MCAZ Medicines Control Authority of Zimbabwe

Medicines Information Bulletin

February 2022

Content

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COVID-19 Vaccines Update

In partnership with Zimbabwe Expanded Program on Immunization (ZEPI) Ministry of Health and Child (MoHCC), the National Pharmacovigilance Centre, MCAZ are the main drivers of vaccine safety surveillance. To date, five COVID-19 vaccines were given Emergency Use Authorisation by MCAZ, namely Sinopharm (China), Sinovac (China), Covaxin (India), Sputnik V (Russia) and Johnson & Johnson (Netherlands). ZEPI-MoHCC and MCAZ conducted several AEFI surveillance trainings of Healthcare Workers (HCWs) during the deployment of COVID-19 vaccines from February 2021 to date, including monitoring and evaluation visits that resulted in increased reporting of Adverse Events Following Immunizations (AEFI). Below is an update of COVID-19 vaccines AEFI reports received at the MCAZ as of 31 December 2021, thanks to the reporters. Signed letters feedback was sent to all the reporters.

- **Summary of number of AEFI reports received and adverse events reported**

Out of the cumulative total of 4.00 million 1st dose and 3.01 million 2nd doses of COVID-19 vaccines administered, 311 suspected COVID-19 Adverse Events Following Immunisation (AEFI) cases have been reported to the MCAZ. Most of the reported reactions were minor/ non-serious, with 24% of the suspected reports being classified as serious.

All reports received by the MCAZ undergo a process known as causality assessment by the National AEFI Committee using the WHO Aide-Memoire on AEFI causality assessment determine if the reactions reported could be due to the vaccines or other causes, such as underlying medical condition(s). After causality assessment, none of the serious reports received were found to be due to the vaccine. Some of the non-serious reactions were found to be due to the vaccine, and these include site adverse events (pain, redness, and swelling), headache, dizziness, fatigue, general body weakness, itchy skin, itchy rash, chills, nausea, vomiting etc. These patients usually recovered after a few days without any treatment.

Causality assessment was conducted by the MCAZ Pharmacovigilance and Clinical Trials division (PVCT) Committee that is also the national AEFI Committee, using the recommended WHO AEFI Causality assessment Algorithm Tool 2019. Of the 15 unfortunate death suspected COVID-19 vaccines reports, two (2) were classified *as coincidental meaning the adverse events were due to other underlying medical conditions.* Two (2) were classified as *B1 indeterminate meaning that there is no evidence that the vaccine caused the reactions, but the reactions occurred within a reasonable time frame after vaccination.* The causality assessment for eleven (11) reports was unclassifiable since post-mortem reports had not yet been submitted despite the follow ups done. Reclassification of these reports will be done when the post-mortem reports have been submitted to the MCAZ.

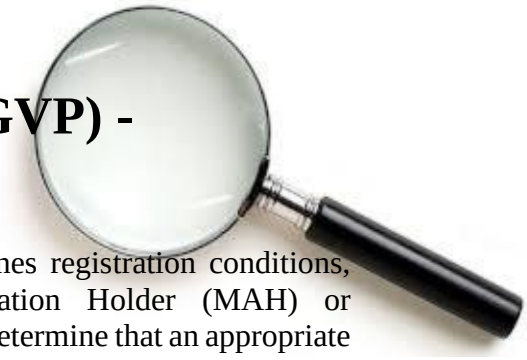
- **Summary of AEFI reports for COVID-19 vaccines by age and gender**

From the 311 AEFI reports received, 192 (62%) were from female COVID-19 vaccine recipients, 118 (38%) from male COVID-19 vaccine recipients and in one (1) report the gender was unknown. The majority of reports 239 (77%) were received from the 18-60 years age range. To note is that the distribution of AEFIs by age group and gender could simply be relative to the total number of people vaccinated in the respective age groups however gender, did not necessarily reflect that a particular age group is more prone to AEFIs. It maybe that more women tend to have been vaccinated more than the men.

Guideline for Pharmacovigilance of COVID-19 Vaccine- AEFI Safety Surveillance

The COVID-19 pandemic has affected Zimbabwe since March 2020. The high numbers of both positive cases and deaths prompted the country to plan for the introduction of vaccines. COVID-19 vaccine doses were secured and vaccination of priority groups commenced in February 2021. Safety of vaccines is an essential part of the success of immunisation programmes. This activity requires the involvement of various stakeholders whose mandate is to monitor safety of vaccines and the vaccination process. A Guideline for Pharmacovigilance of COVID-19 Vaccine-AEFI Safety Surveillance was developed by the Medicines Control Authority of Zimbabwe. It provides guidance on crisis management and communication, reporting of AEFIs during the COVID-19 vaccination programs, the roles of key players in COVID-19 safety surveillance, recommended safety surveillance activities for all countries introducing COVID-19 vaccine, etc. It is available at the MCAZ website or can be access via the link, https://www.mcaz.co.zw/?smd_process_download=1&download_id=3053

Good Pharmacovigilance Practices (GVP) - Pharmacovigilance Inspections



In line with MCAZ Circular 3 of 2022, with regards to medicines registration conditions, pharmacovigilance inspections of each Marketing Authorization Holder (MAH) or manufacturer of products registered in Zimbabwe shall be done to determine that an appropriate pharmacovigilance system is in place to monitor the safety of their products on the market. Copy of the circular 3 of 2022 was sent to all applicants/manufacturers and is also available on the MCAZ website.

The objectives of pharmacovigilance inspections are;

- to determine that the marketing authorisation holder has personnel, systems and facilities in place to meet their pharmacovigilance obligations,
- to identify, record and address non-compliance which may pose a risk to public health,
- to use the inspection results as a basis for enforcement action, where considered necessary.

A pharmacovigilance system is defined as a system used by an organization to fulfil its legal tasks and responsibilities in relation to pharmacovigilance and designed to monitor the safety of authorized medicinal products and detect any change to their risk-benefit balance. A pharmacovigilance system, like any system, is characterized by its structures, processes and outcomes.

In addition to spontaneous ADR reporting, the Market Authorisation Holder (MAH) or manufacturer shall put in place pharmacovigilance measures to actively monitor the safety of their products in clinical practice for a period specified by the Authority. The MAH or manufacturer shall permanently and continuously have at his disposal an appropriately Qualified Person Responsible for Pharmacovigilance (QPPV) or Responsible Personnel for PV.

Qualified Person for Pharmacovigilance (QPPV)

Every MAH or manufacturer who has registered a medicine in Zimbabwe shall designate a responsible person for Pharmacovigilance (PV) or QPPV to be in charge of the pharmacovigilance system. The individual shall be responsible for the safety of the medicines marketed by an applicant or manufacturer in Zimbabwe. However the MAH retains the overall responsibility for their products and is answerable to any issues regarding the products. For administrative purposes the MAH should notify the MCAZ in writing who their responsible person for PV or the QPPV is and submit their curriculum vitae, contact details and their responsibilities. The responsible person should be adequately qualified to execute her or his duties (healthcare professional with a degree in Medicine, Pharmacy, Nursing, Biomedical Sciences, or any other healthcare professional degree recognized by the Authority). The QPPV should have received a formal training in pharmacovigilance recognized by the Authority and should have knowledge of the Zimbabwe pharmacovigilance legislation and guidelines and other international standards for pharmacovigilance.

The MAH should:

1. Provide comprehensive training in pharmacovigilance to the QPPV
2. Ensure that the QPPV has sufficient authority to implement pharmacovigilance activities, provide inputs into Risk Management Plan when necessary, provide inputs into the preparation of regulatory documents to emerging safety concerns (e.g. variations, urgent safety restrictions and as appropriate, communication to Patients and Healthcare Professionals)
3. Ensure that there are appropriate processes, resources, communication mechanisms and access to all sources of relevant information in place for the fulfilment of the QPPV's responsibilities and tasks.
4. Notify the Authority of the absence of the QPPV not later than 30 days after the position becomes vacant.
5. Have a written contract with the QPPV.

The responsibilities of the QPPV are stated in detail in the Pharmacovigilance Guideline for Pharmaceutical Industry which is available on the MCAZ website or can be accessed via the link https://www.mcaz.co.zw/?smd_process_download=1&download_id=2682

References

1. Guideline on good pharmacovigilance practices (GVP), HMA-EMA, 19 June 2012, https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-good-pharmacovigilance-practices-module-iii-pharmacovigilance-inspections_en.pdf
2. Pharmacovigilance Guideline For Pharmaceutical Industry, https://www.mcaz.co.zw/?smd_process_download=1&download_id=2682

Zimbabwe Adverse Drug Reaction (ADR) Reporting in 2021 – Highlights

All medicines used in clinical practice have the potential to cause adverse drug reactions. The World Health Organization defines an ADR as "any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function." ADRs are a serious problem with increasing incidence as more medicines become available and more people become exposed to them.

Pharmacovigilance activities are therefore a necessary component in managing patients and enabling the prevention and/ or treatment of adverse reactions. Pharmacovigilance activities are coordinated by the National Pharmacovigilance Centre, MCAZ in collaboration with the Ministry of Health and Child Care (MoHCC) and all key stakeholders both in the public and private health sector.

Below is the summary of the ADR reports received at the MCAZ from January to December 2021 from patients and consumers; public MoHCC sites; and private sector health care facilities including pharmacies, hospitals and clinics. Thanks to all the reporters. Signed letter feedback was sent to all the reporters.

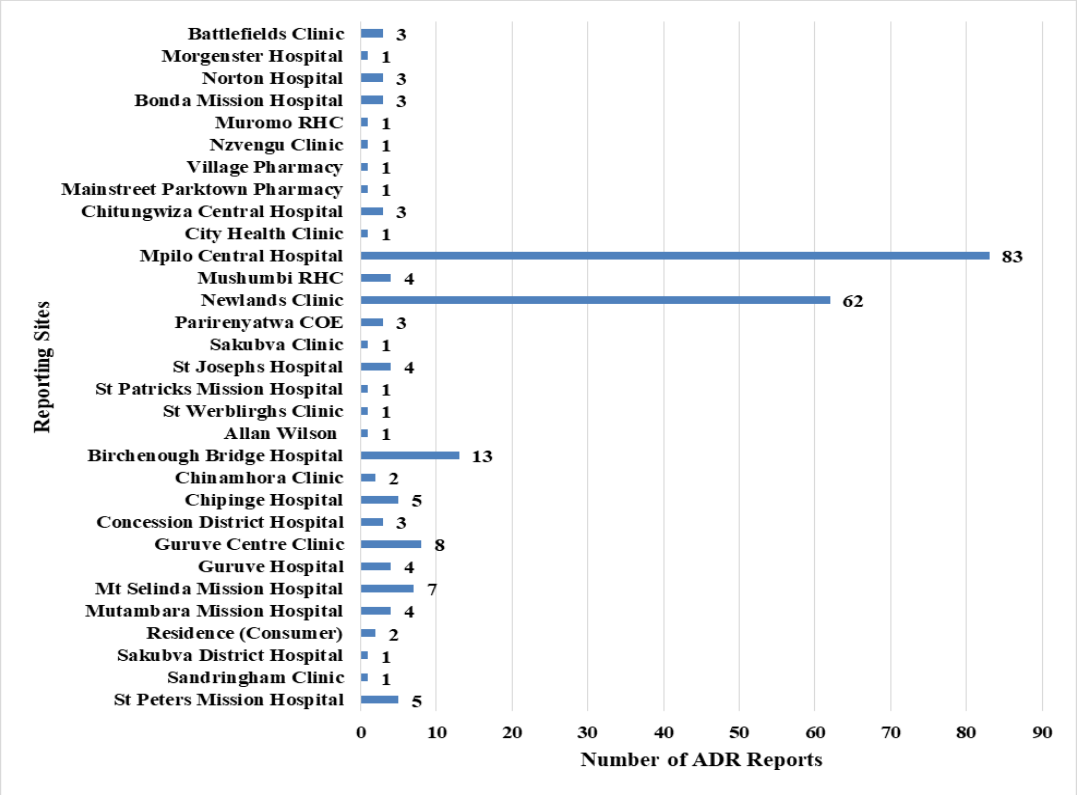
Table 1: Number of ADR reports received and processed by MCAZ in 2021

Type of ICSR reports	ADRs received and processed from January to December 2021
ADRs from the TSR of all essential medicines including ARVs and Anti-TBs from public MoHCC sites and some private sector clinics and doctors.	**233** **Suspected medicines** **107 ARVs** **91 Anti TBs** **1 Anti malaria medicines** **34 other essential medicine**

The majority of the ADR reports received in 2021 were ADR reports associated with Anti-Retroviral medicines (107). The most reported medicines were tenofovir and dolutegravir with renal impairment and weight gain being the most reported adverse reactions respectively. Renal impairment is a known adverse reaction for tenofovir in line with its Summary of Product Characteristics (SPC), labeling and not due to dolutegravir per se. Weight gain is a known SPC adverse reaction associated with dolutegravir. For ADR reports associated with Anti TB medicines, isoniazid was the most reported medicine with dermatological reactions (such as itchy rash, urticaria, skin desquamation, skin hyperpigmentation, etc.) being the most reported adverse reactions. Causality assessment of these reports in line with the WHO causality assessment was 'possible' which means that the adverse reactions could have been due to the medicines or other underlying medical conditions. The reports have been uploaded in an anonymized, de-identified format into the WHO Individual Case Safety Report database called VigiBase for further analysis and signal detection and the MCAZ manuscript publication will be available soon. Health care professionals, patients, consumers, guardians and care givers are

encouraged to continue to be vigilance and report adverse reactions to the MCAZ, where possible prevent and /or minimize the risk factors for adverse reactions occurrence and promote patient safety.

Figure 1: Distribution of ADR reports received at the MCAZ by reporting sites from January to December 2021



The MCAZ appreciates the tremendous support from all the reporting sites, healthcare professionals, patients and consumers in strengthening pharmacovigilance activities in Zimbabwe through their participation in reporting ADRs and promoting patient safety.

Reporters are encouraged to continue reporting adverse reactions by completing the ADR form and submitting them to the MCAZ. ADR reporting forms may be obtained from the following places:

1. The MCAZ offices – for hard copy forms
2. Online reporting using either one of the methods below:

- **Health care workers online reporting**
  https://e-pv.mcaz.co.zw

- **Consumer online reporting**
  https://primaryreporting.who-umc.org/ZW

- **Mobile apps for e-pv system**
  Android – search "MCAZ Pharmacovigilance" on Google Play Store
  iOs (iPhone and iPad) – search "MCAZ PV" on the Apple App Store

- **Desktop apps**

Desktop applications for three major operating systems listed below can be downloaded from the MCAZ website, www.mcaz.co.zw
Windows desktop application
MacOs desktop application
Linux based operating systems

Offline Reporting functionality of the ePV system. The mobile and desktop applications have offline functionality, that is, reports can be completed and saved when the user is offline then be submitted when an internet connection is available. Reporters are also encouraged to provide as much information as possible for the purpose of good quality and statistically sound reports.

Figure 2: Distribution of ADR reports received at the MCAZ by reporting provinces from January to December 2021

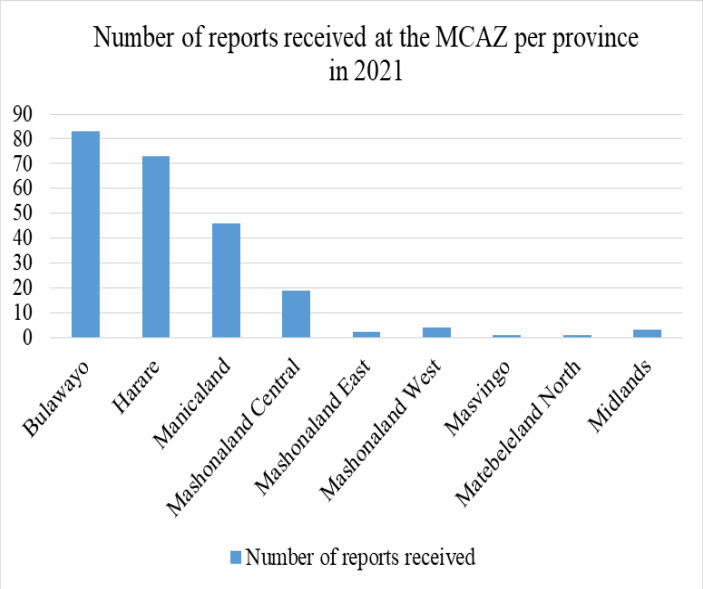
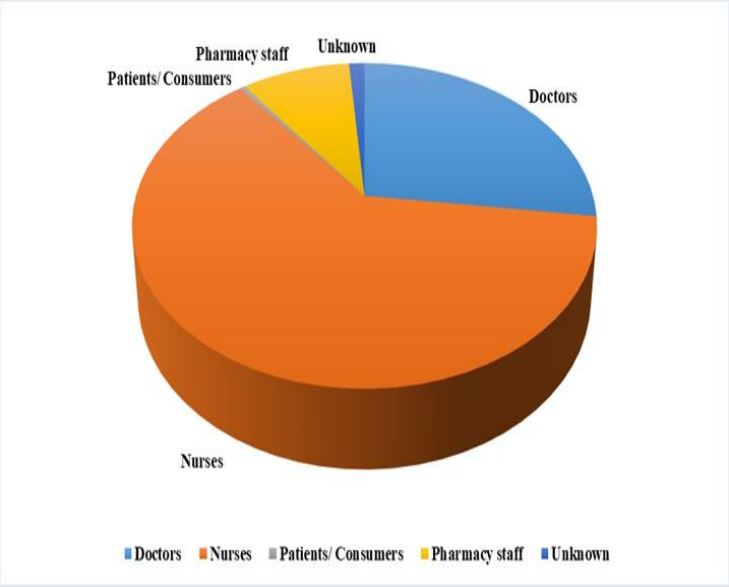


Figure 3: Number of ADR reports received versus types of reporters from January to December 2021



Everyone, including (but not limited to) health care professionals, patients, consumers, guardians and caregivers are encouraged to report all suspected adverse reactions to medicines (including vaccines, X-ray contrast media, complementary medicines), especially when the reaction is unusual, potentially serious or clinically significant. In the 2021, the majority of ADR reports that were received by the MCAZ were reported by nurses, thanks to the nurses' tenacity and assistance in promoting patient safety.

Substandard and Falsified Medicines Alerts

A substandard medical product is an **authorized product** which does not meet quality standards or specifications, produced by a known manufacturer with **no intent to fool or defraud** the patient. A falsified medical product is one that is **deliberately and fraudulently labeled** in a way that misrepresents its identity, source or composition and is often produced in unsanitary and unregulated conditions by an unknown manufacturer. Suspected substandard and falsified products can be reported using Product Defect Forms, available on request and accessible via the MCAZ website.

Summarized below are medicinal products alerts communicated by World Health Organization (WHO) Global Surveillance and Monitoring system for Substandard and Falsified Medical Products in the 2021. Alerts for Falsified Vitamin A (retinol) in WHO Region of Africa (Alert number 1/2021) and Falsified COVID-19 Vaccine BNT162b2 identified in the WHO region of the Americas (Alert 2/2021) were shared in July 2021 MCAZ Medicines Information Bulletin, available on the MCAZ website. Additional information on these alerts can be obtained on the WHO website on the following link: https://www.who.int/teams/regulation-prequalification/incidents-and-SF/full-list-of-who-medical-product-alerts

Alert No	Alert Summary
3/2021 Falsified Misoprostol	**Falsified Misoprostol (CYTOTEC) 200microgram tablets identified in WHO region of Africa:** The genuine manufacturer of the product confirmed to WHO that the products listed in this Alert were falsified. For batch B16519, the batch number did not correspond to genuine manufactured CYTOTEC and laboratory analysis of samples confirmed the product did not contain any active ingredient and did not comply with specifications. For batch 14660, the expiry date (12/2021) on this product was falsified.
4/2021 Falsified Remdesivir	**Falsified Remdesivir 100mg/20ml injection identified in WHO region of the Americas:** Two batches of falsified remdesivir injection 100mg/20ml (5mg/ml) were identified in the WHO Region of the Americas and reported to WHO in July 2021. These products claim to be manufactured by GILEAD. However, GILEAD confirmed that the remdesivir products listed in this alert are falsified and were not manufactured by them. These falsified products were reported at the patient level in Mexico and were illicitly supplied on the internet.
5/2021	**Falsified ChAdOx1 nCoV-19 (COVISHIELD) Corona Virus Vaccines (Recombinant)) vaccine identified in the WHO regions of Africa and South-East Asia:**

Falsified COVISHIELD vaccine	The products identified in this alert were confirmed as falsified on the basis that they deliberately/ fraudulently misrepresent their identity, composition or source: • For Batch 4121Z040, the expiry date (10.08.2021) on this product is falsified • For COVISHIELD 2ml, the genuine manufacturer does not produce COVISHIELD in 2ml (4 doses). • For batch 4126Z079, the batch number on this product is falsified and the product name, COVISHELD is not the correct spelling
6/2021 – Falsified Pfizer-BioNTech COVID-19 Vaccine	**Falsified Pfizer-BioNTech COVID-19 Vaccine identified in WHO region of the Eastern Mediterranean:** One lot of falsified Pfizer-BioNTech COVID-19 Vaccine identified in the Islamic Republic of Iran and reported to WHO in October 2021. The genuine manufacturer of Pfizer-BioNTech COVID-19 Vaccine had confirmed that the product listed in this Alert is falsified. The falsified product was reported at the patient level outside authorized and regulated supply chains and authorized vaccination programmes in the Islamic Republic of Iran. he products identified in this Alert are confirmed as falsified on the basis that they deliberately / fraudulently misrepresent their identity, composition, or source: • The product label and artwork are inconsistent with genuine Pfizer-BioNTech COVID-19 Vaccines • The expiry date on the labels (09/2021) is falsified and inconsistent with the expiry date on genuine Pfizer-BioNTech COVID-19 Vaccine Lot EH9899
7/2021: Falsified COVID-19 Vaccine AstraZeneca	**Falsified COVID-19 VACCINE AstraZeneca identified in WHO region of the Eastern Mediterranean:** This WHO Medical Product Alert refers to falsified COVID-19 VACCINE AstraZeneca (ChAdOx1-S [recombinant]) identified in the Islamic Republic of Iran. The falsified products are illicitly refilled vials of used and discarded genuine COVID-19 VACCINE AstraZeneca (ChAdOx1-S [recombinant]). The metal cap on samples of these falsified products displays evidence of tampering, indicating the metal cap was removed in order to refill the vials, and later replaced onto the vial.
8/2021 - Falsified Combiart (artemether & lumefantrine)	**Falsified Combiart identified in WHO region of Africa:** The products identified in this alert are confirmed as falsified on the basis that they deliberately/fraudulently misrepresent their identity, composition, or source. Laboratory analyses of the products found were conducted and the two expected active ingredients (artemether and lumefantrine) were not detected. Distinguishing features of the falsification: • The expiry date on the packaging is 10/2021, while the expiry date on the blister is 10/2022 • The falsified product has a Tanzania Reg No TZ13H260 on the blister
9/2021 Falsified Soliris (eculizumab)	**Falsified Soliris identified in WHO regions of the Americas, Europe and South East Asia:** This WHO Medical Product Alert refers to several batches of falsified Soliris (eculizumab) identified in Argentina, Estonia, India and Uruguay and reported to WHO between November and December 2021. The products identified in this Alert

are confirmed as falsified on the basis that they deliberately/fraudulently misrepresent their identity, composition or source.

WHO requests increased vigilance worldwide to prevent the distribution of these falsified medical products.

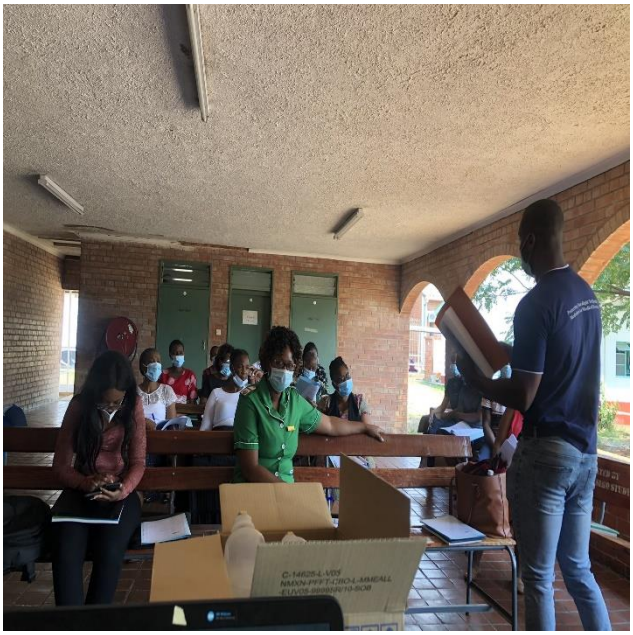
References

1. https://www.who.int/news/item/10-08-2021-medical-product-alert-n-3-2021
2. https://www.who.int/news/item/13-08-2021-medical-product-alert-n-4-2021-falsified-remdesivir
3. https://www.who.int/news/item/31-08-2021-medical-product-alert-n-5-2021-falsified-covishield-vaccine
4. https://www.who.int/news/item/04-11-2021-medical-product-alert-n-7-2021-falsified-covid-19-vaccine-astrazeneca
5. https://www.who.int/news/item/21-12-2021-medical-product-alert-n-8-2021-falsified-combiart
6. https://www.who.int/news/item/22-12-2021-medical-product-alert-n-9-2021-falsified-soliris

2021 Pharmacovigilance trainings

Increasing awareness about pharmacovigilance through trainings is associated with increased reporting of ADRs and improvement in the quality of submitted reports. In 2021, the MCAZ in collaboration with the Ministry of Health and Child Care and with support from the Clinton Health Access Initiative (CHAI) conducted medicine safety monitoring and reporting (Pharmacovigilance) trainings at 24 CHAI Implementing sites for Tuberculosis Preventative Treatment (TPT), Paediatric Dolutegravir (pDTG) and Advanced HIV Disease (AHD) management across Zimbabwe. A total of 414 health care professionals were trained during these trainings.

The main objective of the trainings was to capacitate healthcare workers on reporting and management of adverse drug reactions related to antiretroviral and anti-tuberculosis medicines. These trainings help in strengthening of the national pharmacovigilance system by improving reporting of adverse events and promoting patient safety. Thanks to CHAI, all 24 sites, healthcare workers, PMDs, PP, PNOs, DMOs, DNOs, district pharmacy managers , health information's, and ART & TB -MoHCC, & MCAZ teams for their support and commitment in promoting patient safety.



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REF: B/279/35/3/2022

CIRCULAR 3 of 2022

Date: 17/02/2022

To: ALL CURRENT AND PROSPECTIVE, LOCAL AND EXTERNAL, APPLICANTS, MANUFACTURERS AND PRINCIPALS FOR REGISTRATION OF MEDICINES

RE: CLARIFICATION OF CONDITIONS FOR MEDICINES REGISTRATION REQUIREMENTS AND SUBSEQUENT EXPANSION OF REGISTRATION CERTIFICATE, SECTION 15 FORMAT ANNEXURE.

This circular serves to inform all applicants, manufacturers, and principals, that the Medicines Control Authority of Zimbabwe clarified the conditions for medicines registration and subsequently expanded section 15 of the registration certificate, i.e. "Conditions for registration imposed by the Authority", as an annexure that is meant to capture more information on the medicines registration conditions requirements. The annexure shall include information on:

General conditions of registration
Subject to:

1. Compliance with labelling requirements.
2. Mandatory Reporting of Individual Case Safety Reports(ICSRs) that includes (ADRs, AEs, SAEs, & AEFIs) and/or product defects;
3. Applicant, manufacturer and/or market authorization holder (MAH) is required to have a functional Pharmacovigilance system in place for their medical products;
4. Applicant, manufacturer and/or MAH is required to designate a responsible person for Pharmacovigilance (QPPV) to be in charge of the pharmacovigilance system for the MAH;
5. Compliance with any request by the Authority to conduct post-authorisation safety and efficacy studies whenever the need may arise;
6. Renewal of market authorisation every five (5) years on condition of demonstration of quality, safety and efficacy.

Product specific conditions of registration

- API manufacturer(s).
- Approved batch size(s).
- Written commitment(s) by the FPP manufacturer.
- Approved label.
- Risk management plan.

NB: Please note that the MCAZ registration conditions stated above are also part of the legal provisions for existence of a national vigilance systems based on requirements for sections 33(2) (iii), 33(3) and 29 (1) (b) of the Medicines and Allied Substances Control Act (MASCA) [Chapter 15:03], MCAZ National Pharmacovigilance handbook 2016 Edition, MCAZ circular 1/2000 dated 21st March 2000, MCAZ Pharmacovigilance Guideline for Pharmaceutical

Industry MCAZ/PVCT/GL-02, Guideline for Pharmacovigilance of COVID-19 Vaccines MCAZ/PVCT/GL-03 and Zimbabwe National Adverse Events Following Immunization (AEFIs) Guideline 2017.The use of the new format for the registration certificate will clarify all the registration conditions requirements plus product-specific information to ensure compliance, and vigilance post-registration processes. The clarification of the registration conditions and subsequent new registration certificate format, with the annexure, will be implemented with immediate effect from the date of publication of the circular that is 15th February 2022.

These changes were necessitated by further clarification of medicines registration conditions requirements in line with MASCA Chapter 15:03 including additional compliance with critical international good regulatory best practices to ensure that effective, quality, and safe medicines are available to the public. We thank you for your usual co-operation in regulatory compliance and promoting patient safety.

MEDICINES CONTROL AUTHORITY OF ZIMBABWE

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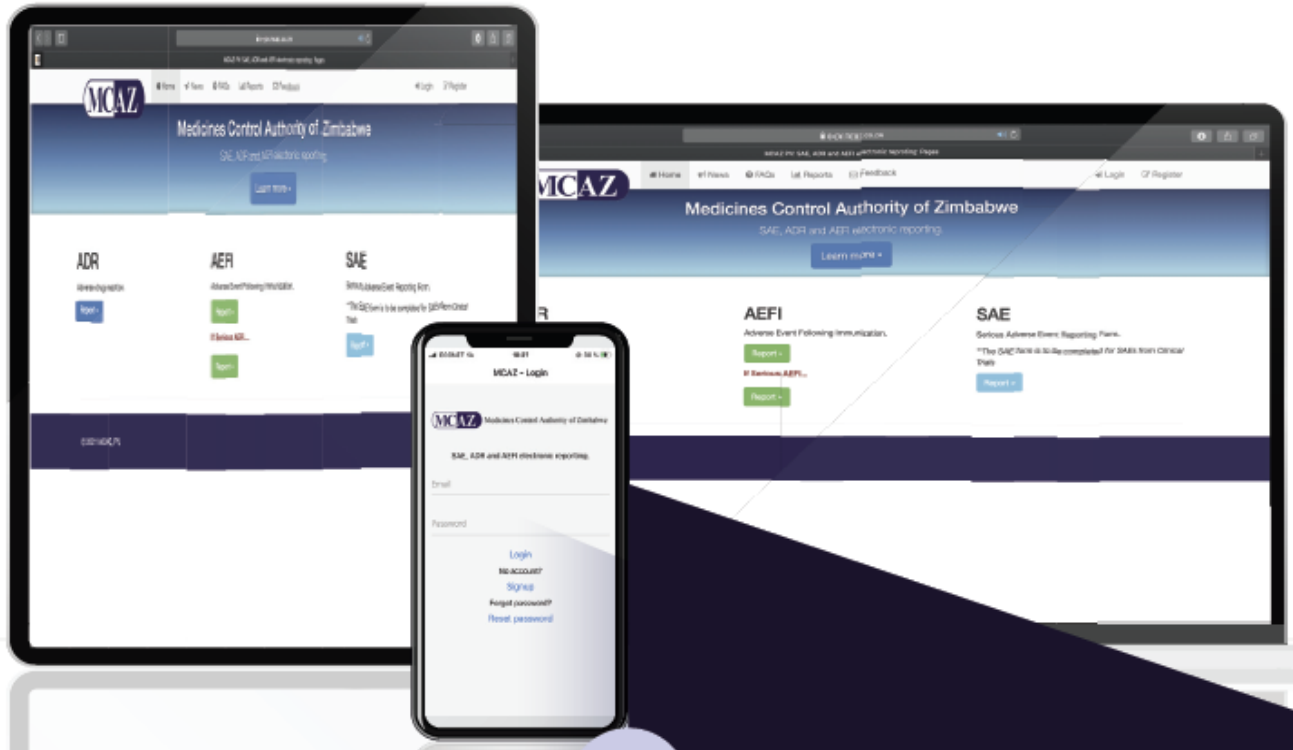
R. Rukwata (Mr.)
ACTING DIRECTOR-GENERAL



e-PV Medicines & Vaccines Monitoring

The Medicines Control Authority of Zimbabwe (MCAZ) with support from the Global Fund To Fight AIDS, TB and Malaria, and in partnership with United Nations Development Programme (UNDP) developed an electronic platform for reporting adverse drug reactions (ADR) or side effects, with both online and offline reporting capabilities. This gives healthcare providers and patients a number of reporting options that would allow the Authority to continuously monitor medicines safety.

Web based reporting
https://e-pv.mcaz.co.zw

Android/iOS Mobile Apps
Search "MCAZ Pharmacovigilance" on Apple App Store or Play Store

Desktop Applications
Windows, MacOs (MacBook) or Linux based operating systems

Patient/Consumer reporting
https://www.mcaz.co.zw/index.php/online-services/pv-reporting/e-reporting

Contact Us

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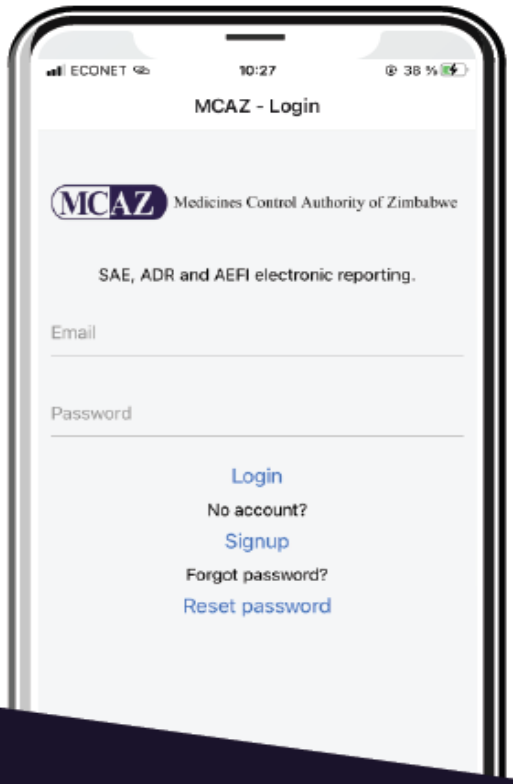

Benefits of the ePV electronic reporting system

- Available as an online & offline reporting system
- Automated email response is provided when:
  - the reports/applications are submitted
  - the Committee considers the report/application
  - feedback is given by the Authority

- The system allows users to:
  - View/download submitted reports/applications
  - Track the progress of submissions made to MCAZ
  - Submit feedback to MCAZ
  - View the Pharmacovigilance and Clinical Trials (PVCT) Committee meeting dates
  - View anonymised public statistics/reports
- Using the ePV system assists in ensuring efficient reporting of adverse drug reactions (side effects), thereby protecting your right to safe, effective and good quality medicines.

MCAZ Medicines Control Authority of Zimbabwe