Medicines Control Authority of Zimbabwe

MCAZ/EVR/GL-05

GUIDELINE ON THE REQUIREMENTS FOR PERMITTING THE MARKETING AUTHORISATION OF PRODUCTS NOT PRODUCED IN ZIMBABWE AND NOT AUTHORIZED IN THE COUNTRY OF ORIGIN

EFFECTIVE DATE: 09/10/2024

Medicines Control Authority of Zimbabwe

106 Baines Avenue

P O Box 10559

Harare

Email: mcaz@mcaz.co.zw

Website: www.mcaz.co.zw

Reviewed by:	..... Signature	03/10/2024 Date
Checked by HoD/HoU:	..... Signature	03/10/2024 Date
Authorised for use by: Quality Manager	..... Signature	03/10/2024 Date
Approved by: Director-General	..... Signature	09/10/2024 Date

TABLE OF CONTENTS

ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
cGMP	Current Good Manufacturing Practices
CHAI	Clinton Health Access Initiative
EU	European Union
GAVI	Global Alliance for Vaccines and Immunisation
GFATM	Global Fund to fight Aids, Tuberculosis and Malaria
GMP	Good Manufacturing Practices
HIV	Human Immunodeficiency Virus
MA	Market Authorisation
MAH	Market Authorisation Holder
MASCA	Medicines and Allied Substance Control Act
MCAZ	Medicines Control Authority of Zimbabwe
MSF	Médecins Sans Frontières
SRA	Stringent Regulatory Authority
TB	Tuberculosis
UNFP	United Nations Population Fund
UNICEF	United Nations International Children's Emergency Fund
USFDA	United States Food and Drug Administration
WHO PQ	World Health Organization Prequalification
WHO	World Health Organisation
WHOPAR	World Health Organisation Public Assessment Report
WHOPIR	World Health Organisation Public Inspection Report

1.0 APPLICATION

The guideline will be used by assessors when they receive dossier applications for drugs that are not produced in Zimbabwe and not authorized in the country of origin.

2.0 PURPOSE

The guideline clearly outlines the exemptions to permitting the market authorisation for products not produced in Zimbabwe and not authorized in the country of origin in support of Section 30 of Medicines and Allied Substances Control Act (MASCA).

3.0 BACKGROUND / INTRODUCTION

Medicines and Allied Substances Control Act Chapter 15:03 states that "*the Authority shall not approve the registration of any medicine manufactured outside Zimbabwe, unless a valid certificate of registration in respect of such medicine issued by the appropriate authority established for the registration of medicines in the country of origin of that medicine has been produced to the satisfaction of the Authority*". However, Section 75 of the MASCA allows exemption of the Market Authorization (MA) of products not produced in Zimbabwe and not authorized in the country of origin. Section 75 is the exemption clause which empowers MCAZ to excuse, subject to conditions as it may specify, any medicine or substance from the operation of any or all of the provisions of the Act.

4.0 DEFINITIONS

4.1 **Marketing Authorization:** Also referred to as a product licence or registration certificate, is a legal document issued by the competent Medicines Regulatory Agency that authorizes the marketing or free distribution of a medical product in the respective country after evaluation of safety, efficacy and quality. In terms of quality, it establishes inter alia the detailed composition and formulation of the medical product and the quality requirements for the product and its ingredients. It also includes details of the packaging, labelling, conditions, shelf-life and approved conditions of use.

4.2 **Dossier:** A dossier contains and/or references the necessary data to demonstrate the quality, safety and efficacy of a medicine.

5.0 GUIDELINES

The guideline indicates the scenarios for exempting the marketing authorisation of products not produced in Zimbabwe and not authorized in the country of origin and the documentation required.

5.1 Exemptions

5.1.1 A Section 75 marketing authorisation can be issued out to life saving medicines which are unregistered or not yet registered in the country of origin and not yet registered in Zimbabwe, in the following circumstances:

i. **Investigational products** that have undergone phase I and phase II clinical trials and phase III studies are ongoing, and the products have already shown a positive benefit-risk balance for patients, and there are no approved alternatives.

ii. **Products for Public Health Programmes**
Products developed and manufactured in well-regulated countries but are not approved and used there because the target infectious disease has low endemicity and/or prevalence (e.g. infectious tropical diseases: malaria, cholera, typhoid, Tuberculosis (TB) and Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome (HIV/AIDS), and neglected tropical diseases: lymphatic filariasis, bilharziasis, river blindness, soil-borne helminthiasis) which still occur in Zimbabwe.

iii. **Products procured by the Government of Zimbabwe to address public health emergencies or shortages** with the support of bilateral (e.g. USFDA, CHAI) and multilateral (UNICEF, GFATM, UNFP, GAVI) development partners and humanitarian organisations (MSF, donors) who have robust or at least functional vendor qualification systems for safety, quality and efficacy.

iv. **Epidemic, Pandemic Response**
A public health emergency caused by a highly transmissible infectious agent with high morbidity or high mortality or both, where there is no approved cure in Zimbabwe and other countries.

v. **Compassionate use of an investigational medicine on a named patient**
Patients suffering from a rare disease where there is no approved treatment in Zimbabwe and in the country of origin, but clinicians have sound expert opinion on the value of using the medication based on published clinical reports.

vi. **Any other unforeseen circumstances** where access to an unregistered product is justifiable and is deemed beneficial to the patient(s).

5.2 Documentation required

5.2.1 Investigational Product still under Clinical Trials

i. Cover letter justifying importation of unregistered medicines.
ii. Product information (package inserts and labels).
iii. Phase I and II Clinical Studies reports.
iv. Chemistry, Manufacturing and Control for the product.
v. Manufacturing license and GMP certificate issued by the regulator in the country of manufacture and/or by other SRAs.
vi. Samples.

5.2.2 **Products for Public Health Programs**

i. Cover letter justifying importation of unregistered medicines.
ii. Product information (package inserts and labels).
iii. Chemistry, Manufacturing and Control for the product.
iv. Manufacturing license and GMP certificate issued by regulator in country.
v. Evidence of GMP inspection by WHO Inspectorate of the manufacturing facility, in the form of a WHOPIR.
vi. Evidence of WHO PQ of the product. A WHOPAR may be provided or,
vii. Evidence of USFDA Tentative Approval or,
viii. European Union (EU) Article 58 Scientific Opinion.

5.2.3 **Other Cases**

The recipient (e.g. Government of Zimbabwe, Zimbabwe Association of Church Hospitals, other Faith based Trusts, Council for the Blind, others) and their external partners or donors should obtain prior advice from the Authority and submit the following:

i. Cover Letter of intent to procure medicines, justifying importation of unregistered medicines.
ii. Details of sponsoring partners.
iii. List of medicines: generic.
iv. Name of Manufacturers, country of manufacturer, license.
v. GMP certificate: The manufacturer(s) should have passed the most recent GMP inspection from MCAZ. Alternatively, proof of cGMP compliance issued within the preceding 12 month within period by any one of the countries considered as WHO maturity level 3 and 4.
vi. Market Authorization Holder (MAH) should provide a list of all countries where the product has been reviewed and approved over the registration period of the product, the registration numbers, and copies of registration certificates, if available.

5.2.4 **Full dossiers**

While Section 75 provides for expeditious access to life-saving medicines on once-off emergency basis for the Zimbabwe Public Health System or patients, the product application should also be submitted for evaluation and issuance of Marketing Authorisation (MA), unless compelling reasons that warrant continued importation of unregistered medicines are communicated in writing to the Director-General and approved by the Authority.

6.0 KEY RELEVANT DOCUMENTS

6.1 Medicines and Allied Substances Control Act Chapter 15:03

7.0 HISTORY

DOCUMENT HISTORY		
Revision Number	Date Approved	**Reason for Change**
0	February 2022	Rolling review **Details of Change** **Section 2.0 Changed from** The guideline clearly outlines the exemptions to permitting the market authorisation for products not produced in Zimbabwe and not authorized in the country of origin in support of Section 15 of Medicines and Allied Substances Control Act (MASCA). **To** The guideline clearly outlines the exemptions to permitting the market authorisation for products not produced in Zimbabwe and not authorized in the country of origin in support of Section 30 of Medicines and Allied Substances Control Act (MASCA). **Section 4.1** **Marketing Authorization:** Also referred to as a product licence or registration certificate, is **a** legal document issued by the competent Medicines Regulatory Agency that authorizes the marketing or free distribution of a medical product in the respective country after evaluation of safety, efficacy and quality. In terms of quality, it establishes inter alia the detailed composition and formulation of the medical product and the quality requirements for the product and its ingredients. It also includes details of the packaging, labelling, conditions, shelf-life and approved conditions of use. (***letter in bold "a" was added***) **Section 5.1.1** **Changed from** A Section 75 marketing authorisation can be issued out to life saving medicines which are unregistered or yet registered in the country of origin and not yet registered in Zimbabwe, in the following circumstances: **To** A Section 75 marketing authorisation can be issued out to life saving medicines which are unregistered or **not** yet registered in the country of origin and not yet registered in Zimbabwe, in the following circumstances:

		Section 5.1.1.ii **Products for Public Health Programmes** **Changed from** Products developed and manufactured in a developed country of origin but are not approved and used there because the target infectious disease has low endemicity and/or prevalence (e.g. infectious tropical diseases: malaria, cholera, typhoid, Tuberculosis (TB) and Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome (HIV/AIDS), and neglected tropical diseases: lymphatic filariasis, bilharziasis, river blindness, soil-borne helminthiasis) which still occur in Low Middle Income Countries including Zimbabwe. **To** Products developed and manufactured **in well-regulated countries** but are not approved and used there because the target infectious disease has low endemicity and/or prevalence (e.g. infectious tropical diseases: malaria, cholera, typhoid, Tuberculosis (TB) and Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome (HIV/AIDS), and neglected tropical diseases: lymphatic filariasis, bilharziasis, river blindness, soil-borne helminthiasis) which still occur in Zimbabwe**.** **Section 5.1.1.iii** Products procured by the Government of Zimbabwe to address public health emergencies or shortages with the support of bilateral (e.g. USFDA, CHAI) and multilateral (UNICEF, GFATM, UNFP, GAVI) development partners and humanitarian organisations (MSF, donors) who have robust or at least functional vendor qualification system**s (*letter "s" added to the word system*)** for safety, quality and efficacy. **Section 5.1.1.v** **Compassionate use of an investigational medicine on a named patient** **Changed from** Patients suffering from a rare disease where there is no approved treatment in Zimbabwe and in the country of origin, but clinicians have sound expert opinion on the value of trying the medication based on published clinical reports.

		To Patients suffering from a rare disease where there is no approved treatment in Zimbabwe and in the country of origin, but clinicians have sound expert opinion on the value of **using** the medication based on published clinical reports. **Section 5.1.1.vi** Any other unforeseen circumstances where access to **an** unregistered product is justifiable and is deemed beneficial to the patient(s). (***The article "an" was added before the word unregistered product***) Section 5.2.1.**v. changed from** Manufacturing license and GMP certificate issued by regulator in country of manufacture and by other SRAs **To** Manufacturing license and GMP certificate issued by the regulator in the country of manufacture and/or by other SRAs. **Section 5.2.2 vi changed from** Evidence of GMP inspection by WHO PQ (WHO Public Inspection Report-WHOPIR) of the manufacturing facility. **To** Evidence of GMP inspection by WHO Inspectorate of the manufacturing facility, in the form of a WHOPIR. **Section 5.2.2.vii** **Changed from** Evidence of WHO PQ (WHO Public Assessment Report – WHOPAR) of the product or, **to** Evidence of WHO PQ of the product. A WHOPAR may be provided or, **Section 5.2.4** While Section 75 provides a window of opportunity for the Zimbabwe Public Health System or patients to expeditiously access life-saving medicines on one-off emergency basis, full dossier, for the product should also be submitted for evaluation and issue of Marketing Authorisation (MA), unless compelling reasons that warrant continued importation of unregistered

		medicines are communicated in writing to the Director-General and approved by the Authority **To** While Section 75 provides for expeditious access to life-saving medicines on once-off emergency basis for the Zimbabwe Public Health System or patients, the product application should also be submitted for evaluation and issuance of Marketing Authorisation (MA), unless compelling reasons that warrant continued importation of unregistered medicines are communicated in writing to the Director-General and approved by the Authority.