The National Pharmacovigilance System in Ethiopia:

a situational analysis at the start of the PAVIA and PROFORMA projects

27-31 August 2018

Part 1

National Medicines Regulatory Authority
Marketing Authorization Holders
Healthcare facilities

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E D C T P

List of abbreviations

ADR	Adverse drug reaction
ADE	Adverse drug event
CEM	Cohort event monitoring
DAC	Drug Advisory Committee
DTC	Drug and Therapeutics Committee
EAC	East African Community
(E)FMHACA	(Ethiopian) Food, Medicine and Healthcare Administration and Control Authority
EPI	Expanded Programme on Immunization
FMoH	Federal Ministry of Health
HCP	Health-Care Professionals
ICSR	Individual Case Safety Report
IPAT	Indicator-based Pharmacovigilance Assessment Tool
MAH	Marketing Authorization Holder
NEPAD	New Partnership for Africa's Development - agency
NMRA	National Medicines Regulatory Authority
NTD	Neglected Tropical Diseases
PASS	Post Authorization Safety Study
PAVIA	Pharmacovigilance Africa
PHP	Public Health Programme
PBRER	Periodic Benefit Risk Evaluation Report
PROFORMA	Pharmacovigilance infrastructure and post-marketing surveillance system capacity building for regional regulatory harmonization in East Africa
PSUR	Periodic Safety Update Report
PV	Pharmacovigilance
QPPV	Qualified Person for Pharmacovigilance
RMP	Risk Management Plan
SAE	Serious Adverse Event
TB	Tuberculosis
ToR	Terms of Reference
UMC	Uppsala Monitoring Centre
WHO	World Health Organisation

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1. Introduction

1.1. PROFORMA and PAVIA

The PROFORMA and PAVIA projects aim to strengthen pharmacovigilance (PV) systems and infrastructure in sub-Saharan Africa. Both projects received funding by the European and developing countries clinical trial partnership (EDCTP) to work on PV capacity development in Africa. Having a similar objective and goals, both consortia are collaborating and work together in Ethiopia and Tanzania, the two overlapping consortium member countries. In March 2018, both projects have started to support and established partnership with the Ethiopian Food, Medicine and Healthcare Administration and Control Authority (EFMHACA) and the Tanzanian Food and Drug Authority. Since the implementation plans of both PROFORMA and PAVIA projects have a baseline assessment of the current PV situation in the country as an initial activity, it was decided to undertake a joint assessment based on a common set of indicators. The assessment tool used was derived from a set of PV indicators agreed by members of the East African Community (EAC), supplemented with a few additional indicators considered essential for the needs of the two projects. Data entry sheets were developed to match the indicator questions.

1.2. Pharmacovigilance

The World Health Organization (WHO) has defined PV as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other possible drug-related problems."[1] The aim of the PV system is to protect the public from medicines-related harm. Currently few low- and middle-income countries have a well-functioning PV system to support the timely identification, collection, and assessment of medicine-related adverse events.

1.3. Pharmacovigilance in Ethiopia

Ethiopia established its national PV system under Food, Medicines and Healthcare Administration and Control Authority (FMHACA) in 2002. In 2009 Ethiopia became a full member of the WHO Program for International Drug Monitoring. The number of adverse drug reaction (ADR) reports received from healthcare providers to the national centre have been limited.

Voluntary reporting has come into effect as of 2002 through the activities performed by the Adverse Drug Reaction Monitoring Division of the Drug Administration and Control Authority. A simple reporting form was developed and was made available throughout all the health facilities. Various trainings were given and face-to-face discussions about adverse drug reaction/events monitoring were also performed. In spite of these activities, still there remain important interventions to be implemented to strengthen the existing system and infrastructure, in monitoring ADR and reduce related harms in the public.

2. Aim and objectives of the situational analysis

This report presents the baseline situational analysis of the various aspects and needs of the PV system in Ethiopia at the start of the PAVIA and PROFORMA projects, including its strengths and weaknesses. The baseline situational analysis will be followed by a workshop with broader stakeholder involvement to discuss the findings, define the desired development goals of the PV system and develop a PV plan to achieve these goals, including

[1] WHO 2009, The importance of pharmacovigilance. Safety monitoring of medicinal products. Geneva.

priorities and activities that can be conducted during the PROFORMA and PAVIA projects' intervention period.

The aim of the baseline situational analysis was to get a good understanding about the strengths and weaknesses of the current PV system in Ethiopia, to understand obstacles for development, to identify the most effective targets of interventions to be addressed by PROFORMA and PAVIA, as well as recommend vital solutions to be addressed by EFMHACA and its local partners. Gaps identified by this particular assessment that will not be addressed by PROFORMA or PAVIA may need interventions led by other partners.

Figure 1. Assessment at EFMHACA (28 and 29 August 2018)

This assessment report will form the basis for assessing the short- and long-term effects of the activities brought about by the PAVIA and PROFORMA projects.

3. Methodology and team

3.1. Assessment strategy

The following strategies were used to assess the baseline situation:

1. Legal and statutory documents governing the EFMHACA execution of the PV system were requested by the external reviewers and were studied prior to the assessment on site.
2. PV indicators were selected from pre-existing indicator sets to form a standardized assessment tool (see paragraph 3.2). Information relevant to the indicator questions were retrieved through interviews with stakeholders, supported by a review of documentation provided.
3. Additional information not specifically addressed by indicator questions, but important for the understanding of the current situation of the PV system was obtained through key stakeholder interviews. The aim was to ascertain needs and get recommendations for the future from the key stakeholders.
4. Site visits at selected Public Health Programmes, Addis Ababa University and a selection of healthcare facilities were conducted. A selection of representatives of marketing authorization holders (MAH), medicine importers and distributors were also interviewed to assess the current reporting behaviour of adverse events at stakeholder and facility level and its barriers and facilitators and their risk mitigation plan for high-risk medicines.

A national kick-off meeting for both projects was held on 27 August 2018 in Addis Ababa, attended by the external assessors representing the PROFORMA and PAVIA consortia and national key stakeholders. After this meeting, the assessment tool was reviewed in detail with delegates of the assessment teams. Teams of external and local assessors were assigned to visit, in varying compositions, and evaluate PV capacity and preparedness in a number of institutions and programmes (see paragraph 3.5).

The visits of stakeholders and interviews with representatives of these were held from 28-30 August 2018. On 31 August 2018, a half-day workshop with national stakeholders was organized to share and discuss the findings of the assessment teams. This session was attended by Paul Tanui representing NEPAD.

3.2. PV indicator assessment tool

PV indicators were assessed using a slightly modified questionnaire developed and already used by the East African Community (EAC) which is based on the WHO PV indicators[2] and the Indicator-based Pharmacovigilance Assessment Tool (IPAT)[3], supplemented with a few additional indicators considered essential for the needs of the two projects. Such indicators were selected from the WHO Global Benchmarking Tool. The following elements were addressed:

- Policies, laws, and regulations
- Systems, structures and stakeholder coordination
- Data Management and signal generation
- Risk assessment and evaluation
- Risk management and communication

The tool for assessment of the national medicine regulatory authority (NMRA), the health facilities and MAHs contains 58,7 and 3 indicators respectively. The indicators are attached as Annex 1.

3.3. Assessment team

The assessment was conducted by several teams consisting of national staff and international consultants:

- Abbie Barry, Project manager for PROFORMA, Karolinska Institutet, Sweden
- Dr Abimbola Opadeyi, clinician, University of Benin, Nigeria, assisting Prof. Ambrose Isah on PAVIA WP2
- Aida Arefayne, Pharmacist, PV coordinator for PAVIA in Ethiopia
- Prof. Ambrose Isah, Consultant Physician/Clinical Pharmacologist, Department of Medicine, University of Benin, Nigeria, PAVIA WP2 lead
- Assefa Ejamo, Pharmacist, Clinical Trials and PV Expert EFMHACA
- Prof. Eleni Aklillu, Principal Investigator for PROFORMA, Karolinska Institutet, Sweden
- Elizabeth Woldemariam, Social Pharmacist, Pharmacovigilance Advisor seconded by USP to EFMHACA
- Prof. Eyasu Makonnen, Clinical Pharmacologist, CDT Africa, Addis Ababa University
- Prof. Gurumurthy Parthasarathi, Consultant PROFORMA, Pharmacovigilance Programme of India, Ghaziabad, India

[2] WHO 2009: pharmacovigilance indicators: a practical manual for the assessment of pharmacovigilance systems.

[3] Strengthening Pharmaceutical Systems (SPS) Program. 2009. *Indicator-Based Pharmacovigilance Assessment Tool: Manual for Conducting Assessments in Developing Countries*. Submitted to the U.S. Agency for International Development by the SPS Program. Arlington, VA: Management Sciences for Health.

- Habtamu Gashaw, Pharmacist, Clinical Trials and PV Expert EFMHACA
- Dr Linda Härmark, pharmacist and epidemiologist, Lareb, the Netherlands, PAVIA WP3 lead
- Dr Jessica Maltha, epidemiologist, KNCV Tuberculosis foundation, The Netherlands, representing PAVIA WP4
- Dr Mekonnen Teferi, Researcher, Armauer Hansen Research Institute (AHRI), Chairman PAVIA Steering Committee
- Sten Olsson, deputy project coordinator, PROFORMA, Karolinska Institutet, Sweden
- Tsegazeab Tekle, Country Coordinator for PROFORMA in Ethiopia
- Workagegnehu Degefe, Pharmacist, Clinical Trials and PV Expert, EFMHACA

Figure 2. Team conducting an assessment at Bishoftu Hospital

3.4. Documents reviewed

- Health Policy of the Transitional Government of Ethiopia, 1993
- Proclamation No. 176/1999, A proclamation to provide for drug administration and control
- Proclamation No. 661/2009 (Food, Medicine and Health Care Administration and Control Proclamation)
- Council of Ministers Regulation No. 299/2013 (Regulation to provide for food, medicine and health care administration and control)
- Guideline for Adverse Drug Events Monitoring (Pharmacovigilance); 3rd ed., 2014. Food, Medicine and Healthcare Administration and Control Authority of Ethiopia
- Standard Operating Procedure for pharmacovigilance centre (no date)
- Summary of Adverse drug Event reports that were sent to the Ethiopian Food Medicine and Healthcare Administration and Control Authority Pharmacovigilance centre on 2010 E.C.
- Adverse drug event monitoring system/ Pharmacovigilance Training manual for health teaching institutions (2011)
- FMHACA organogram

3.5. Sites assessed, and stakeholders interviewed

1. National Medicines Regulatory Authority (EFMHACA)
2. Federal Ministry of Health:

a. Departments: Policy, Planning, Monitoring & Evaluation
b. Public Health Programmes (PHPs):
    i. Expanded Programme on Immunization
    ii. Neglected Tropical Diseases
    iii. Tuberculosis

3. Marketing Authorization Holders (8 of 12 MAHs invited):
    a. Local Pharmaceutical Manufacturers
        i. Addis Pharmaceutical Factory (APF)
        ii. Ethiopian Pharmaceutical Manufacturing Company (EPHARM)
        iii. Julphar Ethiopia
    b. Multinational Companies
        i. Roche
        ii. Sanofi
    c. Pharmaceutical Importers and Distributors
        i. Eyasu Drugs and Medical Supplies Importer and Distributor
        ii. DAT international PLC
        iii. ZAF pharmaceuticals PLC
4. Health Facilities:
    a. St. Peter's Specialized Hospital, Addis Ababa
    b. ALERT Hospital, Addis Ababa
    c. Bishoftu General Hospital, Bishoftu
    d. MDR-TB treatment centre of Adama Hospital, Adama College of Health Sciences, Geda area, Adama (Nazreth)

    All these facilities are DR-TB Treatment Initiation Centres (TICs). The DR-TB wards were visited and assessed in each health facility, while the pharmacy/PV unit was visited in all facilities except Geda health centre to assess PV in general.
5. University in Health Care (Addis Ababa University)

3.6. Analysis of the indicator tool and interviews

The indicator tool was used as a guide for structured interviews. Answers to the questions of the indicator tool as well as additional information provided by interviewees is described in the results section. At the end of the project the same indicator list will be used, and results will be compared to those obtained during the baseline assessment.

3.7. Limitations

There are some limitations to this assessment:
A limited number of health facilities could be visited and assessed during this baseline situational analysis, and these may not represent the full spectrum of health care services offered in the country. However, we do believe that for the diseases of our interest, sufficient information was collected to get a broad understanding of the issues regarding PV in Ethiopia.
Since a lot of information was gathered through interviews and discussions with key representatives of the different stakeholders, statements are to some extent depending on the knowledge, experience and opinion of the informant. It was not possible to verify all statements with objective data or documentation or to ascertain the reliability of such data.

4. Results

4.1 National Medicines Regulatory Authority

Fifteen indicators were assessed at the level of the NMRA (Annex 1)

4.1.1 Policy, law and regulations

Information on twelve indicators were collected for this area (see Annex 1).

The Ethiopian Health Policy adopted in 1993 includes also a Drug Policy. There are also two major legal instruments defining the roles of different authorities and other stakeholders:

- The Proclamation No 661/2009
- The Regulation No 299/2013

These legal documents define the role of the Ethiopian Food, Medicine and Healthcare Administration and Control Authority, EFMHACA, and its responsibility to undertake post marketing surveillance of medicines and to take necessary measures to ensure safety, efficacy and quality of marketed products. The proclamation in force is currently being considered for revision.

The Proclamation covers safety and PV related information (part II article 4 sub-article 5 & 10; and article 14 sub-article 2).

The Regulation states that any health institution shall have the duty to report to the authority regarding unexpected adverse reactions or concerns about the quality or failing efficacy of marketed medicines. The regulation also stipulates that any manufacturer, importer or distributor of medicines should establish a PV function and to continuously monitor the safety of their products and to take measures in case of any irregularities.
The Regulation further elucidates the mandates and powers of as Food, Medicines and Health Care Administration and Control Council of Ministers Regulation.

The stipulations of the legal instruments are described and explained in a 'Guideline for Adverse Drug Events Monitoring [Pharmacovigilance]' issued in its 3rd edition by FMHACA in 2014.

There are no requirements, expectations or plans to request patients themselves to submit reports regarding suspected medicine related harm.

FMHACA has started a process of reviewing the PV guidelines with the intention of publishing an updated version in 2019. The aim is to review the guidelines every four years.

The medicines regulatory agency, EFMHACA, was established in 2010 following the proclamation in 2009 (Regulation 189). The predecessor agency, the Drug Administration and Control Authority (DACA), was established in 1999. FMHACA maintains a public record on its web site of all medical products granted a marketing license in Ethiopia.

4.1.1.1 Market authorization holders, importers, and private health care providers

According to the guidelines Marketing Authorization Holders (MAH) should submit Periodic Safety Update Reports (PSURs) to the authority every six months during the first two years after marketing and thereafter annually for three years. The marketing license is renewed every four years. In practice, some but not all companies do submit PSURs (containing data both from Ethiopia and other countries). Moreover, the staff at EFMHACA has time constraints to review the reports. To date, no PSUR has contributed to detection of new signals. The guidelines also contain detailed instructions for MAHs to develop risk management plans and in which situations such plans should be submitted to FMHACA. There is no specific requirement for the risk management plans to be adapted to the specific

risk situation of the Ethiopian population. MAHs are not required to keep a position as Qualified Person for Pharmacovigilance (QPPV). The regulatory authority does not have the legal mandate to require MAHs to carry out investigations, so called Post Authorization Safety Studies (PASS), if signals have been received about possible problems. However, experience has demonstrated that pharmaceutical companies have carried out specific safety investigations on the direct request of the regulator.

There are no specific requirements for PV systems in the licensing of private healthcare facilities. They are covered by the general requirements in the proclamation, however.

4.1.2 Systems, structure and stakeholder coordination

The FMHACA team for Clinical Trials & Pharmacovigilance constitutes the Ethiopian national PV centre. Tasks are divided between management of applications for clinical trials and PV, but clinical trial applications are few. 70% of the work is devoted to PV. There are plans to create a unit only for PV.

The present PV centre has four regular staff members and one person on secondment. There are no formal Terms of Reference (ToR) for the staff members employed. They are collaborating with six additional persons in the regions with some PV training. The FMHACA staff have undergone formal PV training abroad but no records are being kept documenting staff competence development.

A document with Standard Operating Procedures (SOP) was shared (see below). It is not dated, and no information was provided regarding the regularity of its review.

Figure 3. FMHACA organogram.

4.1.2.1. National budget for PV activities

There is no specific budget for PV activities. FMHACA has a three-year budget cycle on directorate level and the Clinical Trials & Pharmacovigilance unit will have to apply for their share of that budget. In general, 30% of the budget is coming from FMoH and 70% from donors. FMHACA maintains a section for fundraising. A grant of 3 million birr has been received from GAVI for vaccine safety monitoring, to be shared with several other stakeholders.

4.1.2.2 National medicines safety advisory committee

A safety advisory committee was originally set up for causality assessment of Adverse Events Following Immunization (AEFI) but its functions have later been expanded to include causality assessments in general and advice on safety issues. The committee includes the following specialisms: paediatrics, neurology, internal medicine, pathology, microbiology, immunology, epidemiology, pharmacoepidemiology, pharmacology, gynaecology/obstetrics, dermatology, cardiology, and pulmonology.

The committee was intended to meet four times a year, but reports have been few and now the committee members are called upon when there is an identified need. The committee last met about a year ago. There are extensive and recent ToR for the committee and their meetings are minuted.

4.1.2.3 Technical support services

There are potential sources for information about the level of medicine consumption in Ethiopia e.g. the Pharmaceutical Supply Funding Agency for the public sector, the Central Port Coordination office for import and local manufacturers for medicines produced and distributed in the country. None of these sources are being used and no public data is available.

FMHACA does not have access to any library service. The PV staff is depending on open sources on the internet, use of academic libraries including services from the WHO HINARI system for information from the literature.

4.1.2.4. Mechanisms for dissemination of PV information

There is an annual plan for PV communication. It includes disseminating four PV newsletters per year. Because of lack of relevant topics for dissemination only three issues were released in 2017, while in 2016 and 2015, the planned four issues were released. About 4000 copies have been printed and distributed to branch offices, regional health bureaus and sent to reporters of ICSRs. FMHACA also maintains a web site providing information to the public, including safety messages (www.fmhaca.gov.et). A toll-free telephone number is maintained by the agency. The number (8482) is regularly promoted at 7.00 am on national morning radio. Individual case safety reports (ICSR) can be received through this channel and questions can be passed on to the PV unit by the healthcare professional answering the call.

An annual summary of the experiences of the national PV system is published for pharmacists in the journal of the Ethiopian Pharmaceutical Association. An annual two-hour training is also organized for journalists with approximately 40 participants in each batch.

EFMHACA uses the social media through the public relation division of the Ministry of Health. However, PV information has not been disseminated using the media, although there were some attempts to promote ADR reporting on EFMHACA's Facebook page.

4.1.2.5 Pharmacovigilance training – pre-service

In 2013 the PV centre collaborated with some universities and developed a harmonized training curriculum to be used on undergraduate level for medical, pharmacy and nursing schools. This was supported by Ministry of Education, but it is unknown to what extent this training has been implemented.

Ethiopia is participating in the IGAD regional collaboration with Djibouti, Eritrea, Kenya, Somalia, South Sudan, Sudan and Uganda. Discussions on harmonization in pharmacovigilance and PV training are part of this collaboration

4.1.2.6 Pharmacovigilance training – in-service

Standard 2-3-day training modules for in-service healthcare professionals, particularly the lower cadres, have been used with success. Patient safety and PV is covered during about 2 hours and this has led to an increase in reporting. There is a very high turn-over rate of personnel, however. This training was given five times last year with double sessions on three sites. In all about 700 healthcare professionals were trained last year, but no community health workers.

No web-based training tools are available.

4.1.2.7 Stakeholder coordination

EFMHACA has an internal PV-forum, consisting of representatives of its different departments: the quality control unit, the inspectorate, and the PV centre, to discuss safety alerts received. Next to this, there are collaborations with different stakeholders. For example, a Task Force composed of the PV team meets with representatives of public health programmes like EPI, NTD and TB. The Task Force gets together on need basis and discusses harmonization of practices and routines. Several different, non-compatible, formats for data collection are being used. Collaboration in training and technical requirements are discussed

Treatment guidelines are developed in HIV, TB and malaria in public health programme specific processes. For remaining diseases FMHACA is responsible for development of treatment guidelines which are updated every 5 years. Safety data are not routinely considered in the development of these guidelines.

A National Essential Medicines list is available in the country, latest reviewed in 2015. The review is managed by the Federal Ministry of Health (FMoH) and FMHACA is involved in the process.

During the past year ICSRs were received from 84 healthcare facilities out of the >4000 facilities available in the country. From nine facilities the number of ICSRs exceeded 10 during the year.

Ethiopia joined the WHO Programme for International Drug Monitoring in 2009 as member country 88.

4.1.3 Signal generation and data management

Reports received are managed in different ways depending on their source and nature. Reports from the TB programme are received and kept in Excel format. ICSRs received on paper or via telephone calls are entered in the web based VigiFlow system. Reports on product quality defects are kept in a separate system. The Excel files are stored on a computer at EFMHACA, but there is no central FMHACA server nor is there a back-up system. The VigiFlow system, which is E2b-compatible, is operating on a server in Sweden with cloud back-up. Operation of the VigiFlow system requires internet access.

Information from the safety databases is shared with the Medicine facility inspection Directorate, with regional authorities and data entered in VigiFlow is shared with all the countries participating in the WHO Programme for International Drug Monitoring.

There is a standard national adverse drug event reporting form with prepaid postage. It is adequate for reporting of all kinds of medicine related problems including adverse events, lack of therapeutic effect, quality problems, medication errors, drug dependence, problems with medical devices and diagnostics. The reporting form is available from the FMHACA web site, but it cannot be filled and submitted electronically. Instead, it needs to be downloaded, printed, filled, scanned, and then attached to an email to EFMHACA for reporting.
Apart from being available on the website, the paper form is distributed during trainings, through PV partners, and as part of the acknowledgment package for reporters. It can also be requested by health facilities from EFMHACA through the national and the branch offices.
For AEFIs and the TB programme there is a special reporting mechanism, with specific forms, reporting frequency and timelines.
Patients are not encouraged to report directly and there is no specific reporting form for consumers.
The SOP document provides instructions for data management and analysis under the following headings:

1. Quality assurance of adverse drug event reports
2. Causality assessment of adverse drug event reports
3. Processing of received adverse drug events
4. Training of Staff at the centre
5. Communication of drug safety information to health providers

4.1.4 Risk assessment and evaluation

In this area, twelve indicators were assessed at the level of the NMRA (Annex 1).

According to the distribution agreement signed with MAH, all registered products should have a PV plan, but no record is being kept of such plans at FMHACA.
Last calendar year 706 ICSRs were submitted to the national PV centre. Of these 504 referred to adverse drug reactions, none to medication error, and three to therapeutic ineffectiveness, 17 AEFI and 84 concerned suspected quality problems.

During the past calendar year reporting from various sources was as follows:

Source of report	number of reports
Marketing Authorization Holders	128
Public Health Programmes (TB)	235
Healthcare professionals	565
Patients	0

The professional background of the reporters and their rate of submissions were as follows:

Reporter (by background)	number of reports
Medical doctors	285
Nurses	9
Pharmacists	159
Pharmacy technician*	55
Health officers	8
EFMHACA branch offices**	2
Health bureau**	1

Staff of private pharmacies and clinics**	10

* Pharmacy technicians (druggists) have obtained a diploma in Pharmacy, whereas pharmacists have obtained BSc grade; ** these reports are also included in the totals of reports sent by type of health care professional

Ethiopia has about 105 million inhabitants. Thus, in 2017, 4.8 ADR reports per 1,000,000 inhabitants were received.

All reports are entered into a table format. Those referring to adverse drug reactions (504) are entered in VigiFlow. All reports are acknowledged, and each reporter receives two new reporting forms and a copy of the latest ADR newsletter. Only 10 reports were subjected to a formal causality assessment during the past calendar year, based on an assessment of case severity, and community/public health programme concerns. Most of these concerned AEFIs and adverse events among TB patients on new drugs. During the same time period 171 ICSRs were committed to the WHO VigiBase, including cases from the TB programme. Workload issues prevented EFMHACA from submitting all 504 ADR reports to VigiBase. The latest quality score according to the VigiGrade system was 0.8675, out of a maximum 1.0.

An active Cohort Event Monitoring study of anti-retroviral medicines was initiated by FMHACA with the intention of following-up 3000 patients. This project has now been outsourced to Armauer Hansen Research Institute (AHRI), having more resources for the completion of the project. This project is supported by the Global Fund.

The FMHACA PV centre has not undertaken any visits to MAHs to supervise their PV activities.

4.1.5 Risk management and communication

In this area, ten indicators were assessed at the level of the NMRA

During the past calendar year PV activities have resulted in four regulatory actions including four product withdrawals [4]. Actions mentioned referred to drug quality issues (e.g. sodium valproate tablets with wet content in blister), and adverse reactions (e.g. skin burns from iodine tincture).

The last eight years 31 regulatory actions were documented relating to PV activities. In most instances, actions were based on inadequate quality of the product, but they were often identified through reports of adverse reactions.

The average time from first identification of a problem until regulatory action, was stated to be 2 – 3 months, depending on the nature of the investigation needed.

The planned publication schedule for the PV newsletter is four issues per year. Last year, three issues were released (see section 4.1.2.4).

Questions from the outside community to FMHACA regarding issues of medication safety are managed by another department (Health Regulatory Information Centre). No statistical records are kept at the PV centre regarding the number or nature of such questions.

FMHACA has initiated one regulatory action based on information about safety issues received from WHO or other countries (an alert re. codeine received from the US Food and Drug Administration). Such alerts normally do not refer to products available on the Ethiopian market.

[4] Lidocaine with adrenaline, Iodine tincture, Ringer lactate , sodium valproate

No information was provided on the number of training activities related to medicine safety that have been targeted towards the general public.

4.2 Marketing authorization holders, importers and distributors

4.2.1 Systems, structures and stakeholder's coordination

The two multinational companies and the importer have focal persons responsible for PV. Their tasks seem not to be on par with what is normally required from Qualified Persons for Pharmacovigilance (QPPV) internationally, which is not a legal requirement in Ethiopia. In the other companies the professional responsible for quality management is also responsible for management of any safety concerns.

4.2.2 Risk assessment and evaluation

Complaints about failing quality or safety of products are normally collected by members of the company sales force and are passed on to the PV focal person or quality manager. One international company has a process of passing on adverse reaction reports to their office in South Africa, taking care of recording, processing and submission of case reports to relevant authorities.

4.2.3 Risk management and communication

Multinational pharmaceutical enterprises have systems for submission of risk management or risk mitigation plans to the authority. The international (multinational) companies may receive Periodic Safety Update Reports from other African representative offices for submission to FMHACA.

4.2.4 Other information acquired from the representatives of pharmaceutical enterprises

There is a high level of preparedness from industry to comply with possible stricter requirements from the regulatory agency regarding establishment of a QPPV function, regular ICSR reporting, submission of periodic safety updates and risk management plans.

4.3 Healthcare facilities

Two out of three facilities visited had a mechanism in place to disseminate PV information in the health facility:

- one had a Telegram group for health care workers for sharing updates on drug indications, adverse events, etc., a library with drug info, and an information board in the hospital. Also, the PV newsletter from FMHACA is distributed; and
- one had an email service to physicians with safety updates, drugs quality defect communication to the Pharmaceuticals Fund and Supply Agency and departments, a monthly drug information bulletin including PV related information if available, and regular Drugs and Therapeutic Committee meetings, although the latter are not PV specific, but rather focus on drug expiry and stock-out problems.

One other health facility was relying on the regular newsletters from FMHACA for PV information, whereas one health facility said that such newsletters were not received by the facility.

For spontaneous reporting, health care providers can fill so-called yellow forms. These can be filled on paper and sent to FMHACA, or scanned and then sent as pdf by email to FMHACA. SAEs should be reported to FMHACA within 24 hrs after the SAE became known to the health care provider. Therefore, health care professionals are advised to fill out the version of the yellow form available on the website of FMHACA, scan it and send it to FMHACA by email. Not all filled yellow forms are submitted to FMHACA: in one of the visited health facilities, none of the four filled yellow forms had been submitted, whereas in another facility, only 2/4 filled reports had been submitted to FMHACA.
One facility reported one suspected product quality issue to FMHACA, but another facility did not report a drug quality issue (ketamin with visible particles).

5. Conclusions: Strengths and weaknesses of the Ethiopian PV system

5.1. Strengths of the PV system managed by FMHACA

- There is a solid legal foundation of the national PV system expressed in the following instruments:
    a. Health Policy (1993) and Drug Policy
    b. Proclamation (Act) No 661/2009
    c. Regulation No 299/2013
    d. FMHACA Guidelines, 3rd ed 2014

  The guidelines are quite well aligned with international best practice and legal requirements, although gaps do exist. The present guidelines are considered for revision in 2019.

- A national centre for PV with standard premises exists at FMHACA, with well trained staff, supported by a technical advisory committee. Individual plans for competence development of staff are made.

- The Centre is equipped with computerized data management systems and has internet access.

- The activities of the national centre are coordinated with other units within FMHACA and platforms for collaboration with external stakeholders exist. Such stakeholders include Public Health Programmes (EPI, TB, NTD).

- The national PV centre has been active in developing training curricula for PV in collaboration with academic institution and Ministry of Education.

- Training courses have been carried out for in-service healthcare professionals in the regions. Such activities have resulted in higher reporting rates.

- The Centre is actively contributing to a discussion about harmonizing PV standards and methods in the region under the umbrella of IGAD.

- Internal processes for data management and analysis are described in a Standard Operating Procedure (SOP) document, although the frequency of updating is not known or recorded. Well defined and up to date Terms of Reference for the Adverse Reaction Advisory Committee exist

- A standard reporting form is available and is distributed around the country. Postage for returning it to the centre is pre-paid. Any kind of medicine related problem can be reported with the standard yellow form.

- ICSRs shared with the WHO VigiBase database have a high VigiGrade completeness score, which indicates a high information content.

- All individuals submitting ICSRs to the system receive an acknowledgement, accompanied by supporting material

- The centre has initiated an active Cohort Event Monitoring project of antiretroviral medicines, although it was later outsourced to another institute with better resources.

- The reporting system has triggered regulatory actions based on identified problems. In most instances inadequate quality has been the reason for withdrawals.

5.2 Weaknesses and needs

- The Ethiopian PV system has a repertoire of Laws, Regulations which are to some extent aligned with International best practices. However there are notable gaps which should be addressed and the need for intense stakeholder engagement is an important consideration. The use of a Standalone PV policy to draw commitment with more thrust on core PV issues, delineating roles and responsibilities may be a pro-active approach with more positive results.

- Resources at the PV centre are inadequate for the full implementation of provisions in the 2014 Guidelines for Adverse Drug Events Monitoring. The PV function does not benefit from a designated annual budget, allowing its management to plan properly for sustainability and long-term development.

- FMHACA would need to establish a PV inspectorate to ensure that stakeholders e.g. MAH are indeed following the reporting requirements mentioned in the guidelines.

- Although the staff members of the PV centre are experienced and well trained, given the large population size of Ethiopia, they are too few to be able to interact with, promote and engage stakeholders needed to ensure input to the PV system, i.e. healthcare organizations, healthcare professionals, Marketing Authorization Holders, Academia, Public Health Programmes, media and the public. The input of reports of suspected medicine related harm received from these stakeholders is far too low, leading to very limited output and results from the system.

- Currently, there is no specific PV advisory committee. The Drug Advisory Committee (DAC) / AEFI committee is used to serve as such but may not consider all PV issues. Thus, there is a need to establish a formal PV Advisory Committee.

- The inadequate input of observations of suspected harm to the system leads to an under-utilization of the Adverse Reactions Advisory Committee. Members of this committee should be engaged in the promotion of the system nationwide. The fact that only 10% of the ICSRs were subjected to causality assessment is an indication that the available expertise is not fully utilized.

- Ethiopia has a high level of self-medication, including use of traditional medicines. The level of harm from this use of medicines in the community will not be known to authorities unless direct patient reporting is facilitated and encouraged.

- The PV centre is poorly supported by technical facilities. Data management is fragmented. Relevant information is stored in different systems and moved between systems. This invites mistakes and is resource demanding and complicates signal detection. There are no library facilities easy at hand which makes data analysis tedious if not impossible.

- There are questions around the internal quality management; the reliability of keeping data in different IT-systems, the regular review and adherence to the SOPs, the long-term planning of competence development for staff etc.

- Identified signals leading to regulatory actions have mainly concerned product quality related issues, which probably reflects the inadequate input of clinically serious consequences of pharmacotherapy reported from the healthcare system, MAH and Public Health Programmes.

- Although plans for communication of patient safety issues are developed by FMHACA and communication channels are available, they are not optimally used because of inadequate resources, both financial and human. Low visibility leads to a poor understanding in the community of the importance of the system.

5.3. Overall assessment of pharmacovigilance as practiced by marketing authorization holders and distributors

Currently the pharmaceutical corporations operating in Ethiopia are not well equipped in terms of structures, processes and competence to comply with the stipulations of the 'Guideline for Adverse Drug Events Monitoring [Pharmacovigilance]' from 2014. As can be expected representatives of international companies have more advanced routines, although still not fully complying with the guidelines. There is an openness and positive attitude in the industry to stricter demands from the regulatory authority and a preparedness to get engaged in training activities in case all companies would be required to have a Qualified Person for Pharmacovigilance (QPPV). Such steps are not likely to be taken, however, unless there is a new initiative from FMHACA to actively engage MAHs in PV activities and to enforce the 2014 guidelines.

6. Recommendations

6.1. Respondents' recommendations

- Simplify reporting for health professionals by making electronic reporting tool and offer that as an additional option for reporting (next to reporting on paper forms and reporting scanned forms via e-mail).

- Conduct regular trainings about PV for all (especially new) healthcare providers, including general practitioners, nurses and pharmacists; this is especially needed given the relatively high staff turnover.

- Ensure that good internet is available in health facilities

- FMHACA should be more active in sending feedback about the reports to the reporting health care provider

- A focal person for PV (and/or PV data collection) might further increase clinician's awareness about the importance of PV

6.2 Recommendations by external assessors

Interventions that would strengthen the capacity of the National PV System, to be considered and prioritised for implementation by stakeholders involved. The recommended interventions are not ordered in terms of their importance or time sequence in which they should be implemented. This time planning should be carried out in connection with the development of a national PV plan.

6.2.1 Policy, law and regulations

- Consider strengthening the requirements for MAH to contribute to the PV system, as stated in the guideline of 2014, to the level of regulation, making the consequences of non-compliance more serious. As a minimum the requirements should include
    - Mandatory appointment of QPPV
    - Submission timelines for ICSRs, PSUR/PBRER, RMP in line with international standards
    - Mandatory performance and funding of Post Authorization Safety Studies (PASS) relating to identified safety signals, on request by FMHACA

- The MAHs should play an active role in gathering data specifically from the Ethiopian market, and not only submit data from the rest of the world.

6.2.2 System, structures and processes

- Establish a separate PV unit with a dedicated annual budget

- Budget allocations need to be strengthened considerably if only to implement the current PV guidelines and further if ambitions are increased beyond the current guidelines

- Supplement current paper-based ICSR reporting with electronic reporting tools using internet, e-mail and/or reporting applications

- Recruit additional staff necessary for implementation of PV activities in all parts of the country at a level required to support the PV guidelines. Also, staff with competence in communication, both regarding technology and content, should be recruited to the PV system.

- All staff recruited to the PV centre should undergo basic PV training offering an understanding of the full scope of PV, e.g. the different types of harm caused by medicines, methods used for their study and management, and an understanding of the role of the different stakeholders involved.

- All health care professionals actively involved in the ADR reporting system and its management should undergo a course in causality assessment. Apart from this course, the national and regional PV staff should also have a course on signal analysis. Such courses are offered online by the UMC free of charge.

- Organize relevant training for FMHACA staff responsible for assessment of Periodic Safety Update Reports (PSUR) and Periodic Benefit-Harm Evaluation Reports (PBRER) from MAH, to empower EFMHACA staff to retrieve the relevant safety information to identify new safety information of relevance ensuring routine management of necessary changes to user instructions.

- Establish a plan with ToR for engagement of the EFMHACA branch offices to represent the PV system around the country.

- Design a curriculum for recurrent training of staff

- Ensure that enabling technological infrastructure e.g. offices, computers and broad-band internet, is available to all centres involved in the national PV network

- Streamline ICSR data management, ensuring safety data to be stored in only one database, using one tool for data retrieval, statistics and signal analysis. This database should be regularly backed-up at a safe location and it should not only exist on one (stand-alone) computer Transfer of data between different internal systems should be avoided, being wasteful and error prone. The notifications should be stored in such manner that adverse events can be easily retrieved by organ group.

- Organize access to up-to-date reference literature, including the HINARI system, for all professionals involved in causality- and benefit-harm assessments and signal analysis.

- Plan and conduct a mandatory training in e.g. causality assessment, signal analysis and benefit-harm assessment for members of the National Pharmacovigilance Advisory Committee.

- Ensure that the Standard Operating Procedures for the routine operation of the EFMHACA have a review date and are regularly reconsidered for relevance.

- Approach the Pharmaceutical Supply Funding Agency and the Central Port Coordination office, suggesting a collaboration for development of drug utilization statistics for routine use by the PV centre.

- Plan and implement fast and reliable communication channels with key stakeholders in the PV network nationally and internationally for two-way communication. The national PV centre needs to be easy to reach with new safety information and have several communication channels for outward dissemination of information.

- Establish a PV inspectorate function to ensure stakeholder compliance with PV regulations and guidelines. Provide adequate training for inspectors.

6.2.3 Stakeholder coordination

- Establish and formalize the PV Forum (see paragraph 4.1.2.7) as a regular platform for discussions with stakeholders to develop active collaboration and information exchange with representatives of healthcare professionals, PHP, MAH, patient organizations, media etc.

- Make explicit agreements with individual PHPs on the roles and responsibilities of the monitoring of the safety of the drugs deployed in the programmes.

- Plan and budget for participation from the national PV centre in the annual meetings of the WHO Programme for International Drug Monitoring and other professional and scientific conferences in PV

- Once requirements for MAH to establish QPPVs are in place, their responsibilities should be defined, and training offered. Organization of such professional trainings for a QPPV certificate in partnership with academic partners should be considered.

- Building on previous experience in development of an undergraduate PV curriculum for healthcare professionals, academic partners should be engaged in providing basic PV training to undergraduate students in medicine, pharmacy, nursing and dental medicine.

- Approach academic scientists, engaging them in joint patient safety research projects of major importance e.g. the burden of medicine related harm in Ethiopian hospitals. The possibility of writing joint grant applications should be considered.

- Establish relationships with managers of all Public Health Programmes that are using medicines and vaccines as important interventions. Engage them as important partners in the national PV system by e.g.
    - Developing joint guidelines for safety surveillance of medicines used
    - Designing specific training programmes for healthcare workers in the PHP
    - Carrying out joint active safety surveillance when new therapeutic regimens are being introduced in the PHP.
    - Provide PHP managers with specially designed feed-back on reporting and safety profiles of products in frequent use.

- Engage all hospitals as partners of the national PV system through their Drug and Therapeutics Committees (DTC). Guidelines for DTCs should be written to include responsibility for collection, assessment and further reporting of ICSRs to the national PV centre. To motivate committee members training programmes should be designed and offered both electronically and as face-to-face training courses. The DTC members should be made responsible for PV training of HCP in their facility.

- Consider establishing PV sentinel sites at hospitals of clinical excellence in key disciplines. The safety of new medicines introduced in such specialist hospitals can be surveyed in an intensive manner.

- Approach professional societies of medicine, pharmacy, nursing and dentistry offering continuing professional education through short training courses in PV and patient safety. Such training should also be offered to practitioners of traditional medicine.

- Identify and approach community leaders in the civil society, including religious leaders, and discuss how best to educate their community members about safe use of medicines and to find out about their problems when seeking healthcare and taking medicines. Models for such interventions in Africa exist.

- Identify and approach suitable patient and consumer organizations to find out about their perspectives on the safe use of medicines and offer education. Systems for patient reporting should be developed since information on occasional harm from self-treatment is unlikely to reach HCP and the PV system unless serious.

- Establish a communications plan, ensuring that plans and responsibilities for crisis prevention, management and communication are included.

- Produce information and education regarding medicine safety and PV for the general public to be disseminated in different media channels, both printed, broadcast and web based. The general public should understand the purpose of PV and the role of the individual patient in the system.

- PV training for media professionals should be maintained and expanded. The crucial role of media as providers of balanced information for the public should be explained

- With growing media attention to medicine safety and PV, all staff members of the PV system should receive media training.

Annex 1. Assessment tool for NMRA and MAHs

Indicator #	Indicator	Assessment Questions	Answer	Notes & additional comments	Information source
Component 1. Policy, Law, and Regulation					
1.1	Existence of a policy document that contains essential statements on pharmacovigilance or safety of medicines, health products and technologies (stand alone or as a part of some other policy document)	Is there a national policy on pharmacovigilance or medicine safety, or a more general medicines policy that contains essential statements?	Yes	National Health Policy Article 7.4 Mention Safety of Products. Established by Parliament Drug Policy (Article 4.5)	EFMHACA TEAM
		When was the policy last reviewed? *Date* (DD/MM/YYYY)	2000	Under revision	
1.2	Existence of specific legal provisions for pharmacovigilance in the national medicines legislation or similar legislation	Are there legal provisions for pharmacovigilance or medicine safety in the medicines act or law?	Yes	Proclamation – Mandate to EFMHACA 2009. Under revision – consideration of mandatory reporting and sanctions to be included in regulations for health care workers	
1.3	Legal provisions for Marketing Authorization Holders to monitor and report the safety and quality of their products	Is it mandatory by law or regulations for MAHs to		it is mentioned in the regulation, guidelines provide more information from MAHs, these are quite specific	
		- conduct post marketing safety activities?	Yes		
		- report adverse drug reactions/medicine safety related issues?	Yes		
		- regularly submit periodic safety update reports (PSUR) or periodic benefit-risk evaluation reports (PBRER)?	Yes	Regulations exist but no capacity. Per guideline: new drugs – every 6 months for two years, thereafter annually for 3 years licensing is only for 4 years at the moment no PV inspection plan, but there is general inspection directorate	
1.4	Existence of legal provisions empowering the national regulatory authority to require Marketing Authorization Holders to submit proof of their proactive pharmacovigilance planning as part of an application for product licensing	Does the national regulatory authority have the power to require MAH to submit any of the following documents prior to product licensing?		High risk if substance has not previously been registered in Ethiopia. Registration and PV in same directorate, not involved in the evaluation process, when it moves to post-authorization it will be the responsibility of the PV unit, but in practice this does not happen	
		I. Pharmacovigilance plan	Yes	Requested for during Registration process	
		II. Risk management plan	No	Country specific RMP not in place	
		III. Risk minimization/ mitigation plan	No	Activities limited by number of personnel	

		Are MAHs required to adapt the plans to the particular risk situation of the population in the country?	No		
1.5	Existence of national pharmacovigilance guidelines developed or reviewed within the past 5 years	Does a national guideline for PV (or a related document) exist?	Yes	Last published/ circulated in 2014 Under revision. MAH input requested.	National PV guideline
		Has the national PV guideline been developed or reviewed within the past 5 years?	Yes	Under revision	
		When were the guidelines last reviewed? *Date*		Revision started in 2014. MAH is circulated to receive their comments, new version is expected to be finished in 2019	
1.6	Regulations and guidelines encourage distributors, importers exporters, health- care institutions, other stakeholders and consumers to report ADR and/or AE to the MAH and/or NRA	Do regulations and guidelines encourage distributors, importers exporters, health-care institutions, other stakeholders and consumers to report ADR and/or AE to the MAH and/or NRA	Yes	Not yet with Consumers. Toll free line 8482 in Aramaic	
1.7	The legal provisions and/or regulations allow NRA to require manufacturers and/or MAHs to conduct specific studies on safety and effectiveness under specific conditions	Does the national regulatory authority have the mandate to require manufacturers and/or marketing authorization holders to conduct and present results from specific studies addressing identified safety concerns?	No		
1.8	Legal provisions, regulations and/or guidelines require manufacturers and/or marketing authorization holders to designate a Qualified Person responsible for vigilance.	Do legal provisions, regulations and/or guidelines require manufacturers and/or marketing authorization holders to designate a Qualified Person responsible for vigilance?	No		
1.9	Existence of updated National Essential Medicines List that was reviewed with consideration of medicine safety information	Is there an essential medicines list in use?	Yes	EFMHACA in consultation with MoH. EFMHACA is driver of the process.	www.EMFHACA.gov.net
		Does the essential medicines list selection committee consult medicine safety information?	Un-clear	To be confirmed	
		When was the list last reviewed? *Date*	2015		
1.10	Existence of a medicines regulatory authority or agency	Is there a drug regulatory authority or agency?	Yes	Drug Administration and Control Agency (DACA) established 1999. Definitively established 2010 with Proclamation 2009 ET. Regulation 189.	

1.11	Existence of official records of licensed medicinal products	Is there an official source of information on medicinal products that are licensed for use in the country?	Yes		
1.12	Accreditation of private health facilities includes requirements for the existence of a pharmacovigilance system	Does the public authority responsible for accreditation of private health facilities require that a pharmacovigilance system is in place?	No		
Component 2. Systems, Structures, and Stakeholder Coordination					
2.1	Existence of a national pharmacovigilance center with a clear mandate and structure	Is there a National PV center or any other body assigned the responsibility of monitoring safety of medicines?	Yes		
		Is there a clear mandate and organizational structure for the pharmacovigilance center?	Yes	EFMHACA Responsibility shared – PV 70%; Clinical Trials 30%	
2.2	The pharmacovigilance center has designated, qualified human resources to carry-out its functions	How many staff members (full-time equivalent) does the PV center or system have who are specifically responsible for carrying out its functions (technical and administrative)?	4	Four staff; 6 Regional Offices with 1 focal person/office (but the latter are not only for PV and have no terms of reference – they are the main contacts for training. HR is responsibility of civil service ministry and it is therefore very difficult to get extra staff.	
2.3	Existence of a dedicated financial provision or statutory budget for the pharmacovigilance center	Is there an annual budgetary allocation for PV activities or for the PV Center?	Yes / No	Flexible budget from government + Donor funding (e.g GAVI)	
		In the last fiscal year, how many funds were allocated by the government and donors for pharmacovigilance activities? *Please specify the amount & currency*		Budget is based on directorate level, not specified per unit. PV has a 3 year project now and has a specific budget, 30% of the project from government and 70% from donors. Has a fundraising unit which facilitates in getting funding.	
2.4	Existence of a functional national medicine safety advisory committee	Does a national medicine safety advisory committee exist with the responsibility to provide technical advice on the safety of medicines to the regulatory authority?	No	Technical Committee for AEFI exists	
		Has the national medicine safety advisory committee met at least twice in the previous calendar year?	No	Last meeting was about a year ago because of serious AEFI reports	ToR, minutes
2.5	Existence of standard operating procedures (SOPs) for conducting pharmacovigilance activities	Does the NMRA / PV center have SOPs for pharmacovigilance activities?	No	Only for AEFI	
		When were the SOPs last reviewed? *Date.*		NA	

2.6	Existence of a source of data on consumption and prescription of medicines	Are there any sources of information on sales or consumption of medicines on a national, regional or local level? .	No	Availability at Port Health Office for import, Pharmaceutical Funding Supply Agency for public sector, local manufacturers for production	
		Are they publicly available?	No	Drugs distributed by Pharmaceutical Supply Agency	
2.7	Existence of a library or other reference source for drug safety information	Does the PV center has access to a library or electronic sources providing up-to-date information on medicine safety and the progress of scientific knowledge in the domain?	No	No links. No drug information service Use of freely available internet sources, WHO, Hinari. Plan to subscribe to Micromedex and Pubmed	
2.8	Existence of a mechanism to disseminate pharmacovigilance information (including one or more of the following: newsletters, information bulletin, website or phone line for dissemination of pharmacovigilance information)	Is there a communication plan in place to disseminate PV information?	Yes		
		Is there a newsletter or information bulletin for dissemination of PV information?	Yes		
		How many issues of the medicine safety bulletin are supposed to be published per year	4		
		How many issues of the medicine safety bulletin were published in the previous calendar year?	1	2016: 2 issues, 2017: 1 issue, 2018: 1 issue	
		Is there a website for dissemination of PV information?	Yes	www.fmhaca.gov.et. Managed by IT directorate within EFMHACA (Need for a Webmaster inhouse)	
		Is there a publicly advertised phone line to receive and provide medicine safety and PV information?	Yes	Toll free 8482 for general EFMHACA issues.	
		Are findings published in national/international journals?	Yes	Use of Local Ethiopian Pharmacy Association Bulletin	
		Is there another mechanism for dissemination of PV information? *Please describe the mechanism in Notes*	Yes	FMHACA is providing training for journalist, 3 rounds of training this year, in about 40 different regions; printed media, radio, PR directorate, FMHACA IT policy says that on a department level you are not allowed to use social media	
2.9	Existence of harmonized pharmacovigilance curricula for key healthcare workers - **Pre-Service**	Is PV incorporated into the national pre-service curricula of doctors?	Yes	Training materials developed 5-6 years ago. FMHACA approached all universities for inclusion of PV in curriculum in 2013. Collaboration with Ministry of Education. No follow up.	
		Is PV incorporated into the national pre-service curricula of nurses?	Yes		
		Is PV incorporated into the national pre-service curricula of pharmacists?	Yes		
		Is the curriculum in use for pre-service training of healthcare workers the EAC harmonized PV curriculum?	No	HCP rotate all the time, especially the lower levels, nurses, pharmacists and health care workers	

2.10	Existence of harmonized pharmacovigilance curricula for key healthcare workers - **In-Service**	Is there a pharmacovigilance training module, manual, or curriculum for **in-service** training of health care workers?	Yes	2-3 d training at health care facilities, for 20-30 HCP, about 2 hours sessions: present PV system, yellow card and how to fill it. EFMHACA mainly in Addis; in the regions, regional branches carry out these tasks. AEFI has separate training curriculum.	
2.11	Number of healthcare workers trained in pharmacovigilance in the previous calendar year through in-service training program	How many healthcare workers has the center/program trained on PV in the previous calendar year (through **in-service** training)?		Done at clinics. In-service training is shown to be very productive: higher number of reports, appointment of focal PV person. Follow up is important. Staff interested to come but lack of resources for scale-up.	
		a. Health professionals	700		
		b. Community health workers	0?		
		How many training events/sessions were conducted in the previous calendar year?			
		a. For health professionals	5, double events	3 health facilities visited based on demand	
		b. For community health workers	0?		
2.12	Adoption and use of harmonized web-based pharmacovigilance training tools	Are web-based PV training tools available?			
		a. For health professionals	No	There are computers but no access to internet	
		b. For the general public	No		
2.13	Existence of a functioning platform, mechanism or strategy for the coordination of pharmacovigilance activities - **National Level**	Does a platform, mechanism or strategy for the coordination of pharmacovigilance activities (such as PV technical working group, forum or regularly scheduled meetings) exist among **national stakeholders**?	Yes	Internal PV forum, inspectorate and quality control directorate, regional branch coordination office (to collect samples), external coordination with TB and neglected tropical diseases, EPI (immunizations team).	
		Have the key **national stakeholders** convened at least once in the previous calendar year?	Yes		
2.16	Submission of AE reports by health-care facilities in the previous year	From how many health facilities were AE reports received in the previous calendar year?	84		
		How many health facilities are there in the country?	3800 + 400	3800 governmental HF, 400 hospitals not including private sector	
		How many health facilities submitted >10 reports to the PV center in the previous calendar year?	9		

2.17	Evidence of consideration of safety data when developing and updating standard treatment guidelines	When developing standard treatment guidelines is evidence on safety data being described and taken into consideration?	No	PHPs TB/HIV/Malaria have program-specific guidelines; EFMHACA is responsible for treatment guidelines of other diseases which are updated every 5 years. Safety date is not routinely taken into account.	
2.18	National PV center is a full or associate member of the WHO Program for International Drug Monitoring	Is the national pharmacovigilance center a full or associate member of the WHO Program for International Drug Monitoring?	full member	nr 88, in 2009	
Component 3. Signal Generation and Data Management					
3.1	Existence of a national database for pharmacovigilance information	Does a central database exist for managing PV data?	Yes	ADRs are entered into VigiFlow. 706 reports received, 504 ADRs, 84 product defect problems.	
		Does the central database contain data from various PV sources and methods (including PHPs?)	Yes		
		Is there a dedicated computer for pharmacovigilance activities?	Yes		
		Does the computer have internet access?	Yes		
		Is data stored on a cloud/server? *Please specify*	No		
		Is there a back-up system? *Please specify*	?		
3.2	Evidence of a process or mechanism for sharing information with other regulatory functions, other regulatory agencies and global databases	Has information in the database been shared (either electronically or via report) with other regulatory functions, other regulatory agencies and/or global databases?	Yes	Inspectorate, regions, with PHPs the reports that are specific to that program; through VigiFlow shared with VigiBase	
3.3	Existence of a standard adverse event (AE) reporting form and subset indicators	Is there a standard AE reporting form?	Yes	Yellow form, AEFI form, special TB form	
		How is the reporting form offered? (e.*g.* paperform, web, app)		paper, available for download on the website	
		Are there relevant fields in the standard AE form (or a separate form) to report:			
		- adverse drug reactions?	Yes	Standard AE reporting form	
		- Suspected medication errors?	Yes	From TB program	
		- therapeutic ineffectiveness?	Yes	Standard AE reporting form / separate form	
		- misuse, abuse and/or dependence on medicines?	Yes	Standard AE reporting form / separate form	
		- suspected/ observed poor quality issues?	Yes	Standard AE reporting form	

		- adverse events following immunization?	Yes	Separate form	
		- medical devices and diagnostics?	Yes	Standard AE reporting form	
3.4	Existence of a form or mechanism for the public to report AEs (Patient reporting system)	Is there a standard reporting form for the general public to report AEs?	No	General public can report by calling toll-free number.	
3.5	Existence of electronic AE reporting system that complies with international reporting format standards	Is there an electronic AE reporting system?	No	There is interest in implementing the WEB-RADR app, website electronic format as in Kenya and Tanzania or the e-reporting tool from the UMC	
		If yes, please provide technical details.			
		Is the system compliant with the international reporting standards (E2B)?	n/a		
3.6	A process is in place for collection, recording and analysis of ADR reports	Is there a process in place for collection, recording and analysis of ADR reports?	Yes	There is an SOP, e-mail specific for pharmacovigilance, automatic reply acknowledging report, as well as official letter. Missing information is asked for by telephone, for all incomplete reports. For SAE reporters are always contacted. Data entered into the local database. ADRs are entered in Vigiflow. All SAE are sent to the advisory committee for causality assessment.	
Component 4. Risk Assessment and Evaluation					
4.1	Number of registered products with a PV plan and/or a risk management strategy	How many registered products with a pharmacovigilance plan and/or a risk management strategy from market authorization holders exist in the country?	None	As part of distribution agreement all products have a PV plan. There is no record of a submitted plan to the Regulatory Authority.	Product Registration and Licensing Directorate
4.2	Total number of AE reports received in the previous calendar year (also expressed as number of AEs per 100 000 persons in the population). And number of reports of sub-indicators	What is the total number of AE reports received in the previous calendar year? Of the total, what is te number of reports of:	706		
		- ADR?	504	3.02 per million inhabitants (235 from TB program)	
		- suspected medication errors?	1		
		- therapeutic ineffectiveness?	1		
		- suspected misuse, abuse, dependence?	0		
		- AEFI?	17		
		- medical devices and diagnostics?	0		
		- suspected counterfeit / substandard drugs?	84	95 product quality defect reports received	

		What is the total population of the country?	104.9 million		http://www.worldometers.info/world-population/ethiopia-population/
4.3	Number and percentage of total AE reports received by the national pharmacovigilance center in the previous calendar year from:	What is the number of AE reports received by the national pharmacovigilance center in the previous calendar year from:			
	- Marketing Authorization Holders	- Marketing Authorization Holders	118		
	- PHPs	- PHPs	235	from TB program, through aDSM and STREAM trial	
	- Health care providers	- Health care providers	565	of which 235 are from TB program	
	- Patients	- Patients	0	There is no system in place for patients to report	
	-Distributors	-Distributors	128	From importers	
	-Suppliers	-Suppliers			
4.4	Number and percentage of total AE reports received that are entered in the national database in the previous calendar year	What is the total number of AE reports received that have been entered in the national database in the previous calendar year?	504		
4.6	Number and percentage of total AE reports acknowledged and/or issued feedback in the previous calendar year	What is the total number of AE reports acknowledged/issued feedback in the previous calendar year?	504	including clinical trials, acknowledgement, two more report forms, and the newsletter	
4.7	Number and percentage of AE reports subjected to causality assessment in the previous calendar year	What is the total number of AE reports subjected to causality assessment in the previous calendar year?	10		
4.8	Number and percentage of AE reports submitted to VigiBase in the previous calendar year	How many of the AE reports received at the national PV center were submitted to Vigibase in the previous calendar year?	171	reports from clinical trials are not entered, aDSM data are being entered into Vigiflow	
4.9	Average completeness score of quarterly reports submitted to VigiBase in the previous four quarters (= one year)	What was the average completeness score of quarterly reports submitted to Vigibase in the previous calendar year? *Consult quarterly reports from VigiGrade for completeness scores of submitted reports*	0.8675		PV center

4.10	Number of active surveillance activities initiated, ongoing or completed during the previous three years	How many active surveillance studies have been conducted in the last three years (36 months)?	1		
		Indicate what type (e.g. cohort event monitoring, targeted spontaneous reporting, etc.) and stage of completion (e.g. initiated, on-going or completed) for each study. *Request research protocol*		Cohort event monitoring on Antiretroviral medicines, the surveillance is ongoing. CEM first managed by FMHACA but now out-sourced to AHRI. AHRI has its own database for this purpose. 3000 patients targeted, now 2000 included.	
4.11	Number and percentage of total AE reports received at the national pharmacovigilance center in the previous calendar year from healthcare providers by type of provider	What is the number of AE reports received in the previous calendar year submitted by:			
		- doctors?	285		
		- nurses or midwifes?	9 nurses		
		- pharmacists?	159	55 from druggists	
		- manufacturers and pharmaceutical companies?			
		- dentists?			
		- the general public?			
		What is the total number of AE reports received in the previous calendar year?	556	Other HCP also reported: 25 Health officers, 12 Health extension heads, 1 laboratory technologist	
4.12	Evidence of supervision visits to marketing authorization holders by NMRA that address PV	Does the NMRA conduct supervision visits of MAHs that address PV?	No		
		How many supervision visits have been conducted in the previous calendar year?	n/a		
Component 5. Risk Management and Communication					
5.1	Number of regulatory actions taken in the previous calendar year as a consequence of national pharmacovigilance activities. *Request documentation to verify*	How many regulatory actions were taken in the previous calendar year as a consequence of pharmacovigilance activities that resulted in:	3	This data is only form the PV Center, additional Data has been requested from PMS/Inspection team.	
		- product label changes (variation)?			
		- safety warnings on medicines to health professionals?			
		- safety warnings on medicines to the general public?			
		- withdrawals of medicines?	4		
		- treatment guideline/policy changes?			
		- other restrictions on use of medicines?			

5.2	Number of signals detected in the past 5 years by the pharmacovigilance center	How many signals were detected in the past 5 years by the pharmacovigilance center?	31	in the past 8 years, all led to recall, mainly quality defects.	
		If any signals were detected, which ones and how were they identified?		On Measles Vaccine, It was detected from post campaign report. Causality analysis was done and recommendations were communicated to the Ministry of Health.	PV center
5.3	Average time lag between identification of safety signal of a serious ADR or significant medicine safety issue generated nationally and communication to health care workers and the public	How long does it take from when a safety signal or significant safety issue is identified to when it is communicated to health workers and the public? *Please answer in days for each signal identified in the previous calendar year.*	n/a		
5.4	Number of suspected product quality issues detected through the pharmacovigilance system	What is the number of suspected product quality issues detected through the pharmacovigilance system in the previous calendar year?			
5.5	Percentage of planned issues of the medicine safety bulletin (or any other health-related newsletter that routinely features ADR or medicine safety issues) published in the previous calendar year	How many issues of the medicine safety bulletin are supposed to be published per year?	4		
		How many issues of the medicine safety bulletin were published in the previous calendar year?	1		
5.6	Number of products voluntarily withdrawn by marketing authorization holders because of safety concerns in the previous calendar year	How many products were voluntarily withdrawn by marketing authorization holders because of safety concerns in the previous calendar year?	1		
5.7	Number and percentage of medicine safety information requests addressed in the previous calendar year	How many requests for information about medicine safety were received in the previous calendar year?	n/a	There is a different department dealing with information requests (Health Regulatory Information Center). Information is not shared with PV center.	
		Of the total received, how many requests for medicine safety information were addressed in the previous calendar year?	n/a		
5.8	Number of summaries of product characteristics updated by MAH because of safety concerns in the previous year	Of the total received, how many requests for medicine safety information were addressed in the previous calendar year?	n/a		

5.9	Number of medicine safety issues of local relevance identified from outside sources (e.g., from another country, from region or international sources) and acted on locally in the previous calendar year	How many medicine safety issues identified from outside sources were acted on locally in the previous calendar year?	None	Safety issues about medicines communicated to FMHACA from WHO were not registered in Ethiopia.	PV center
5.10	Number of public or community education activities relating to medicine safety carried out in the previous calendar year	How many public or community education activities relating to medicine safety were carried out in the previous calendar year?	n/a		

Annex 2. Spontaneous reporting form

Food, Medicine and Health Care Administration and Control Authority of Ethiopia (FMHACA)
Adverse Drug Event reporting form

Patient Name (abbreviation) ----------	Card No ----------	Age, Date of birth ----------	Sex ---------	Weight ----------	Height ----------
Ethnic group ----------		Substance of abuse ----------			

Information on suspected drug/vaccine S=suspected drug C=concomitantly used drugs

Drug name(write all information including brand name batch no and manufacturer	S/C	Dose/dosage form, route, frequency	Date drug taking was started (D/M/Y)	Date drug reaction started (D/M/Y)	Date drug taking was stopped (D/M/Y)	Indication (Reason for drug use)

Adverse drug event description(include all available laboratory test results)

_____
_____
_____
_____
_____
_____
_____
_____
_____.

Reaction necessitated Discontinuation of drug/s □ YES □ No Hospitalization prolonged □ YES □ No	Reaction subside after D/C of suspected drug □ YES □ No □ Information not available Reaction reappear after restart of suspected drug □ YES □ No □ Information not available

Treatment of reaction

_____
_____
_____

Outcome: □ Died due to the adverse event □ Died, drug may be contributory □ Not yet recovered
□ Recovered without sequelae □ Recovered with sequelae □ Unknown

Sequelae

Relevant medical conditions such as allergies, renal disease, liver disease, other chronic diseases, pregnancy etc_____

Reported by: Name ----------	Profession: ----------	Email address: ----------	Telephone ----------
Name of health institution			Date

Product quality problem: Color change, separating of components, powdering, crumbling, caking, molding, change of odor, incomplete pack, suspected contamination, poor packaging/poor labeling, etc (Write if anything different than given above)

Drug trade name	Batch No	Registration no	Dosage form and strength	Size /type of package

For office use only	
Received on:	Registration no:

Key: D/M/Y ; Date /Month/Year D/C; Discontinue treatment Y;YES N;NO

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what to report

All suspected reactions to drugs
Unknown or unexpected reactions
Serious adverse drug reactions
Unexpected therapeutic effects
All suspected drug interactions
Product quality problems
Treatment failures
Medication errors

NB. Drugs includes
Conventional drugs
Herbal drugs
Traditional medicines
Biologicals
Medical supplies
Medicated cosmetics

This ADE reporting form was prepared by FMHACA in collaboration with MSH/SPS and the financial support from USAID

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Business Reply Service License No HQ2

From ----------

Postage prepaid

Food, Medicine and Health care Administration and Control Authority of Ethiopia

Food, Medicine and Health Care Administration and Control Authority
Regulatory Information Development and Dissemination Team
P.O.Box 5681-Tel.0115-523142
Addis Ababa, Ethiopia

Annex 3. Further information about this report

This report was prepared for the PAVIA and PROFORMA project in February 2019, and composed by Sten Olsson, Linda Härmark, Jessica Maltha, Edine Tiemersma, Aida Arefayne, Eleni Aklillu, Ambrose Isah, Abimbola Opadeyi, Abbie Barry, Tsegazeab Tekle and Eyasu Makonnen.