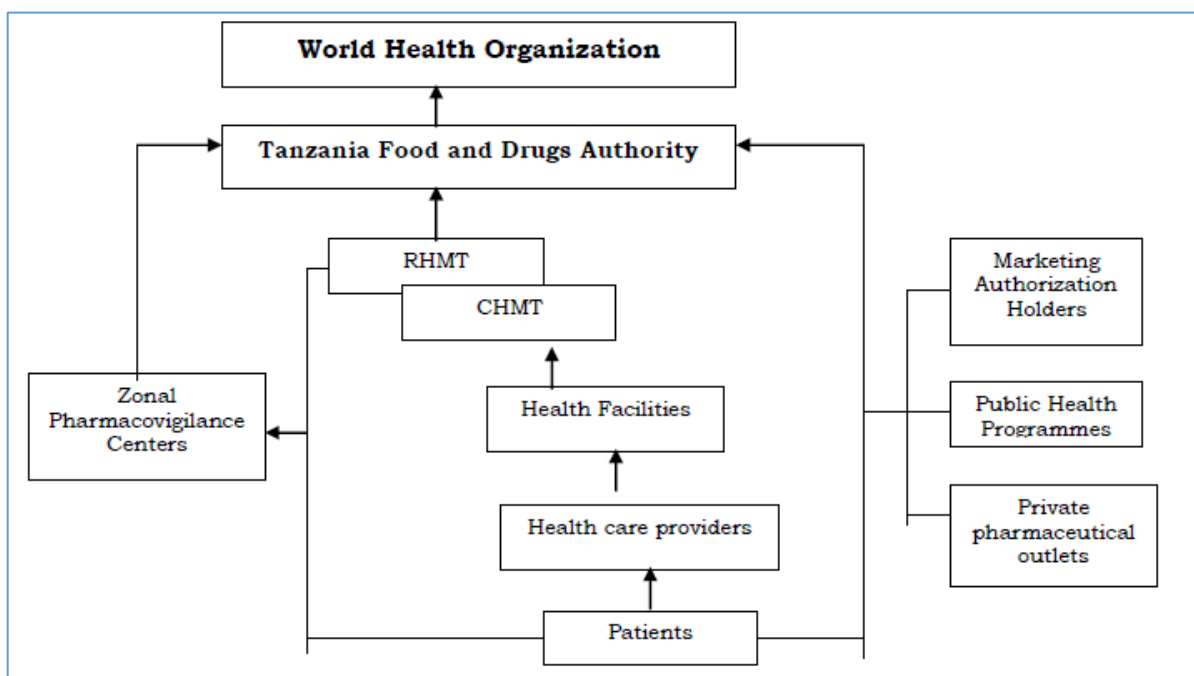


Figure 3 - Flow of ADR information

9 Under-reporting in Tanzania

Under-reporting is a major limitation of spontaneous reporting systems. On one hand, a high rate of under-reporting prevents risk from being quantified, and on the other hand, it leads to excessive delay in triggering signals.

Underreporting in Tanzania remains a challenge due to the following factors:

- lack of awareness on ADR by health care professionals;
- lack of reporting by pharmaceutical industry (not mandatory);
- lack of priority setting within TMDA and public health programs;
- lack of technical and financial resources;
- weak organizational structure, leading to uneven distribution to and collection of standardized ADR reporting forms (“yellow card”) from health facilities.

To improve its PV system, TMDA plans to carry out these activities:

- incorporate PV into health care teaching curricula (physicians, pharmacists, nurses, etc.);
- institute mandatory ADR reporting by pharmaceutical industry;
- increase collaboration with public health programs within MoH;
- increase ADR awareness among health professionals;
- make ADR forms (“yellow card”) available to each health facility nationwide;
- establish more zonal DICs.

10 Keypoints

- ✓ Adverse drug reactions can be reported by: web-reporting, calling TMDA, mail or e-mail.
- ✓ All suspected adverse reactions should be reported whether known or unknown, serious or not, including minor ones.
- ✓ All health care providers including specialists, doctors, dentists, pharmacists, nurses, patients and manufactures can report ADRs.
- ✓ Any suspected ADR should be reported as soon as possible.
- ✓ Expedited reports should be submitted to TMDA immediately and not later than 15 calendar days from receipt of the minimum information required for an ADR.

11 Intermediate Questionnaire

According to the local legislation, who is allowed to report ADRs in Tanzania?

- a. both healthcare providers and Marketing Authorization Holders, not patients
- b. both healthcare providers and patients, not Marketing Authorization Holders
- c. healthcare providers, patients and Marketing Authorization Holders**

d. only healthcare providers, not patients and Marketing Authorization Holders

Teaching

All health care providers including specialists, doctors, dentists, pharmacists and nurses can report ADRs.

Which of these elements must always be present in an ADR report?

- a. a patient and the outcome of the ADR
- b. a drug and the outcome of the ADR
- c. a drug and the patient's relevant medical history
- d. a drug and a patient**

Teaching

A patient, an ADR, a drug and a reporter must be present in the report.

11 Local data on Spontaneous reporting in Tanzania from Vigibase

1 E-learning objectives

At the end of this session, participants should be able to report main features of spontaneous reporting data in Tanzania.

2 Data from Vigibase

Tanzania **joined the World Health Organization** international drug monitoring program in **1993**. To date (20th May 2019), Tanzania has sent **2689 reports** (0.01% of the total). The following data shows some features of these reports.

Figure 4 shows Tanzania ADR Reporting trend from 1994 to 2019. From January of this year we can observe a very high growth.

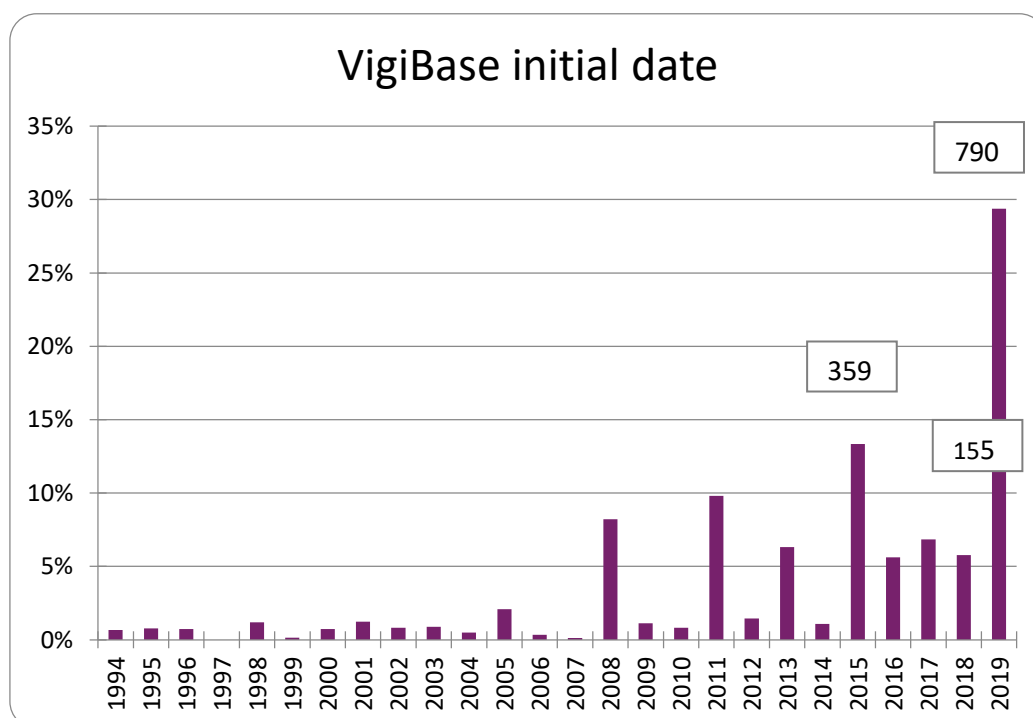


Figure 4 - Tanzania ADR reporting trend from 1994 to 2019 (20 maggio 2019)

Figure 5 shows patient age related to 2689 reports. Most reports concern a range of patients between the ages of 18 and 44 years of age.

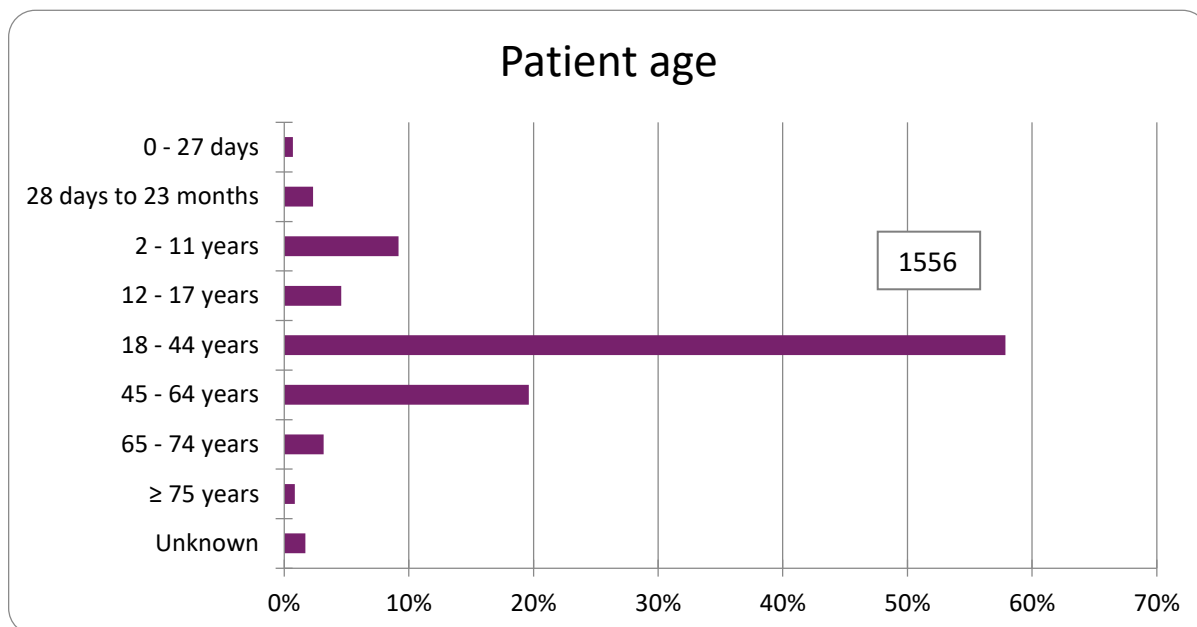


Figure 5 - Patient age related to 2689 reports

Figure 6 shows patient sex related to these 2689 reports. More than 60% of reports concern women.

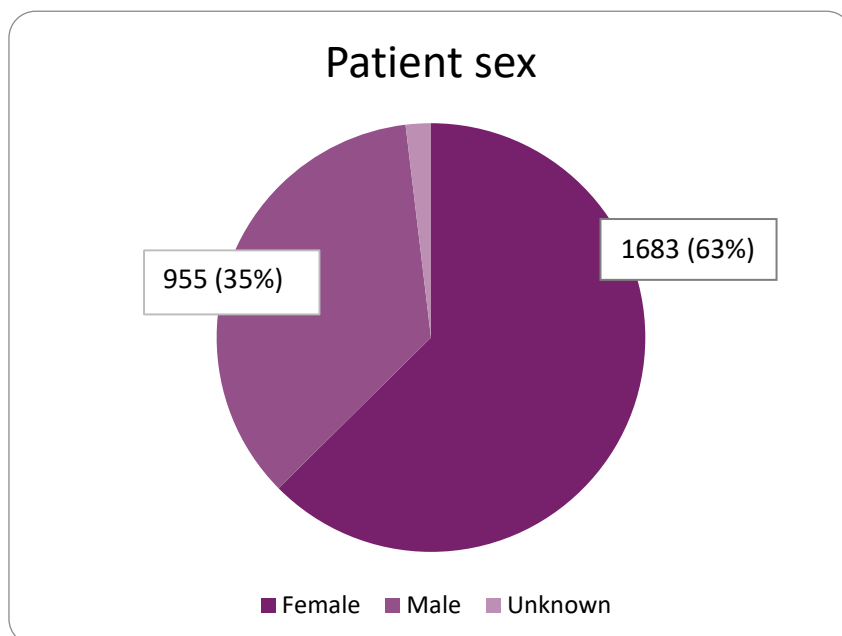


Figure 6 - Patient sex related to 2689 reports

Figure 7 shows Top reported ATC (Anatomical Therapeutic Chemical classification system) Antiinfectives for systemic use are drugs most involved.

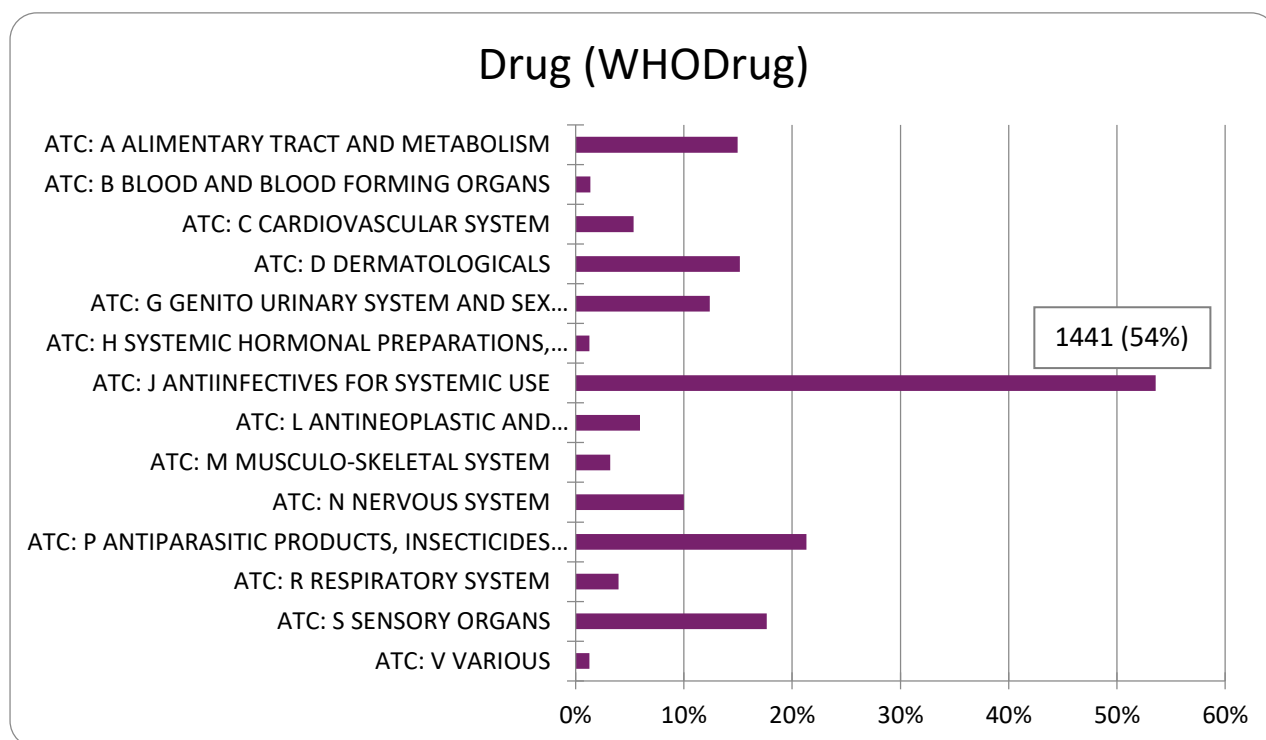


Figure 7 - Top reported ATCs

Figure 8 shows Top Ten Reported Active Ingredients.

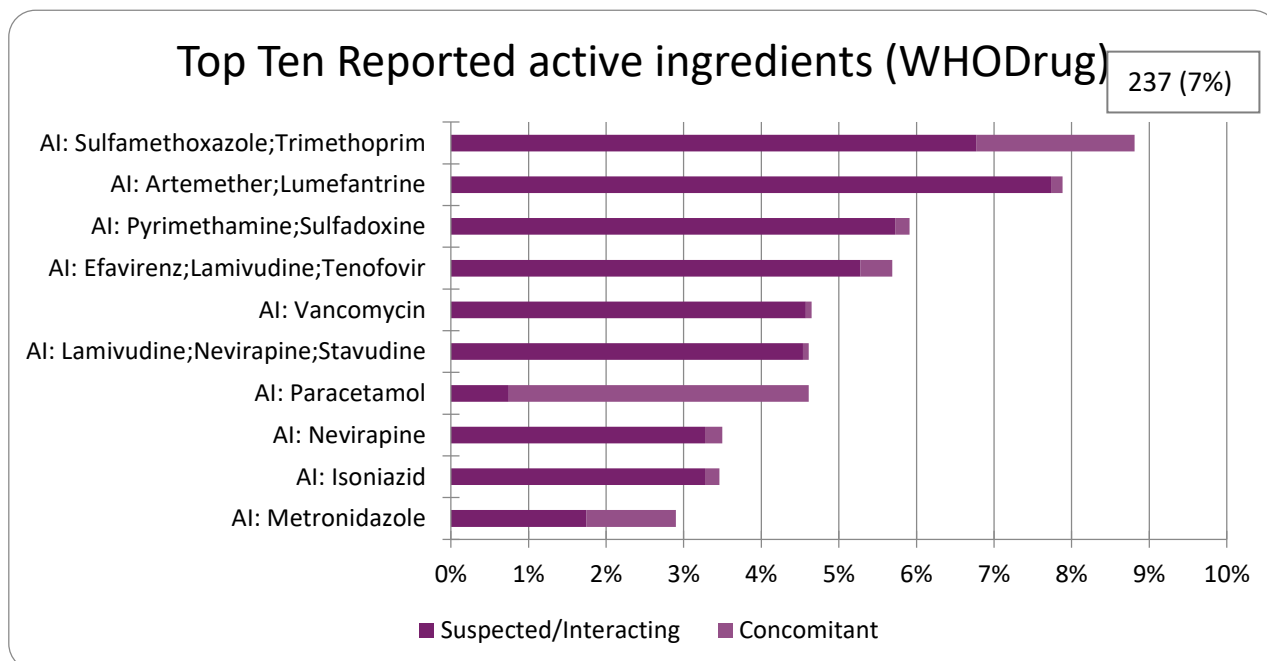


Figure 8 - Top ten reported active ingredients related to 2689 reports

Figure 9 shows classification Reaction related to 2689 reports. The most commonly reported ADRs were skin and GI disorders.

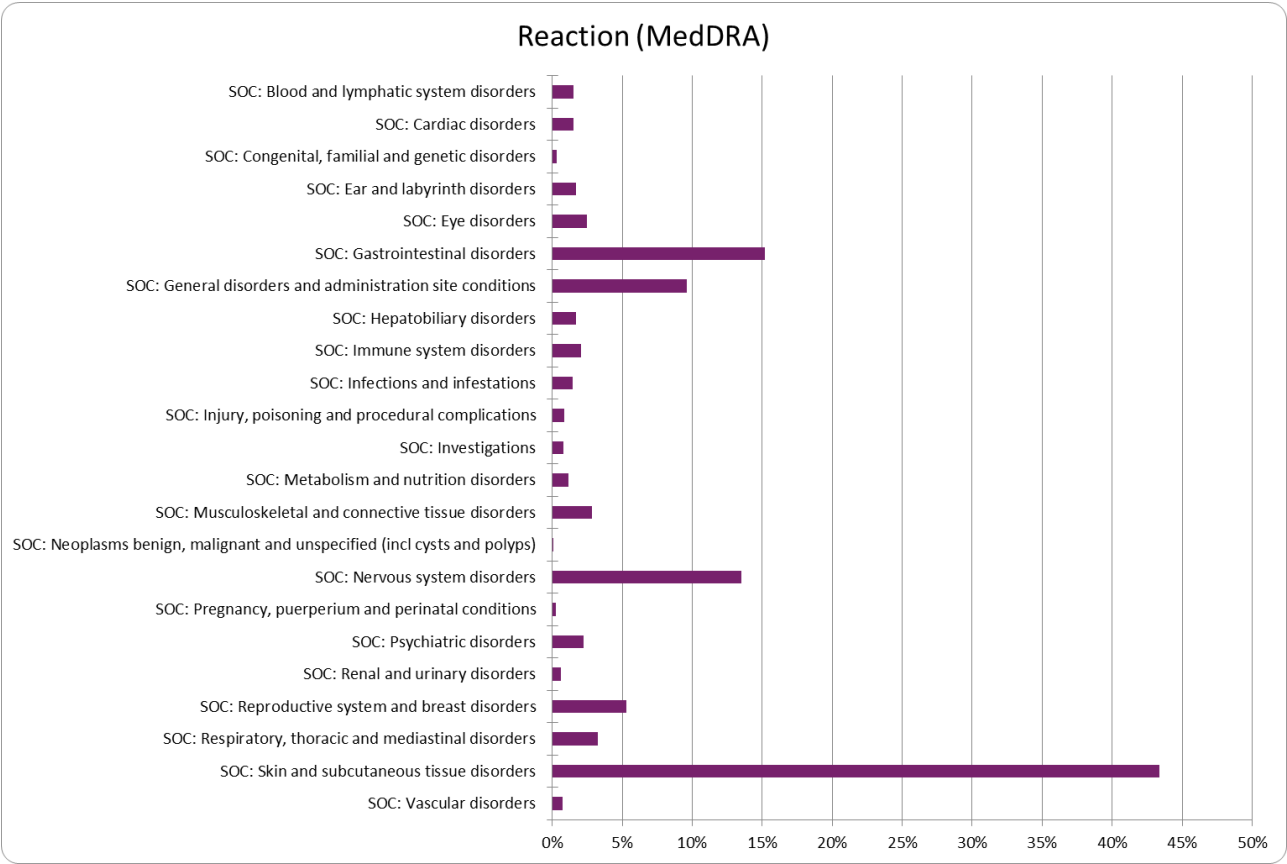


Figure 9 - Classification reaction related to 2689 reports

Figure 10 shows Top Ten Reported Preferred Terms related to 2689 reports.

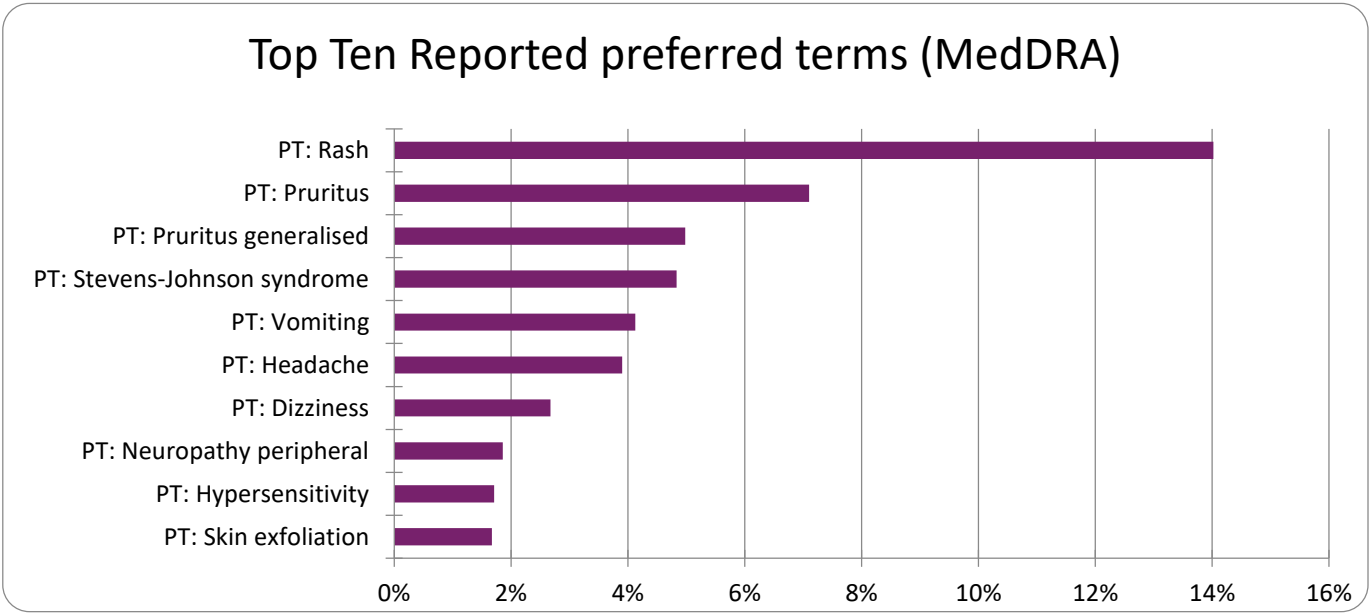


Figure 10 - Top ten reported Preferred Terms related to 2689 reports

3 What can you do to improve the system?

From January of this year we can observe a very high growth. An improvement is possible. You can contribute to this improvement. We have presented this data not to discourage you, but to present the initial situation from which to start.

4 Keypoints

- ✓ Tanzania joined the World Health Organization international drug monitoring program in 1993.
- ✓ To date (20th May 2019), Tanzania has sent 2689 reports (0.01% of the total).
- ✓ Most reports concern a range of patients between the ages of 18 and 44 years of age.
- ✓ More than 60% of reports concern women.
- ✓ Antiinfectives for systemic use are drugs most involved.
- ✓ The most commonly reported ADRs were skin and GI disorders.

5 Intermediate Questionnaire

Which are the most commonly reported ADRs in Tanzania?

- a. nervous system disorders and hepatobiliary disorders
- b. nervous system disorders and skin disorders
- c. gastrointestinal disorders and skin disorders**
- d. gastrointestinal disorders and hepatobiliary disorders

Teaching:

The most commonly reported ADRs were skin and GI disorders

Which are the most reported drugs in Tanzania?

- a. antiinfectives for systemic use**
- b. antineoplastic and immunomodulating agents
- c. dermatologicals
- d. antiparasitic products, insecticides and repellents

Teaching:

Antiinfectives for systemic use are drugs most involved.