Medicines Control Authority of Zimbabwe

MCAZ/LED/GL-06

GUIDELINES FOR HANDLING OF TEMPERATURE AND TIME SENSITIVE PHARMACEUTICAL PRODUCTS

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1.0 APPLICATION

These guidelines apply to all pharmaceutical manufacturers and distributors handling temperature sensitive medicines.

2.0 PURPOSE

This guideline is to be used for handling of temperature and time sensitive medicines throughout the supply chain.

3.0 BACKGROUND / INTRODUCTION

Monitoring of temperature in storage facilities and during transportation using calibrated measuring devices is necessary in order to provide assurance that conditions are under control, and that product quality is maintained. Specialized monitoring devices may need to be considered to enable sound transport validations, temperature mapping and online temperature control to ensure that product integrity within the specification limits is maintained. For many medicinal products, storage and transportation temperatures are highly significant factors in maintaining the quality throughout the distribution chain.

4.0 DEFINITIONS

4.1 **Service level agreement (SLA) or contract**: It is a negotiated agreement between the customer and service provider that defines the common understanding about materials or service quality specifications, responsibilities, guarantees and communication mechanisms. It can either be legally binding, or an information agreement. The SLA may also specify the target and minimum level performance, operation or other service attributes.

4.2 **Temperature Mapping:** It is a process of predetermining if a storage area can maintain temperature within predefined limits.

4.3 **Temperature-controlled**: This phrase includes any environment in which the temperature is actively or passively controlled at a level different from that of the surrounding environment within precise predefined limits.

4.4 **Time- and temperature-sensitive pharmaceutical product** (**TTSPP)**: Any pharmaceutical goods or product which, when not stored or transported within predefined environmental conditions and/or within predefined time limits, is degraded to the extent that it no longer performs as originally intended.

4.5 **Temperature excursion**: It is a deviation from given instructions in which a TTSPP is exposed to temperatures outside the range(s) prescribed for storage and/or transport. Temperature ranges for storage and transport may be the same or different; they are determined by the product manufacturer, based on stability data.

4.6 **Temperature data logger**: It is a portable battery powered device with temperature probes. It should be capable of continuous recording of temperature with an ability to display the maximum temperature on a specified time interval.

5.0 GUIDELINES

5.1 Enabling Provisions in the Legislation

The Medicines and Allied Substances Control Regulations (S.I. 150 of 1991) 'Third schedule" section 2(d), provides for the need for *'; adequate refrigeration. This guideline will go on further to provide guidance to manufactures, wholesaler, retailers and any other distributors of TTSPs on fulfilment of this requirement.*

5.2 Provisions

5.2.1 Manufacturers and Applicants

All manufacturers and applicants supplying time and temperature-sensitive pharmaceutical products to Zimbabwe are to ensure that medicines are transported within the product specifications. The following policy changes are made:

i. Transport validation should have been conducted for climatic zone IVa.
ii. Risk assessment should have been conducted with all the risk factors and mitigating procedures put in place to ensure maintenance of TTSPPs.
iii. Contracts should ideally be available with all the participants in the supply chain, for example transportation, warehouse facilities and brokers to ensure responsibilities are defined.
iv. Each consignment should have a calibrated digital data logger whose data can be downloaded and verified at the port of entry or at any other time as requested by the Authority. The data from the data logger should be electronically kept and/ or physical records maintained for up to one year post the shelf life of the product. Alternative means such as vial monitors for vaccines are acceptable.
v. Accelerated stability data should be readily available to support any unforeseen temperature excursions.
vi. Where possible, and where necessary ensure that all temperature controlling equipment for temperature sensitive storage (i.e. refrigerators, freezers, building management systems, heating, ventilation and air-conditioning (HVAC) systems, compressors, air-handling units, monitoring systems, alarms and related computer equipment) are connected to an uninterrupted power supply (UPS) system.
vii. Provide calibrated temperature alarm systems for temperature-controlled rooms, cold rooms, freezer rooms, refrigerators and freezers, used to store TTSPPs. These should have a mechanism of immediately informing/alerting the supervisors off-site of any temperature excursions.
viii. All cold rooms or refrigerators should be qualified and/or records of temperature mapping conducted should be maintained
ix. Standard Operating Procedures (SOPs) for handling TTSPP should be readily available

5.2.2 Wholesalers

i. There should be SLA between wholesalers and applicants or manufacturers to ensure that the TTSPPs conditions are maintained throughout the transportation and distribution of TTSPPs. These should explain the roles and responsibilities of both parties.
ii. Vaccines and other biological products that are sensitive to freezing should be protected from sub-zero temperatures
iii. Data from each consignment's data loggers is to be kept as part of the product records up to one (1) year after expiry of the products.
iv. All cold rooms or refrigerators should be qualified and/ or Appropriate temperature mapping should be conducted.
v. Online temperature monitoring for cold chain rooms or refrigerators is required. Alert and action limits should be set to ensure that the products are always in the specified range of the TTSPP Data should be readily available for inspection. Records should be checked daily and independently reviewed on a monthly basis by the supervisor
vi. Additional emergency mechanisms such as cooler boxes and ice packs should be available as contingency plans for emergencies.
vii. All TTSPPs dispatched from the facility should be dispatched using temperature regulated and monitored means. This involves use of cooler boxes with data loggers and gel packs.
viii. There should be recorded product handover and take over between the wholesaler and the health institution.
ix. Temperature excursions and deviations should be recorded and impact assessment should be carried out. Major excursions and deviations should be reported to the Authority.
x. Temperature controlled vehicles should be used when transporting TTSPPs. These should have been qualified.
xi. SOPs for handling TTSPPs should be available.

5.2.3 Shipping services and cargo handling

i. Service Level Agreement (SLA) should exist between importer and clearing agents to ensure that temperature sensitive products are cleared through customs rapidly. Only certified agencies should be used for handling TTSPPs.
ii. Online monitoring of the cold chain store rooms is required.
iii. Cold air distribution, qualification and calibration reports should be available for all TTSPPS storage facilities.
iv. These storage facilities should be open for inspection by the Authority.
v. Continuous online temperature monitoring using calibrated devices should be implored.

5.2.4 Pharmacies and Health institutions

Pharmacies and Health Institutions should have mechanisms to ensure "adequate storage conditions. These include the presence of the following:

i. It is mandatory that calibrated digital temperature monitoring devices whose data can be downloaded and verified are used. This involves the use of portable data loggers. The data shall be inspected during routine inspections of facilities.
ii. There should be uninterrupted power supply provided by suitable means.
iii. Product dispatch mechanisms that maintain the cold chain or specified temperatures should be used. This involves the use of cold packs and ice blocks. Vaccines that are sensitive to freezing should be protected from sub-zero temperatures
iv. Standard operating procedures for maintenance of the appropriate cold chain or temperature sensitive products should be available.
v. The Authority holds the right to disqualify any facility from dealing in temperature sensitive medicines, should there be sufficient evidence of failure to guarantee the maintenance of the cold chain.

6.0 KEY RELEVANT DOCUMENTS

6.1 Taylor J, Recommendations on the control and monitoring of storage and transportation temperatures of medicinal products. The Pharmaceutical Journal, 28 July 2001, Volume 267, pages 128-131.
6.2 EU Guidelines on Good Distribution Practice (GDP) of Medicinal Products for Human Use.
6.3 Health Products Regulatory Authority 'Guide to Wholesaling and Brokering of Medicinal Products for Human Use in Ireland.'
6.4 WHO TRS 961 Annex 9 Model guidance for the storage and transport of time- and temperature sensitive pharmaceuticals.

7.0 HISTORY

DOCUMENT HISTORY		
Revision Number	Date Approved	Date Reviewed: N/A
		Reason for Change and Amendments None as this is a new guideline.