MCAZ Medicines Control Authority of Zimbabwe

GUIDANCE ON GOOD PRACTICE (GxP) INSPECTIONS DURING EMERGENCIES/DISASTERS INCLUDING THE COVID- 19 PANDEMIC

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EFFECTIVE DATE 19/6/2020

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1.0 APPLICATION

1.1 This guidance document outlines how to submit records and what evidence will be required to be submitted to support facilities level of compliance with GxP requirements during emergencies/disasters including the COVID- 19 pandemic. MCAZ will assess the evidence against GxP standards according to the MASCA 15:03 and its associated regulations and guidelines.

1.2 These guidelines for the GxP inspection of medicine and applies equally to products for human and for veterinary use. The sequence of doing these audits across the GxP spectrum will depend on the readiness level of systems both at MCAZ and at facilities/ sites.

1.3 This document clarifies the functions and requirements of good practice for:

1.3.1 Pharmaceutical Holder of Certificate of Registration,

1.3.2 Pharmaceutical Manufacturers,

1.3.3 Pharmaceutical Wholesalers,

1.3.4 Pharmaceutical Quality Control Laboratories

1.3.5 Cannabis production sites

2.0 PURPOSE

This guide provides guidance on the inspection processes to be undertaken during unexpected emergencies/disasters including the COVID- 19 pandemic. It is important to understand it cannot replace an on-site auditor's scrutiny and hence **is only an interim measure.** This guidance is established to handle and conduct remote audits in cases of travel restriction due to unexpected events / circumstances that prevent an on-site audit. **There will be a greater emphasis on the quality management system in place, which should continually be handled as per approved procedures at the facility/ site.**

These guidelines are defined for inspection during emergencies/disasters including the COVID-19 pandemic and focusses on the good practices (GxP) evidence and the regulatory requirements for conducting pharmaceutical wholesaling, distribution, and manufacturing for MCAZ licence /approval holders.

3.0 BACKGROUND / INTRODUCTION

3.1. With the complexity of global supply chains, the demand for inspecting pharmaceutical facilities far exceeds what any Regulatory Authority can accomplish during emergencies/disasters including the COVID- 19 pandemic and a framework is required to assist Regulators in managing quality risks posed by the increasingly complex pharmaceuticals global supply chain.

3.2 GxP inspections are conducted for purpose of product registration and also for the purpose of the system of licensing the manufacturing and distribution of medicinal products. An informed decision on the GXP compliance of manufacturing / distribution/ importation/ exporting/ of medicines can be made, in certain circumstances, based on the outcome of virtual or remote inspection by the Regulatory Authority.

3.3 Confirming GxP compliance through virtual/ remote inspection, where appropriate, without undertaking an onsite inspection could potentially ensure:

3.3.1 The periodic re-evaluation or re-assessment and monitoring of medicines, medical devices and IVDs,

3.3.2 Compliance with existing legislation is controlled through a process of active inspection and investigation and

3.4 This Guideline sets out appropriate steps for meeting the responsibility of importation, manufacturing, sale of medicine during emergencies/disasters including the COVID- 19 pandemic.

3.5 This document should be read in conjunction with the Guidelines on Good Manufacturing Practice.

3.5.1 This guideline supports legislative requirements as outlined in the MASCA and its Regulations.

3.5.2 MCAZ ensures that medicines meet the requirements of quality, safety and efficacy.

3.5.3 Medicines should comply with the information that has been evaluated and approved by the MCAZ.

4.0 DEFINITIONS

The definitions provided below apply to words and phrases used in these guidelines. Facilities / sites should also consider the definitions as prescribed by the Medicines and Allied Substances Control Act 15:03 and the various guidelines as published by the World Health Organisation, WHO.

4.1 **Pharmaceutical product**: Any substance or combination of substances marketed or manufactured to be marketed for treating or preventing disease in human beings, or with a view to making a medical diagnosis in human beings, or to restoring, correcting or modifying physiological functions in human beings.

4.2 **Quality control**: All measures taken, including the setting of specifications, sampling, testing and analytical clearance, to ensure that raw materials, intermediates, packaging materials and finished pharmaceutical products conform with established specifications for identity, strength, purity and other characteristics.

4.3 **Quality Management System**. An appropriate infrastructure, encompassing the organizational structure, procedures, processes and resources, and systematic actions necessary to ensure adequate confidence that a product or service will satisfy given requirements for quality.

4.4 **Quality system**: The sum of all features that are necessary to implement an Organization's quality policy and meet quality objectives. It includes organizational structure, responsibilities, procedures, systems, processes and resources. Typically, these features will be addressed in different kinds of documents, such as the quality manual and documented procedures.

4.5 **Remote Virtual Inspection:** This is Inspection of a facility conducted using information sharing platforms which is agreed upon prior to inspection. Platforms that can be used include Zoom, WebEx, Microsoft Teams Software, Whatsapp etc.

4.6 **Covid-19 pandemic:** The COVID-19 pandemic, also known as the coronavirus pandemic, is an ongoing pandemic of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

4.7 **Desktop inspection:** A review of the requested and submitted documents remotely. This can be in conjunction between MCAZ and the Company

4.8 **GxP:** Good Manufacturing Practice, Good Wholesaling practice, Good Dispensing practice, Good laboratory Practice

5.0 GUIDELINES

5.1 REMOTE AUDIT

5.1.1 A remote audit is an audit which is performed via remote tools (examples include: landline or mobile telephone, e-mails, Skype, WhatsApp, Zoom, Webex, Microsoft Teams, etc.), with the exchange of electronic documents using internet-cloud system when the size of document cannot be transferred by direct mails (e.g. WeTransfer, Dropbox, Mimecast).

5.1.2 A remote audit is different from a questionnaire assessment or teleconference as there should be a direct discussion between the auditor and the auditee. The use of a video-conferencing system is considered as essential. The auditor shall have the opportunity to read and assess written audit evidence; therefore, the use of shared screen is encouraged as well. The auditor may also be granted temporary secure access to the organisation's electronic validated GxP IT systems to observe information directly.

5.1.3 Strict confidentiality commitment is essential according to the MCAZ Code of Conduct for the following considerations:

5.1.3.1 The realisation of a remote audit does need to exchange documents, data, videos and photographs through internet-based virtual support software. Therefore, both the auditor and the auditee shall accept to share information for the purpose of the audit only and

5.1.3.2 There should be commitment to keep confidential information shared before and during the audit, and to make auditee aware of storage and archiving of any photographs, videos or documents provided by the auditee.

5.1.4 It shall be agreed during the audit preparation phase, the communication tools to be used, and their connection and availability to both sides. The ability to exchange documents should be tested before the audit day. The inspection programme will be conducted in four phases to allow for controlled and smooth process. Inspection scheduling to the applicant will be via emails, telephonic communications and a proposed inspection plan and document list will be submitted. The phases are shown in table 1.0:

Figure 1.0 General flow of approach to remote GMP clearance at MCAZ

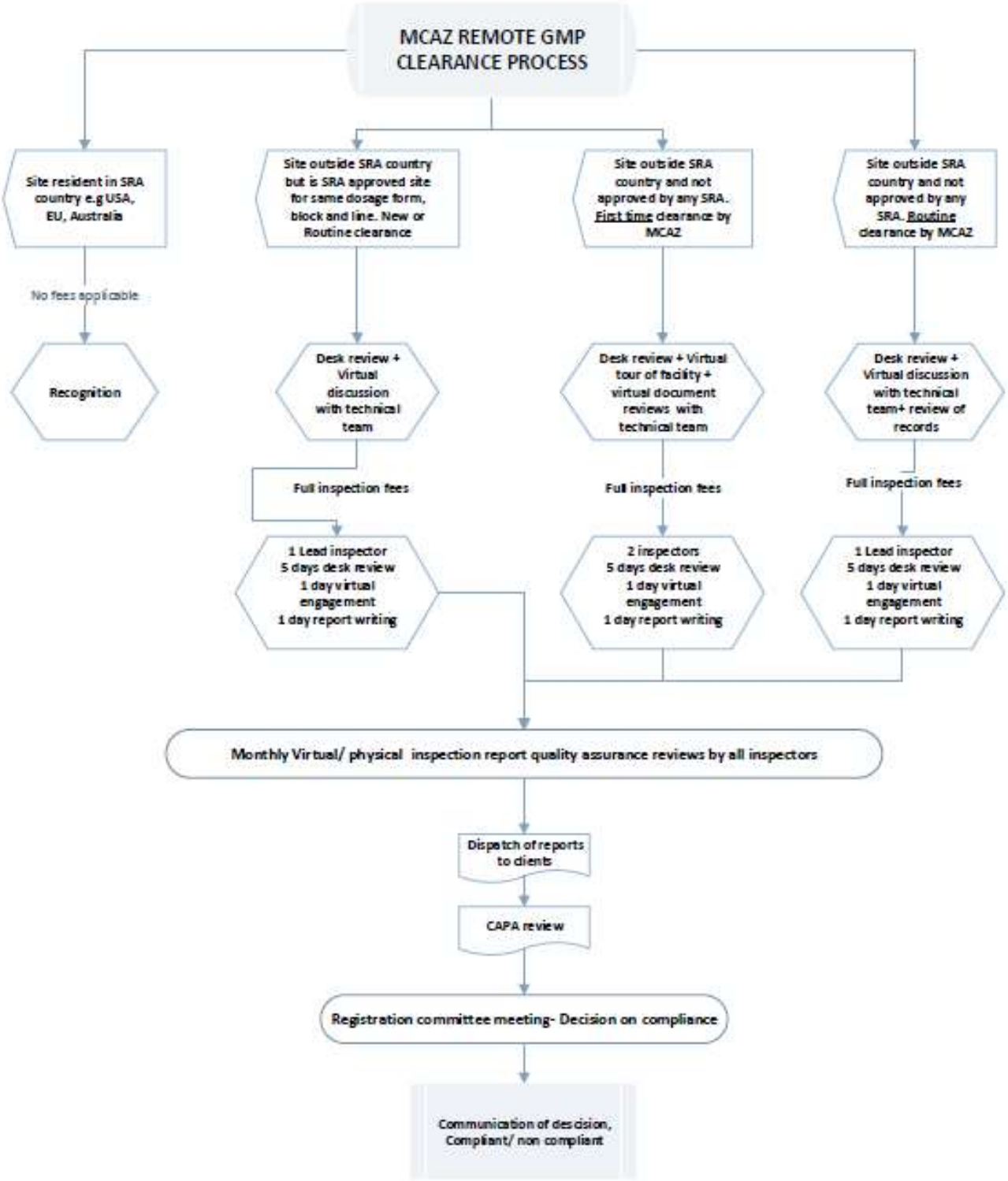

TABLE 1.0 PHASE-WISE REMOTE INSPECTION PROGRAM

Phase 1*	**Planning and scheduling** 1. Scheduling of inspection and request for SMF 2. Payment of inspection fees 3. Notification letter and proposed inspection plan	 MCAZ Site MCAZ
Phase 2 Day 1	**Virtual opening meeting** 1. Outlining how the inspection will be conducted 2. Review of any Regulatory correspondences between site and the Authority, e.g CAPA, Registration Queries, Variations 3. Discussions about documents listed on the inspection plan	 MCAZ MCAZ/SITE MCAZ
Day 2	**Desktop Inspection/Review**	MCAZ
Phase 3 Day 3	**Remote Virtual Inspection:** 1. The auditor will connect with the auditee on the agreed secure remote virtual communication platform (landline or mobile telephone, e-mails, Skype, WhatsApp, Zoom, Webex, Google Teams etc.). 2. The auditor shall provide the site/facility with feedback from Phase 2: Desktop Inspection/Review and will provide the site/ auditee the opportunity to present more evidence and/or additional evidence of procedures/processes to address noted gaps or deficiencies. 3. The Auditor shall request a remote live video walk through the plant or specific sections of the manufacturing plant, guided by the auditee.	 MCAZ/SITE MCAZ/SITE MCAZ/SITE
Day 4	**Virtual Closing meeting** A closing discussion on the findings from the inspection shall be conducted between the auditor and the auditee. Interim report will be emailed to the auditee after the discussion and agreeing to the raised findings.	 MCAZ/SITE MCAZ

Day 5	**Final inspection reporting** The interim report shall be referenced, at least for all major and critical non-conformances, peer reviewed, signed and dispatched to the auditee	MCAZ
Phase 4	**Corrective action and preventive action, CAPA and inspection closure** 1. The site shall respond to the final report with a comprehensive CAPA using email or internet-cloud storage platforms like WeTransfer, Dropbox, Mimecast etc. 2. Review of CAPA and closure of the inspection	SITE MCAZ

**The individual sequence of phases can change to facilitate ease of audit*

5.2 Submission and assessment of documentary evidence and information

5.2.1 When the site is subject to a remote audit, they should ensure that auditee representatives for each topic and each function is available. Therefore, the continuous communication between the auditor and the auditee's Team Leader is crucial for adapting the agenda continuously.

5.2.1.1 Submission documentary evidence

Submissions of the requested documents in the inspection for each site should be submitted or access granted to web based documentation system by the auditee Team Leader to MCAZ.

5.2.1.2 Assessment of documentary evidence and information

Desktop assessment (and remote virtual inspection) involves a detailed evaluation of the specified documentary evidence supplied by the site/facility against GxP guidelines and regulations as determined by the Authority

5.2.1.3 General requirements for documents

Documents to be submitted to MCAZ as evidence of compliance to GxP standards and systems that are implemented at the facility should adhere to the following general requirements:

i. All certificates and other supporting documents should be in English,
ii. Where the document is not in English, it should be submitted with a certified translation. A signed and dated statement by the certified translator, stating that each document is a true and accurate translation of the original document, must accompany translated documents,
iii. Submitted documents should be the most recent and reflect current activities and practice and approved and dated accordingly (draft, expired or superseded documentation cannot be used to justify non-compliance, but maybe shared or mentioned for noting) and
iv. Documents must provide sufficient information to cover the scope of activities for which confirmation of GxP compliance is to be determined.

All documents, whether the original format is paper or electronic, are to be submitted electronically (for example as Electronic transfer systems, DVD's, CDs etc.) and are not required to be certified as original copies. Certification of a document may be requested if, for example, there is concern over the validity of the supplied documents. MCAZ can request certified copies of original documents at any time.

5.3 Authenticity of documents

It is important that documentary evidence provided by the applicant as the basis for granting approval for good practices be current, accurate and authentic. It is the responsibility of the auditee to ensure this. The Head of Quality Assurance should include a **declaration** statement, in the acceptance response to the notification of inspection, that all the documents to be submitted are authentic, accurate and correct.

Submission of inaccurate or false information may result in declaration of the manufacturer, wholesaler, and distributor, holder of certificate of registration or quality control laboratory as non-compliant and possible rejection of registration/variation application, possible rejection of license renewal or possible suspension/cancellation of Marketing Authorisation.

5.4 Failure to submit documentary evidence

If the auditee is unable to provide adequate documentary evidence, including information on current compliance, or to submit the documents before a specified deadline or fails to submit documents as required, the Authority will issue non-compliance resolution.

In such circumstances, approval of GxP should only be granted after the on-site inspection has been conducted, and the manufacturer, holder of certificate of registration, outsourced quality control laboratory, wholesaler or distributor has been found compliant.

5.5 Responsibilities of the Facility/Site

The main responsibilities of the facility/site for GxP compliance inspection during emergencies/disasters including the COVID- 19 pandemic are summarized below:

5.5.1 Ensuring that all required evidence documents are submitted during GxP compliance inspection. Incomplete submissions will be rejected, and the facility/site will be required to reapply with payment of prescribed fees,

5.5.2 Ensuring that all necessary arrangements are in place to ensure uninterrupted video conference interviews and electronic access to QMS as required,

5.5.3 Remitting the inspection fee(s) prior to the GxP inspection

5.6 MCAZ Assessment of the GxP evidence

After MCAZ's assessment of the GxP evidence, a resolution will be assigned to the facility/site:

5.6.1 Compliant – issued when the evidence is deemed acceptable and demonstrates GxP compliance.

5.6.2 Non- compliant – issued when the evidence is deemed unacceptable and does not demonstrate GxP compliance.

Terms and conditions may be added to the Regulator resolution if other factors (such as the facility's compliance history, drug type, medical necessity, category, dosage form or activities conducted at the facility) require additional GxP oversight.

5.7 Remote Audit Times

The inspection shall be done during routine working hours of the auditee, i.e between 08:00 am and 17:00pm. Any changes to these shall be communicated during the inspection and agreed upon.

5.8 Emergencies/disasters including the COVID- 19 pandemic inspection process fees

The normal inspection fees are applicable and the exact fee vary from site to site. To determine the inspection fee, the site must send the current SMF and list of products registered or submitted for registration to gmp@mcaz.co.zw and request for an inspection proforma invoice accordingly.

5.9 Exemption from the emergencies/disasters including the COVID- 19 pandemic inspection schedule

Generally, a facility/site will not be exempted from the emergencies/disasters including the COVID- 19 pandemic inspection schedule. Sites/ facilities are expected to be operational with office operations not absolutely interrupted by the emergencies/disasters including the COVID- 19 pandemic regulations therefore complying with good practices as determined by the Regulator.

However, you may still request exemption in some justified exceptional circumstances. If you intend to request that we exempt your facility/site from the inspection schedule, you should ensure that you provide the appropriate level of detail and justification upfront via a cover letter in an email to MCAZ at gmp@mcaz.co.zw .

5.10 MCAZ on-site inspection in exceptional circumstances

An on-site inspection during risky pandemics and emergencies will only be done after Authority approval based on advice from local and international health authorities. This consideration will only be explored for high risk products, urgently needed and may not wait for the disaster/ emergency situation to end. All less risky alternatives for assessment of compliance should have been explored and found not inadequate.

Important - MCAZ has the right to inspect the facility/site regardless of what other evidence you supply—for example, we may as a regulator:

i. have identified issues during the desktop inspection and/or virtual inspection and
ii. have received other regulatory information or have concerns about the facility/site ’s level of compliance.

The guidance only applies during emergency/ disaster and pandemic situations.

6.0 KEY RELEVANT DOCUMENTS

6.1 The MCAZ Good manufacturing practice guideline

6.2 SAHPRA guidance on good practice (GXP) inspections during emergencies/disasters including the Covid- 19 pandemic

6.3 Medicines and Allied Substances Control Act 15:03 and its Regulations.

7.0 HISTORY

DOCUMENT HISTORY		
Revision Number	Date Approved	**Date Written**: June 2020
0	June 2020	**Reason for Change and Amendments:** None This is a new guideline