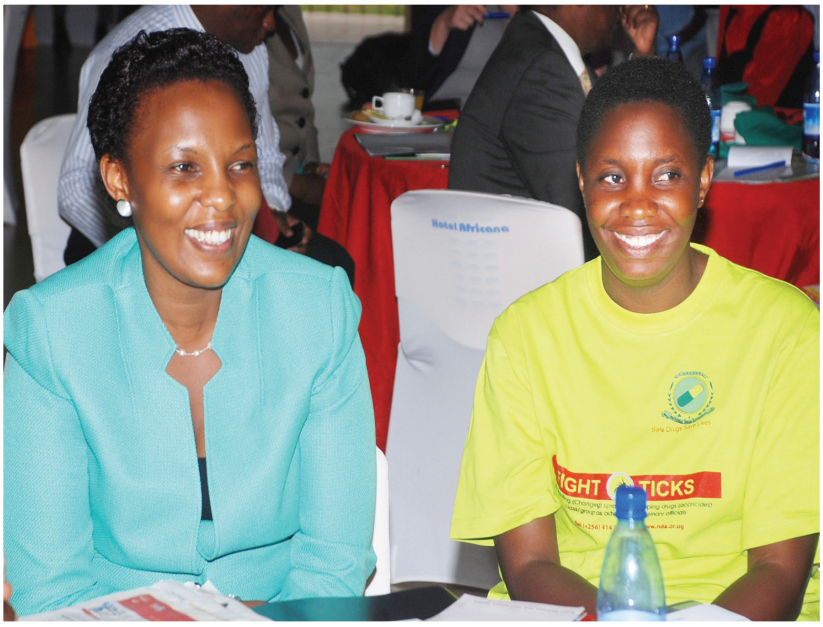
National Pharmacovigilance Center



National Drug Authority Report

FOREWORD

Director Product Safety

In 2016-2017 the National Pharmacovigilance Center priorities and innovations included: a national program for voluntary reporting by health care professionals and consumers, Mandatory Reporting of Marketing Authorization Holders, Drug Safe ty Communication, Market Complaint Tracking, Medication Errors Initiatives, Community Engagement, safety surveillance and tracking and collaborative approaches to pharmacovigilance. While many challenges lay on the path to achieving our objective, we report a steady progress towards a lasting improvement in patient safety in Uganda.

Seven out of twelve pharmacovigilance centers scattered all over the country continued to receive our technical assistance and financial support from the National Pharmacovigilance Center to improve their competences in safety monitoring and protecting the populations.

From our spontaneous reporting system, a total of 301 reports were received from various districts and different health facilities.
These reports are fewer than expected and as a matter of improvement, and in order to encourage more reporting, we plan to facilitate direct patient reporting. We encourage patients to report directly their suspected adverse drug reactions (ADRs) with extra details to enhance our knowledge about the medicines as well as clinical decision making.
We have also initiated community sensitization where we have sensitized the leaders of patient care organization and expect them to teach patients about pharmacovigilance

This year we were able to come up with a guidance document for marketing authorization holder to report ADRs to the regulatory body.
In order to build a young generation that has knowledge in drug safety, we are partnering with UMC on PV for children using comics read more on Meet Annie and Mac – the new pharmacovigilance on the block

A well-functioning pharmacovigilance systems can significantly contribute to safe and effective medical products in the country. To this end, we would want to acknowledge the valuable financial contributions from the National Drug Authority. I also wish to appreciate the contribution of the Pharmacovigilance Working Group for their invaluable guidance.
Most important, I wish to appreciate our dear reporters without them we would have nothing to report on.

Helen Byomire Ndagije;
Director, Product Safety

CONTENTS

Chapter 1

Spontaneous Reports from Health Care Professionals and Consumers

1.0 Status of individual case reports (icsrs): reporting, collation and analysis Financial Year 2016/2017

A total of 301 ADR reports were received at the National Pharmacovigilance Center (NPC) with more than half (n = 214; 73%) reported as serious. The cumulative reports over the months are shown in figure 1 below.

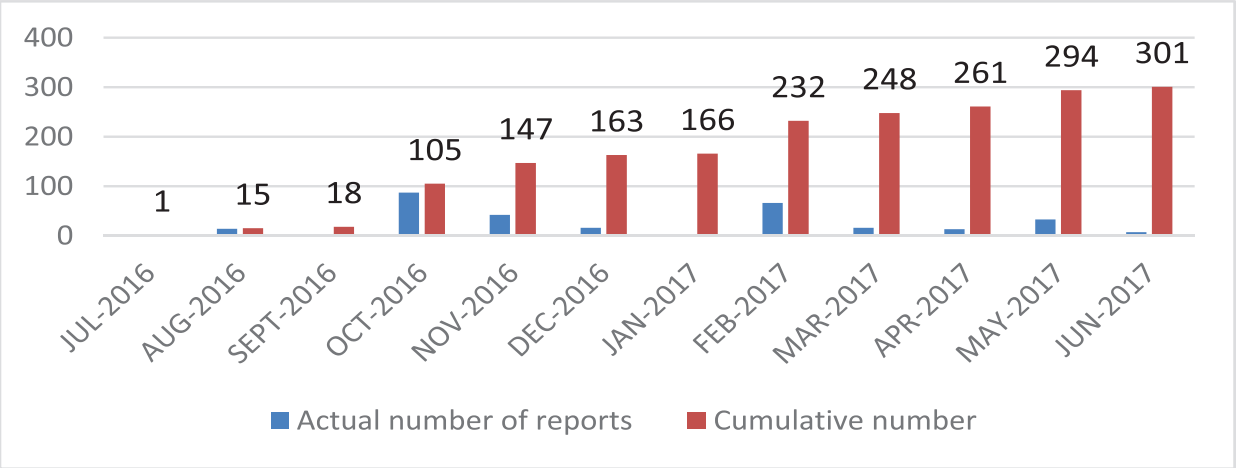


Figure 1: ADR reports received in each month

Over all, Masaka district reported most (25%) followed by Wakiso(15.6%) and Kampala(16%) as shown in figure 2 below.

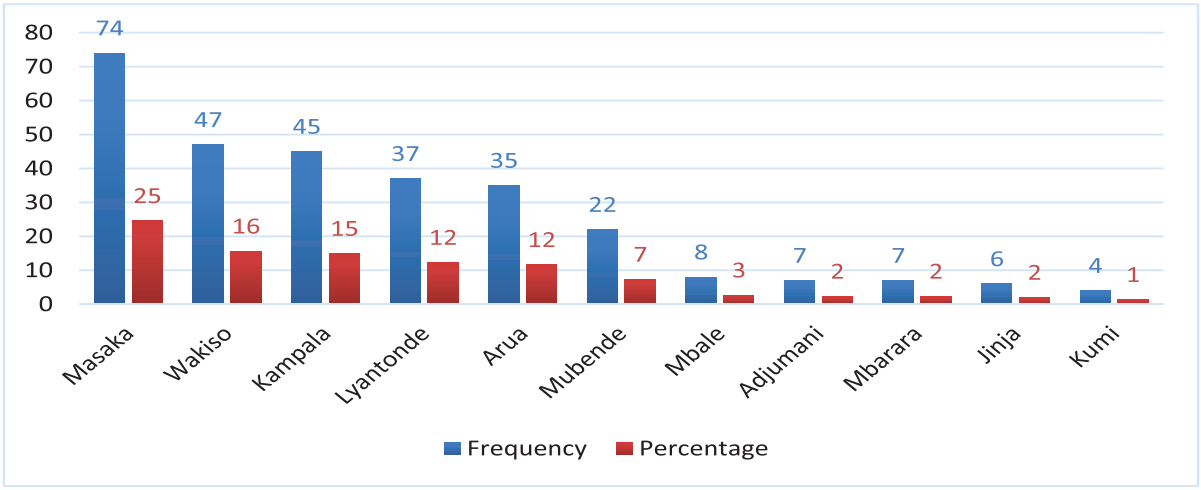


Figure 2: DISTRICTS THAT SUBMITTED REPORTS

Despite this performance, all districts are represented by mainly one health facility, indicating low reporting rates. Figure 3 shows the faclitaties that were able to submit reports. Overall, Uganda Cares (Masaka Hospital) submitted the highest number of reports (72 reports) followed by Mildmay Uganda with 48 reports.

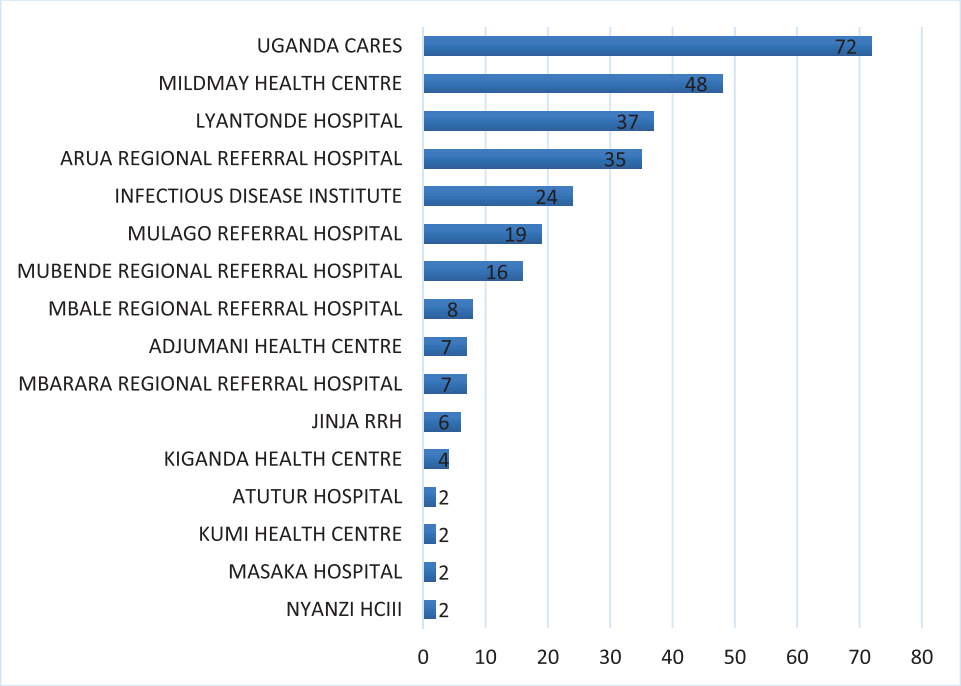


Figure 3: HEALTH FACILITY THAT SUBMITTED ADR REPORTS

Type of reporters

Overall, Clinical officers (n=93; 30.9%) reported most, followed by medical officers (n = 80; 26.6%) and Pharmacist as indicated in figure 4 below. There is still low reporting from the consumers of medicines in Uganda.

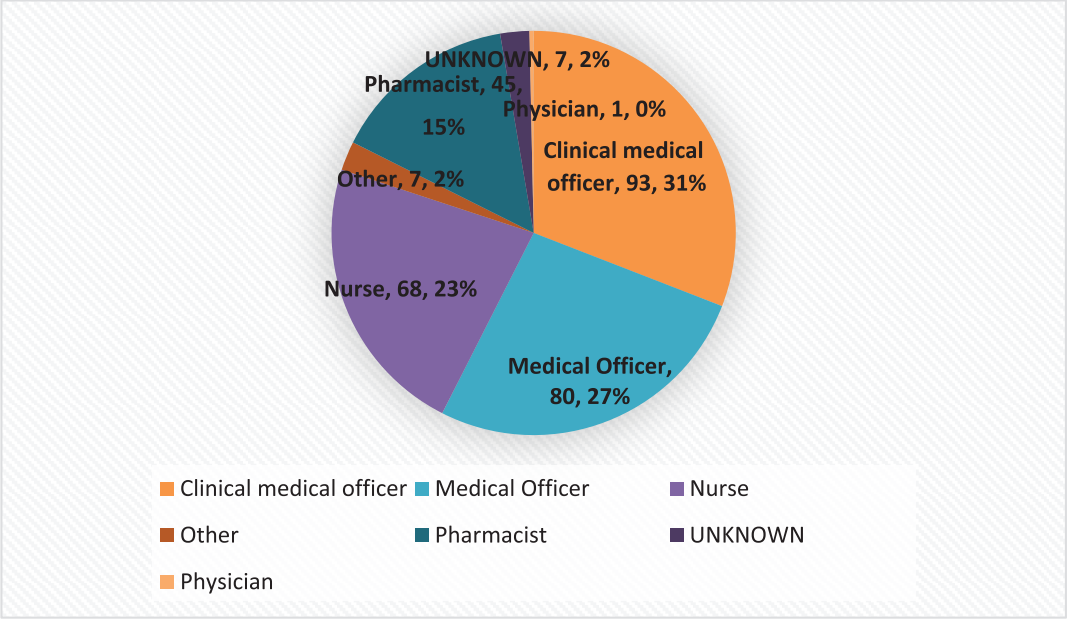


Figure 4: TYPE OF CADRES REPORTING

3.1.6 Common Reported Drugs

Antiretroviral drugs had the highest number of reports (56.8%) followed by TB drugs as shown in figure 5 (appendix 1).

Tenofovir, Efavirenz, zidovudine and kanamycin had the highest number of ADRs reported. Tenofovir was reported to be associated with renal abnormalities and masculo-skeletal disorders (figure 6 annex 1), while Zidovudine was majorly associated with aneamia with a few with on lipodystrophy. Efavirenz was mainly associated with gynaecomastia and hepatotoxicity. Table 2, Annex II, shows the common adverse drug reactions associated with each individual drug reported.

Community engagement

SENSITIZATION OF THE COMMUNITY ON PHARMACOVIGILANCE FOR THE PATIENT ORGANIZATIONS IN UGANDA

One of the priority activities of the Directorate of Drug Safety of the reporting period was to engage the community. The NPV engaged the patient care organization by way of training them on pharmacovigilance and encouraging them to report all adverse events to the contact persons within their different disease area. In collaboration with Community Health and Information Network (CHAIN) we planned and trained all patient care organizations

ACHIEVEMENTS:

42 leaders of patient care organization were sensitized on pharmacovigilance as a means of patient empowerment. A reporting framework for adverse events reporting was created by the workshop. This will be key in soliciting for adverse event reports. We were able to distribute some materials prepared for such exercises following this training we expect more involvement of the community in ADR and other drug related problems' reporting.

Chapter 2

Vaccine safety Monitoring

The directorate of product safety set out to profile the safety of HPV Vaccine among the school going children. For effective monitoring, data management and follow-up, NPC partnered with Makerere University Centre for Health and Population research (MUCHAP) to conduct a pilot vaccine pharmacovigilance program in Iganga-Mayuge Demographic Surveillance Site (DSS).

Achievements

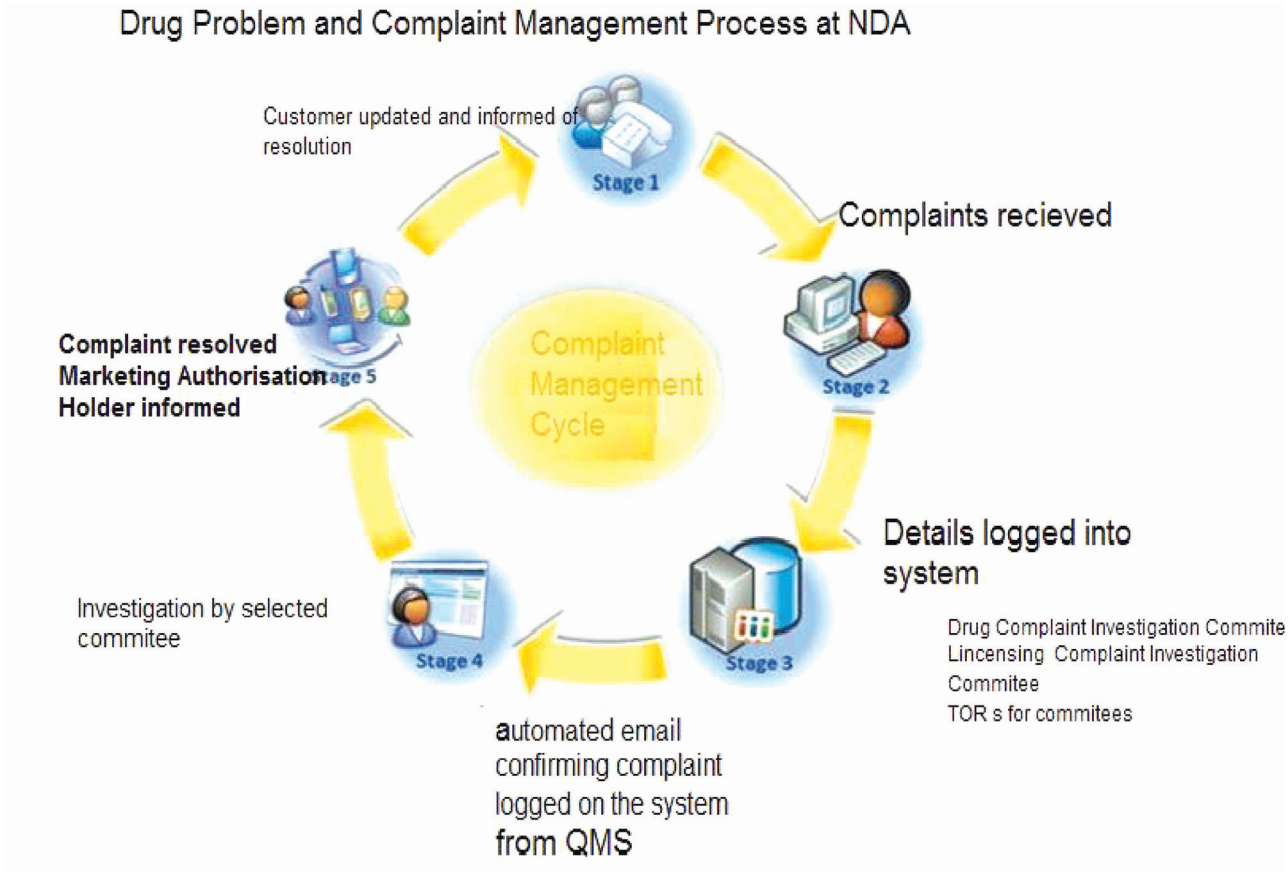
93 people from different health centers were trained on soliciting for ADR and entering them on ADR form. We anticipate seeing a vigilant population that will provide data on the safety of HPV in the country

Community sensitization on ADR

Chapter 3

SAFETY SURVEILLANCE AND TRACKING

How to Report Product Problems and Complaints to the NDA
The National Drug Authority protects the public health by helping to ensure the safety, efficacy, and security of human and veterinary drugs and biological products. We call upon you to support NDA to carry out safety surveillance and tracking by reporting all product problem complaints
If you have a problem or concern about any of the products that the agency regulates, NDA wants to hear from you.



Which products should you report on?

1. Human prescription and over-the-counter (OTC) drugs
2. Medical devices
3. Veterinary products, including foods and drugs for animals
4. Biologics, including vaccines and cosmetics

Why should you report problems?

Information about problems or unexpected reactions can help the NDA protect the public health. For instance, if you report a problem to the NDA, you could help identify an unknown risk. And your report could help the NDA know when to carry out preventive and protective actions, which can include requiring labels to provide new warning information and issuing safety messages to the public. Products also can be potentially removed from the market.

What kinds of problems can you report—and when?

If you have a medical emergency related to an NDA-regulated product, seek medical assistance immediately. After you've received the medical attention that you need, you can report the issue to the NDA.

Note: Even if you have a problem and do not seek medical attention, you still can report the issue to the NDA. Similarly, you can report problems with animal drugs whether you sought veterinary assistance or not.

Examples of problems you can report include:

Known or Unexpected side effects or adverse events: These can include everything from skin rashes to more serious complications.

Product quality problems: These issues can happen if a product isn't working

properly or if it has a defect like change in color.

Potentially preventable mistakes. These can be caused by various issues, including

choosing the wrong product because of labels or packaging that look alike. (For instance, confusing two products that have similar brand or generic names.) Mistakes also can be caused by difficulty with a device due to hard-to-read controls or displays, which may cause you to record a test result that is not correct.

Therapeutic failures. These problems can include when a medical product does not seem to work as well when you switch from one generic to another.

How should you submit your report?

You can report a problem to the NDA online (https://primaryreporting.who-umc.org/Reporting/Reporter?OrganizationID=UG) via phone, or via mail (druginfo@nda.or.ug), Reports can also be submitted electronically, by going to the NDA website http://www.nda.or.ug, you may also contact NDA at 0800101999.

Chapter 4

Photo by courtesy of WHO /UMC REPORT

DRUG SAFETY COMMUNICATION

Several important safety communications to assist health care professionals in prescribing and monitoring the safety of drug therapy have been shared. These communications, are based on safety signals generated locally and from post-marketing surveillance data solicited world over .
Two most important drug warning in this year are:

Issue 1: Migration of implants into the vasculature system and lungs

Medicine and Healthcare Products Regulatory Agency (MHRA) of UK. received and communicated several reports of Nexplanon® implants migrating in the vasculature and lungs. This is supported by a report by the license-holder who estimates the risk to be approximately 1.3 per million implants sold worldwide.
National Drug authority although has no report in the country as such about this safety signal, it evaluated this information together with the current product information and advises that both patients and healthcare providers should be aware of this risk.

ADVICE TO HEALTHCARE PROFESSIONALS

It is strongly recommended that implants like Implanon used for family planning be inserted and removed only by healthcare professionals who have completed training for the use of the implants Women should therefore be shown how to locate the implant immediately following insertion and advised to check the position of the implant frequently for the first few months. Tell your patients to contact their doctor immediately to report the disappearance of the implant

If an implant cannot be palpated at its insertion site in the arm, it should be located as soon as possible and removed at the earliest opportunity. It is also advised that chest imaging is performed, should this occur correct subdermal insertion reduces the risk of these events. If they are located early enough it is possible to remove them.

Evidence from literature shows that implants found in the vasculature can become endothelized into the pulmonary artery. A cumulative (1998-2015) search of the Company global safety database identified 18 spontaneous post marketing reports describing implants (radiopaque and non-radiopaque) found within the vasculature, lung or chest wall. The reporting rate of migration of etonogestrel implant into the vasculature (including the pulmonary artery and lung) is approximately 0.6 per million implants sold. For the radiopaque etonogestrel implant (which permits additional methods by which to detect them) the reporting rate is approximately 1.3 per million implants sold.

You are encouraged to report negative side effects of implants to the National Pharmacovigilance Center at National Drug Authority.

You may also contact our Drug Information Department at 256-414--255665 if you have any questions about the information contained in this bulletin.

Issue 2: Very Serious Heart Complications Associated with the use of Sildenafil (Viagra)

Serious cardiovascular events, including myocardial infarction, unstable angina, sudden cardiac death, ventricular arrhythmia, cerebrovascular haemorrhage, transient Ischaemic attack, hypertension and hypotension have been reported with a temporal association with the use of Viagra.

Most, but not all, of these patients had pre-existing cardiovascular risk factors. In Uganda, there have been reports of sudden deaths in lodges that may be linked to use of sildenafil. These deaths were reported to occur during or shortly after sexual intercourse and a few were reported to occur shortly after the use of Sildenafil without sexual activity. Also Visual defects and cases of non-arteritic anterior ischaemic optic neuropathy have been reported in connection with the intake of sildenafil.

Of significant importance to public is the potentiation effect of some ART drugs on Sildenafil.
Co-administration of the HIV protease inhibitor ritonavir, which is a highly potent P450 inhibitor, at steady state (500mg twice daily) with sildenafil (100mg single dose) resulted in a 300% (4-fold) increase in sildenafil Cmax and a 1,000% (11-fold) increase in sildenafil plasma AUC. At 24 hours, the plasma levels of sildenafil were still approximately 200ng/ml, compared to approximately 5ng/ml when sildenafil was administered alone.

Advice to healthcare Professionals

Prior to prescribing sildenafil, you should carefully consider whether your patients has certain underlying conditions and interacting drugs.Sildenafil has vasodilator properties, resulting in mild and transient decreases in blood pressure leading to fainting or even instant death. Of significant importance to public, is the potentiation effect of ART drugs on Sildenafil. The patient should also be advised on identifying all possible symptoms of cardiovascular events, and consult a physician immediately.

Chapter 5

COLLABORATIONS

Stakeholder engagement and collaboration is one of the key strategic priorities for NDA. Infectious Diseases Institute (IDI) is one of our key partners that supported us as reported in this chapter.

'Infectious Diseases Institute (IDI) is a Ugandan not-for-profit organization whose mission is to strengthen health systems in Africa, with a strong emphasis on infectious diseases, through research and capacity development. The IDI Outreach Department through KCCA, West Nile and Mid-Western HIV/AIDS CDC-PEPFAR funded projects support comprehensive HIV care across 3 regions namely Kampala, Mid-western and West Nile. The programs use technical teams to support health facilities provide quality medicine and supply chain services including Pharmacovigilance.

To strengthen Pharmacovigilance, the project has supported various strategies including assessment of availability for Adverse Drug Reactions (ADR) forms and knowledge pertaining the reporting process for ADRs. This was done with support from the District Logistics Focal persons (DLFP) and District Medicine Management Supervisors (DMMS) in 120 health facilities across Mid-western and West Nile Region. To address gaps identified, mentorships were conducted across all the aforementioned facilities and 50 ADR books were distributed. Following the communication pertaining drug safety on use of Tenofovir Disoproxil Fumarate, 6 facility based continuous Professional Development sessions (CPDs) attracting 219 health workers were conducted across Kiswa, Kisugu, Kisenyi, Kawaala, Komamboga and Kitebi health units in Kampala. Main focus was placed on equipping health workers with knowledge pertaining identification of signs and symptoms as well as investigations and management of the syndrome. Relatedly 11 facility based CPDs focused on the reporting mechanism for ADRs to National Drug Authority (NDA) were also conducted.

Furthermore, to increase awareness for Pharmacovigilance, an SMS reminder highlighting both the manual and online National reporting platforms for ADRs was developed with support from National Pharmacovigilance Center at NDA. In this regard, a total of 452 SMS were sent targeting clinicians and facility in charges in 114 supported health facilities in Kampala and West Nile regions. Similarly leveraged on platforms such as the IDI Annual supply chain forum and the Regional Training of Trainers for the 2016 ART guidelines to present the online mechanism for reporting ADRs to various stakeholders including Regional Performance Monitoring Team (RPMT), DMMS, DLFP, District TB Focal Persons and health workers.

This was done with support from the National Pharmacovigilance Center and IDI respectively.

In the subsequent quarters, these interventions coupled with other activities such as identification of Pharmacovigilance focal person and functionalization of Medicine Therapeutic Committees will be adopted to further expand Pharmacovigilance.

Annex 1:
SUMMERY OF REPORTING FREQUENCY BY ATC CATEGORIZATION

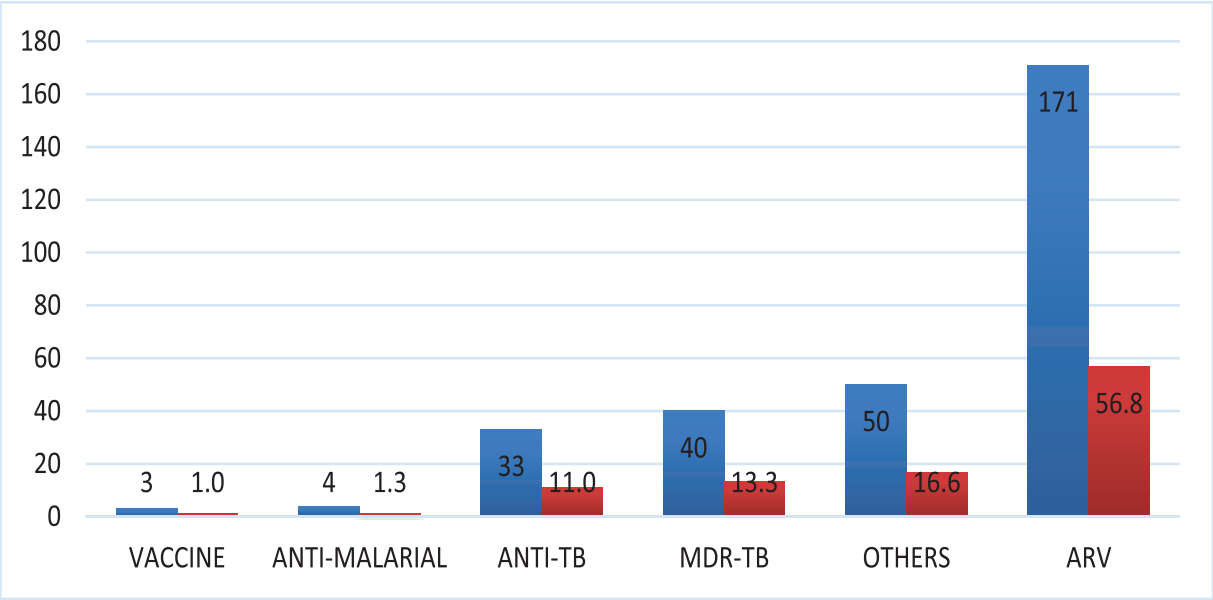


Figure 5 reporting frequency by ATC categorization

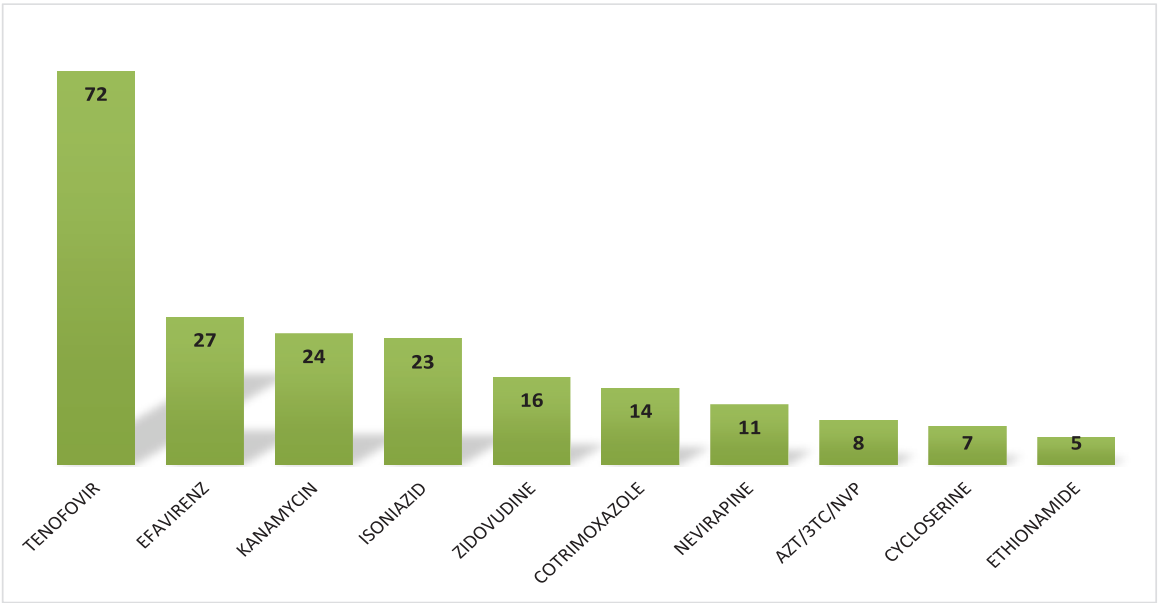


Figure 6.Top ten commonly reported individual drugs

Annex 2:
TABLE 2: DRUG –REACTION COMBINATIONS 2016/2017

DRUG REACTED TO	REACTIONS REPORTED
Tenofovir	Renal insufficiency, dizziness, nausea, headache, Fanconi syndrome, increased creatinineosteomalacia, abdominal pain, dysuria
Efavirenz	Dizziness, Gynaecomastia, hepatotoxicity, bed wetting, joint ache, skin reactions
Kanamycin	Tinnitus, Hearing impairment, skin reaction, deafness,
Isoniazid	Skin papular rash, drug hypersensitivity reaction, Hepatotoxicity, peripheral neuropatthy, disabling back pain
Nevirapine	Generalised body weakness, renal insufficiency, Generalized skin rash, pain in the limbs, toxic epidermal necrosis
Zidovudine	Neutropenia grade III, lipodystrophy grade II, anaemia, darkened nail beds, palpitations, weak knee jonts, Peripheral neuropathy
Cycloserine	Sleeplessness, aggression, incoherent speech, mood swings and insomnia, hallucinations,irritability,overtalking, convulsions, increased libido
Ethionamide	Abdominal pain, gynaecomastia, nausea, vomiting, epigastric pain
Cotrimoxazole	Thrombocytopenia, anaemia, stevens-johnson syndrome, hypersensitivity skin, toxic epidermal necrosis, itchy and body swelling
Aciclovir	Excessive dermatitis
Agopril	Skin reaction, diarrhea, blurred vision
Albendazole	Skin eruptions
Amoxacillin	Excessive rigors
Ampicilin/Ppf	Rash pruiritic
Ampiclox	Drug eruptions(skin eruptions)
Artesunate	Skin reaction, diarrhoea, skin rash
Albumin	Itchy skin and vomiting

Atazanavir/Ritonavir (Atv/R)	Ocular jaundice, yellowing of eyes, severe dizziness, fanconi syndrome.
Bedaquiline	Death, headache, neausea, epigastric pain, vomitting
Benzyl Penicillin	Paralysis and numbness of fingers
Blood	RigorS, Urticaria
Captopril	Skin reaction of impentigo, dry cough, chest pain, insomnia
Ceftriaxone	Wheal form rash and body itching, hypersenstivity
Chlorhexidine Gluconate And Cetrimide Solution	Blisters burning sensations
Ciprofloxacin	Burning skin and darkening around the lip and neck
Cloxacillin	Itchy body rash
Co-Amoxiclav	Mouth sores, dysphagia
Coartem	Facial and limp oedema, skin reaction, diarrhea
Fansidar	Itchy macula-papular skin rash with erythema
Fluconazole	Hepatotoxicity and SJS
Hep. B Vaccine	Body rash affecting face, thoracic and pelvic regions
Human Papiloma Vaccine	Fever and rash
Hydroxyurea	Neutropenia
Lamotrigine	Drug Hypersnsitivity Reaction
Levofloxacin	Convulsions, tremor and seizures
Linezolid, Tdf,Levofl	death
Misoprostol	Convulsion and psychosis
Osteomin, Ligaba, Tegretol	Ulcerated lips,drooping of saliva and oral sores
Oxytocin	Swelling of the sight and burn-like has extende to the whole upper thigh
Pyrizinamide	Yellowing of eyes,abdominal pain
RHEZ	Acute kidney injury, generalised itchy rash on the trunk later had darkening of palms and soles of the feet
RIF/INH/ETH/PZD	Maculopapular rash
Rifabutin	Hepatotoxicity, severe jaundice, hepatocellular damage, jaundice, abdominal pain, gynaecomastia
Salbutamol	Croup
Tetanus Toxoid	Stevens-johnson syndrome

IMPORTANT DATES TO NOTE

Annual meeting draws Pharmacovigilance Experts to Kampala 2017

Pharmacovigilantes from nearly 60 countries will be converging in Kampala for the 40th International annual pharmacovigilance meeting of the WHO Programme for International Drug Monitoring

Dates: 7th -10th November 2017

Safe Drugs Save Lives

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