INTRODUCTION
Zimbabwe is a landlocked country located in the southern part of Africa. It is categorized under the low-to-middle income countries in the world. The national and health-care products in Zimbabwe are regulated by the medicines control authority of Zimbabwe (MCAZ). The MCAZ authority was first established in 1969 as the drug control council. Under the act of parliament, medicines and allied substances act (Chapter 15:03), the MCAZ became a successor of the Drug Control Council and Zimbabwe Regional Medicines Control Laboratory in 1997. The MCAZ reports to the Minister of Health and Child Welfare, but it has a 100% funding derived from fees collected for services. The MCAZ is responsible for ensuring that all medicines available for sale to the public of Zimbabwe are safe, effective, and of good quality. This authority will ensure that every medicinal product that needs to be marketed in Zimbabwe is registered first before it is distributed to the public. The evaluation and registration division (EVR) is designated to assess the applications for medicinal products [1].

The MCAZ is one of Africa's triumph stories regarding the regulation of medicines and many other health products. In 2012, the MCAZ received a certification from the WHO prequalification program which has led to the expansion and improvement of MCAZ serves in the chemistry laboratory. The quality testing of medicinal products at MCAZ has proved to meet international standards. The MCAZ has supplementary advanced into a laboratory in 1997. The MCAZ reports to the Minister of Health and Child Welfare, but it has a 100% funding derived from fees collected for services. The MCAZ is responsible for ensuring that all medicines available for sale to the public of Zimbabwe are safe, effective, and of good quality. This authority will ensure that every medicinal product that needs to be marketed in Zimbabwe is registered first before it is distributed to the public. The evaluation and registration division (EVR) is designated to assess the applications for medicinal products [1].

The MCAZ is one of the founding member states of the Southern African Development Committee (SADC) which is known as ZAZIBONA. This is a centralized procedure in which the objective is to provide access to safe, effective, and quality medicines by work sharing in the analysis of applications for registration. This centralized procedure allows inspection of manufacturing testing facilities. The aim is to allow

However, MCAZ still has a long way to go to meet the world international market of medicinal products. Stringently regulated countries such as the European Union (EU) have set a standard for the marketing and authorization of medicinal products in the world. EU is a giant in the drug regulating markets; it has very stringent requirements for drug development, drug processing, and drug approval. The Medicines Agency (EMA) is a decentralized body of EU which is in charge for the safety and promotion of public health and animal health, through the evaluation and supervision of medicines for human and veterinary use. The EMA was established in 1995 and has worked across EU and globally to facilitate public and animal health assessing medicines to severe scientific standards and by providing partners with independent science-based data. The main objective of the EU pharmaceutical legislation is to safeguard public health while protecting free movement of medicinal products [3].

The EMA is accountable for the assessment of applications for European marketing authorization for medicinal products (centralized procedure). In this centralized procedure, companies must succumb a single marketing authorization application to the EMA which will constantly monitor the safety of medicines through a pharmacovigilance program. The EMA will take appropriate action if adverse drugs report suggests changes to the benefit-risk balance of a medicinal product [3].

MATERIALS AND METHODS
Registration requirements in EU
For a medicinal product to be placed on the market in Europe, a marketing authorization has to be issued by the competent authorities
### Table 1: Comparison for EMA and MCAZ

| Contents | EU | Zimbabwe |
|----------|----|----------|
| Authority | EMA | MCAZ |
| Committees | 1. Committee for human medicinal products | 1. Evaluation and registration committee |
| | 2. Pediatric committee | 2. Licensing and advertising committee |
| | 3. Committee on herbal medicinal products | 3. Legal committee |
| | 4. Pharmacovigilance risk assessment committee | 4. Pharmacovigilance and clinical trials |
| | 5. Committee for advanced therapies | 5. Laboratory committee |
| | 6. Committee for orphan medicinal products | 6. Veterinary committee |
| | 7. Committee for medicinal products for veterinary use | 7. National procedure |
| Types of registration procedure | 1. Centralized procedure | 1. National procedure |
| | 2. Decentralized procedure | 2. The WHO collaborative procedure |
| | 3. Mutual recognition procedure | 3. ZAZIBONA procedure |
| | 4. National procedure | 4. National procedure |
| Types of application | 1. Full dossier application | 1. New chemical entity application (biological and biosimilar medicines are included under this group) |
| | 2. Generic product application | 2. Generic drug application |
| | 3. Hybrid application | 3. Line extension application |
| | 4. Biosimilar application | 4. Biosimilar application |
| | 5. Bibliographic application | 5. Bibliographic application |
| | 6. Fixed dose application | 6. Fixed dose application |
| | 7. Informed consent application | 7. Informed consent application |
| CTD presentation | eCTD | Paper CTD |
| eCTD year implemented | 2005 | Not yet |
| Fees structure marketing authorization application | €282,100 for the whole process | $3000 for NCE registration process |
| | | $2 500 generics $1 500 line extensions |
| Stability requirements | 2 | 3 |
| Number of batches | Northern Europe Zone I | Zone II |
| Climatic zone | Southern Europe Zone II | |
| Storage conditions long-term intermediate accelerated | 25°C±2°C/60% RH±5% RH or 30°C±2°C/65% RH±5% RH 12 months | 25°C±2°C/60% RH±5% RH or 30°C±2°C/65% RH±5% RH 12 months |
| | 30°C±2°C/65% RH±5% RH 6 months | 30°C±2°C/65% RH±5% RH 6 months |
| | 40°C±2°C/75% RH±5% RH 6 months | 40°C±2°C/75% RH±5% RH 6 months |
| Container closure system | Testing to be conducted on the dosage form packaged in a container closure system proposed for marketing | Testing is done in dosage form packaged in the container closure system for marketing |
| Quality personnel certification | Required | Required |
| Bioequivalence requirements | Audited EMA | Audited MCAZ |
| Clinical research organization | As recommended by EMA | As recommended by MCAZ |
| Number of subjects | Minimum 12 | Minimum 12 |
| 1. Acceptance criteria for bioequivalence | 90% confidence interval | 80–125% Cmax |
| 2. Acceptance criteria for bioequivalence for special class drugs | 80–125% Cmax | 80–125% Cmax |
| | Narrow therapeutic index drugs 90% confidence interval | 90.00–111.11% |
| | Highly variable drugs 69.84–143.19% | 75–133% |
| Supporting documents | ICH E3 Guidelines | ICH E3 Guidelines |
| Manufacturing and control requirements | | |
| Number of batches | 3 | 3 |
| Batch size | A minimum of 100,000 units | 100,000 |
| Finished product control requirements | | |
| Color identification | Required | needed |
| Disintegration | Required | Required |
| Water content | Not required | Required |
| Supporting documents | ICH Q6A | WHO TRS 95,2009 |

EMA: European medicines agency, MCAZ: Medicines control authority of Zimbabwe
Table 2: Summary of key national differences

| EU | MCAZ |
|----|------|
| i. Administrative information such as cover letter specified for the particular country, application form applicable in that country, exclusivity statement, proof of payment to clinical investigators, proof of establishment of the applicant in EEA | Administrative information correspondence table of contents (M1–5) administrative information product information specific requirements proof of payment and regional summaries |
| ii. A4 (210 x 297 mm) paper size is used for the dossier preparation with font size 12 in Times New Roman | Similar to EU |
| iii. 1.3 Product information SPC (summary of product characteristic) is provided about the drug product in labeling | SPC, package inserts, patient information leaflet are provided in the labeling braille labeling not required |
| iv. 1.3.1. Mock-ups and specimens of labels and cartons sent with the application as appropriate. Braille is used for the labeling conditions on the labels | Any member of the MCAZ is selected |
| v. 1.4 Information about experts who sign the module 2 summaries. A qualified personnel is selected | No specific requirements biowaiver request is provided in module 1 in 1.2.8 |
| vi. 1.5 Specific requirements for different kinds of applications (summary to support generics, hybrid, bibliographic, extension) | No GMO or Non-GMO certification |
| vii. Request for waiver is not provided in module 1. | Evidence linking to an orphan drug is not required in this section |
| viii. 1.6 Environ risk certification 21 is given with the information for GMO or Non-GMO. The fresh/new certificate is provided | No information related to pharmacovigilance required in this module |
| ix. 1.7 Information relating to orphan market exclusivity | Most generic drugs are registered in Zimbabwe. Clinical trials information is obtained from MCAZ |
| x. 1.8 Data associated with pharmacovigilance. A separate additional section is provided for the pharmacovigilance system for surveying and controlling the post-approval undesired effects of the drug | |
| xi. 1.9 Information relating to clinical trials | |
| Module 2: It is the same for EU and MCAZ | |
| Module 3: Quality | |
| i. 3.2.5 Drug substance data may be submitted as an EU part DMF (open part to be reproduced in 3.2.5) or as a reference to pharmacopeia European certificate of suitability, for an EU monograph substance | Drug substance data are submitted to the MCAZ in the form of DMF and QIS with reference of the pharmacopeias used. A complaint has been already raised. |
| ii. 3.2.7 Stability storage requirements to be stated in accord with CHMP guideline | 1.2 S7 stability  
Storage requirements as per MCAZ quality guidelines |
| iii. 3.2. P Description and composition colors to be on the European permitted list. Excipients to be designated as conforming to European national pharmacopeia where there is a monograph 3.2 P 4 excipients to conform to European national pharmacopeia if described in a monograph. | 3.2 P Reference may be in DMF supplied directly to MACZ by excipient and container closure manufacture |
| iii. 3.2. P 5 Control of drug product | 3.2 P 1 Description and composition. Colors to be on MCAZ permitted list. Excipients to be designated as confirm to monograph. |
| Module 4: There are no major differences in this module. | |
| Module 5 | |
| Module 2.3 Quality overall summary and module 2.5 clinical overview summarize this module | 1.3 4 Excipients to confirm to MCAZ guidelines |

MCAZ: Medicines control authority of Zimbabwe, EU: European Union

of the member state to the applicant. The legal requirements and procedures for making an application for a marketing authorization are outlined in Directive 2001/83/EC and in Regulation (EC) No 726/2004. There are four marketing authorization procedures in EU which are the centralized procedure, decentralized procedure, mutual recognition, and national procedure. The centralized procedure is the authorization of medicines, whereby a single application, a single assessment and a single approval throughout the EU. This type of procedure enables the applicant to market the medicinal product and make it available to patients and health-care professionals all over Europe because of a single marketing authorization [4].

Mutual recognition procedure is when the applicant gets marketing authorization in several member states where the medicinal product in question has already received a marketing authorization from one of the member state at the time of application. After the first marketing
authorization in the community is granted, the marketing authorization holder may request one or more member state to recognize an authorization granted by the reference member state by submitting an application in accordance with article 28 of Directive 2001/83/EC. The reference member state will provide a list of documents to the concerned member state and applicant which will be validated in 90 days. The documents to be submitted include the assessment report, summary product of characteristics, labeling, and package leaflet. The concerned member state shall assess and approve these documents and inform the reference member state (Kumar, 2015).

The decentralized procedure is whereby an applicant obtains a marketing authorization in several member states where the medicinal product in question has not yet received a marketing authorization in any member state at the time of application. A national procedure is the starting point for mutual recognition and decentralized procedure, this procedure is when an applicant submits an application to an individual competent member state authority of the EU.

Centralized procedure in EU
Flowchart of centralized procedure show in Fig. 1.

Flowchart: Mutual recognition procedure show in Fig. 2.

Flowchart of decentralized procedure show in Fig. 3.

MCAZ
To obtain approval to market, sell, and distribute the medicinal product for human or animal use in Zimbabwe, an applicant should register with the Medicine Control Authority of Zimbabwe. The EVR of MCAZ is designated to assess the applications of medicinal products. This division is responsible for reviewing the safety, quality, and efficacy of medicines intended for marketing, sale, and distribution in Zimbabwe. There are three ways of obtaining marketing authorization in Zimbabwe. One is through the national procedure by MCAZ, second is by the WHO Collaborative Procedure, and third is by The ZAZIBONA procedure.

The WHO Collaborative Registration Procedure serves to expedite and fast-track registration of products which have already been assessed and prequalified by the WHO Prequalification team. In the ZAZIBONA process, it is a collaborative registration initiative among four national medicines regulatory authority in Zambia, Zimbabwe, Botswana, and Namibia. The objective of this procedure is to assist in the provision of good quality medicines through work sharing in the assessment of applications for registration and inspection of manufacturing and testing facilities. Medicinal products that pass the evaluation are then provided with an approval for marketing authorization in the participating countries in which applications for registration would have been submitted [5].

Flowchart medicinal product registration by MCAZ show in Fig. 4.

A schematic overview of the collaborative registration procedure [6].
RESULTS AND DISCUSSION

Comparison of CTD modules.

The Table 4 gives detailed information about procedures and timelines for variations in EU and Zimbabwe [7,8,9 and 10].

This study systematically challenges MCAZ regulatory requirements and procedures by comparing them with the EU standard drug regulations. It helps process improvement in Zimbabwe drug regulatory system [11]. This will enable the MCAZ to determine what actions are necessary for them to be in compliance with the new EU guidelines and requirements. The study provides MCAZ with an insight into areas that have room for improvement [12, 13, 14, 15].

Current GMP Supervision of Manufactures and Inspections need to be upgraded. However, currently, in Zimbabwe, there are inadequate internal audits, inadequate quality departments to do the validation and self-inspection in pharmaceutical industries [16-40]. The MCAZ can resolve this by ensuring that pharmaceutical industries implement frequent inspections determined on risk-based approach as done in EU [41-56].

Braille requirement

In Zimbabwe, the MCAZ lacks in the area of braille labeling on drugs primary package. It can harmonize the braille requirements with that of EMA and address applicants to implement these necessities on the carton of a medicinal product [57-73].

Pharmacovigilance

A very big gap in this area underreporting of ADR due to common phenomenon of technical and psychological issues.

- Lack of knowledge and understanding regarding the adverse drug reactions reporting system.
- Fear of negative competence among health-care professionals.
- In most hospitals, there is an underestimation of the true size of a problem resulting in ignorance for ADR reporting.
Thus, to stimulate the reporting system in Zimbabwe, there should be easy access to reporting forms and other means of reporting. There should be public education regarding adverse drug reaction reporting as is done in EU, it helps the public to be aware of ADR. (ATUL KHURANA, 2014) MCAZ PVCT team can establish a mobile application in which health-care professionals and consumers can report ADR.

**Digitalization**

There is a huge gap in the online application for a marketing authorization in Zimbabwe by the regulatory authority of MCAZ. MCAZ should harmonize their webpage with that of EMA. All important documents should be easily accessed on the website, for example, the GMP guidelines must be available on the website rather than to let an applicant visit the MCAZ premises to collect the guidelines. The website must be updated on a daily bases. There is a gap in the capacity of assessing and registering new products and to carry clinical trials of new drugs for neglected diseases that are necessary to establish safety and efficacy in Zimbabwe. The SADC has pursued harmonization of registration procedures with a mutual recognition process akin to that of Europe. There is still a gap in the effort put by SADC in relation to focus on NCEs. The SADC should put more effort to harmonize formulation of NCEs rather than on generic products only.[74-81]

**CONCLUSION**

EU with its communal and mutual recognition procedures to enable one dossier to oblige for all is a well-established exemplary for harmonization of drug registration. Thus, the MCAZ and SADC should correspond with EU guidelines to enable improvement of a common scientific framework for assessing medicines and safeguarding the legislation which is enacted to support the assessments. Harmonization of EU and SADC documentation will enable manufacturers to prepare the same dossier for each authority, although there are still country-specific requirements such as the product information documents. Registration of medicines needs to be vigorously embarked on by the MCAZ. Factors responsible for the small number of registered medicines need to be determined so that remedial action can be taken. Subsequently, Zimbabwe is resource constrained, allocation of information, and facilities to register medicines in the subregion must be stimulated. To address the human resources, restraints for MCAZ investment in the training of the human capital for efficient implementation of various functions of regulation should be mandatory. To ensure greater value for harmonization and benefits, the MCAZ and Zazibona member states should build capacity.
for better sharing of resources. To strengthen WHO QP programs, 
tolerable funding is required to support operations and regional 
activities. Consequently, Government should offer an adequate grant 
to support program implementation by MCAZ; the manufacturing 
pharmaceuticals should access and use most of the industry fees for 
production of new drugs.

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CONFLICTS OF INTEREST

None.

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