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# VOL-01

# PERFORMANCE QUALIFICATION PROTOCOL

**FOR**

## COLD ROOM

**OF**

## DR REDA PHARMACY STORE

*KAFR AL-SHIEKHA*

CLIENT:

QUALIFICATION PROVIDER:

**Package Content:**

| | |
|---|---|
| VOL.-01 | Performance Qualification Protocol |
| | Annex-01.01) Results Data Sheets |
| | Annex-01.02) Turn Over Package (Attachments) |


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## Table of Content

## 1. PROTOCOL REVIEW AND APPROVAL

- Prior to the initiation of qualification testing activities, this document will be issued, reviewed and approved by the appropriate personnel.
- The signatures below signify prior approval of the format and content of the final report, ensuring an accurate representation of the qualification activities planned for DR REDA PHARMACY STORE.

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**DR REDA PHARMACY STORE Approver(s)**

| Name | Title | Company | Date | Signature |
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| | | | | |
| | | | | |

**Change History**

| No. | Revision No. | Amended Page No. | Reason for change | Issue Date |
|---|---|---|---|---|
| 1. | 00 | NA | Original | 18-06-2025 |

**Note:** Any amendment will be indicated with italic and bold font.

## 2. INTRODUCION

### 2.1. Glossary/Abbreviations

- **Performance Qualification (PQ):** The process of obtaining and documenting evidence that the premises, equipment and supporting systems, as connected together, will consistently perform in accordance with the approved process method and specifications. It is the final step of qualification. In this phase, the qualification and validation team verify and document that the user requirements are verified as being met and to ensure that every part of the system will maintain a stable temperature during use.
- **Key operating parameters:** parameters that must be maintained in order to process or produce products with consistent quality attributes and those that may have an impact on the proper operation of the system.
- **Controller:** A device that interprets a mechanical, digital or analogue signal, generated by a sensor, to control an equipment or component.
- **Sensor:** A mechanical device (pressure switch, bimetal temperature switch, etc.), or a digital or analogue transducer (limit switch, pressure sensor, temperature sensor, etc.) that generates a mechanical or electrical signal to an instrument or a controller in order to be interpreted.
- **Electronic data logging monitor (EDLM):** A small portable device that measures and stores temperature readings at predetermined time intervals by means of an electronic sensor. They have programmable alarm capabilities, integrated displays, and can create reports and graphs which may be permanently stored, shared and analyzed via proprietary hardware, software, desktop applications or through hosted databases.
- **TTSPP:** time- and temperature-sensitive pharmaceutical product.
- **Temperature-controlled:** Includes any environment in which the temperature is actively or passively controlled at a level different from that of the surrounding environment within precise pre-defined limits.
- **Mapping:** Documented measurement of the temperature distribution within a storage area, including identification of hot and cold spots.
- **Maximum Temperature:** refers to the highest value recorded in the mapped space over the study period, and it may be outside the specified acceptance criteria for the store.
- **Minimum Temperature:** refers to the lowest temperature recorded in the mapped space over the study period, and it may be outside the specified acceptance criteria for the system.
- **Mean Kinetic Temperature:** If you have a set of temperature readings across a certain period of time, the Mean Kinetic Temperature across this period means the effective average thermal value for this period. This temperature value is what the stored goods effectively feel during the mentioned time. This is not the arithmetical average of the readings.
- **Hot Spot:** refers to the highest temperature(s) recorded in the area studied over the study period, but these highest temperature(s) remain within the specified temperature range.
- **Cold Spot:** refers to the lowest temperature(s) recorded in space over the study period, but these lowest temperature(s) remain within the specified temperature range.

- **Worst Locations:** It refers to hot and cold spots determined in the space over the study period during the thermal qualification study.
  Note: It is also important to look at the overall high and low trends rather than just the highest and lowest temperatures. Average values can be useful to help confirm true hot and cold spots.

## 2.2. Rationale

- The rationale behind this protocol is essential for verifying the thermal performance of the Cold Room located at DR REDA PHARMACY STORE and to confirm that it functions as intended and produces reliable results essential for maintaining product quality and ensuring TTSPPs stored within it are maintained under appropriate conditions. By conducting performance qualification, it becomes possible to identify any deviations from the desired temperature range, reduce risks of product degradation, and maintain quality assurance measures. We aim to minimize the risk of errors or inaccuracies in testing procedures, ensuring that the system operates within specified parameters.
- Performance Qualification Protocol will provide the methodology of qualification studies, formats for recording the observation, Criteria of qualification and a guideline for documentation of the study.

## 2.3. Protocol Purpose

- To evaluate the heat distribution profiles and trends throughout the Cold Room located at DR REDA PHARMACY STORE.
- To ensure uniformity and compliance with regulatory standards and to verify that the Cold Room meets regulatory requirements for temperature control.
- To identify the scope of qualification required by DR REDA PHARMACY STORE.
- To determine the responsibilities of TAG and DR REDA PHARMACY STORE.
- To clarify the rationale of this work scope and to clarify the rationale behind the chosen study design and its methodology.
- To describe the followed procedure used to study the heat distribution throughout the Cold Room () located at DR REDA PHARMACY STORE and to ensure uniformity and compliance with regulatory standards.
- To identify the personnel of charge that will perform and follow-up this scope.

## 2.4. Protocol Scope

The scope of this protocol covers the performance qualification of the of the Cold Room () located at DR REDA PHARMACY STORE for full load cycle(s) for 1 day (24 hrs.) and performing the power failure test for 40 min and open-door test for 5 min.

## 2.5. Documents Execution Instructions

Prior to the initiation of Performance Qualification testing activities, this document will be generated, reviewed and approved by the appropriate personnel.

The testing specified in this approved Protocol will be conducted in accordance with the instruction detailed in the test cases.

Additional documentation requirements for protocol and report are as follows:

- Each person recording or reviewing the information in this document must complete the Signature Log
- After completing entries in the test cases, the initials and date of the individual responsible for the entry must be entered in the appropriate column
- Any blank entry space or box must have a line drawn through it, initialed, and dated.
- Any correction entry must be marked with a unique line drawn through the data to be changed, initialed, and dated. After correction, wrong data must remain readable.
- General datasheets and/or supporting documentation must be inserted as near to the related test datasheet as possible and must include the following information:
  - Reference to supplemented datasheet
  - A unique id number (i.e. number of the supplemented datasheet + [a], [b], ... [aa], [ab], etc.
  - Page number
- Supporting documentation not related to a specific datasheet can be attached at the end of this document. Attachments list has to be used to assign a unique id number.
- Attachments are to be intended both as digital/magnetic and paper supported.
- When approved vendor documentation (Protocols) is available and approved by DR REDA PHARMACY STORE, it will be possible to use it for the execution of the Protocol tests at the condition that the documentation meets the minimal requirements listed above.

Any test exception and failure verified during the protocol execution shall be noted on the "Deviation Report" form (Data Sheet Number 01.01.03.01 in Annex 01.01 (PQ Results Data Sheets)). Every exception and its conclusion (intended as foreseen corrective action results) shall be documented inside the related qualification summary.

## 2.6. Responsibilities

For the submission/approval, execution of this protocol and its final report, the responsibility of all personnel involved with the verification and documentation process are as follows:

### 2.6.1. COPMANY_NAME

- Provide the necessary information needed for the performance qualification protocol issue.
- Review and approve the protocol for compliance before qualification execution and ensure that the protocol aligns with regulatory requirements and company policies.
- Responsible for the operational aspects of the system being qualified.
- Provides access to the system being qualified, coordinate and assist in addressing any system-related issues that may impact the mapping process.
- Develop the project timeline and oversee the entire thermal qualification project, including planning, coordination, and execution.
- Provides any documents required in the performance qualification test such as layouts.
- Assign tasks to the responsible team members, ensure adherence to the approved protocol, and manage communication with stakeholders.
- Ensure that the thermal qualification process meets regulatory requirements and quality standards.
- Monitor data collection procedures, verify accuracy of results, and assess compliance with industry guidelines.
- Review any deviation in the deviation form, determine the corrective actions, and evaluate results of corrective measures and approve them.
- Review and approve the report and test results for compliance after execution and ensure that the report aligns with regulatory requirements and company policies.

### 2.6.2. TAG

- Design and prepare the qualification protocol, including all the recommendations and corrections that are required by DR REDA PHARMACY STORE.
- Review and approve the protocol for compliance before qualification execution and ensure that the protocol aligns with regulatory requirements and company policies.
- Execute the qualification only after this protocol has been approved by DR REDA PHARMACY STORE.
- Develop the project timeline and oversee the entire thermal qualification project, including planning, coordination, and execution.
- Assign tasks to the responsible qualified team members, ensure adherence to the approved protocol, and manages communication with stakeholders.
- Assure that any instrument used during qualification has been previously calibrated and that a copy of the calibration certificate is attached.
- Distribute the monitoring devices, ensure data collection at specified interval and troubleshoot any technical issues incident by TAG.
- Conduct and oversee the technical aspects of the thermal qualification study.
- Perform data analysis and interpret results to ensure the accuracy and reliability of the study and compare test results with the acceptance criteria and determine if it conform or not conform.
- Identify temperature trends, generate reports, and communicate findings and any deviations to DR REDA PHARMACY STORE for further action.
- Assure that data from tests, executed by TAG, are properly recorded in an acceptable format on work sheet and on the report.
- Ensure that all original data, final form and tables are signed and dated, that these documents are attached to final Report or that a note with their storing location is specified.
- Ensure that the description of the tool used for tests and/or verifications, its serial number and its ID number are Reported on data collection worksheets and/or forms.
- Prepare the Performance Qualification Report including all the advices and amendments pointed out by DR REDA PHARMACY STORE and submit for it for review and approval by the concerned DR REDA PHARMACY STORE departments.
- Maintain records of protocol, data collection procedures, calibration certificates, and final reports and ensure that all documentation is accurate, organized, and accessible for future reference.

### 2.7. Signature Log

Each person records, review and approve the information in this document must complete the signature log.

### 2.8. System Brief Description

The scope of this protocol intends to cover the performance qualification procedure of Cold Room () located at DR REDA PHARMACY STORE with the following description:

| System Brief Description | |
|---|---|
| Description | Cold Room |
| Dimensions/Volume | -- |
| Manufacturing | NA |
| Model | NA |
| S.N. | NA |
| Code | -- |
| Acceptance Criteria | (2 - 8) °C |
| Location | Warehouse |
| Load Description | Loaded |
| Key Operating Parameters | Temperature |

## 3. PERFORMANCE QUALIFICATION METHODOLOGY

### 3.1 Pre-Requisties

- Performance Qualification activities will only start after this Protocol is approved by the Officials deputed by DR REDA PHARMACY STORE.
- After this approval, the signed original of the Report will be filed in a suitable archive dedicated to Performance qualification/validation documents while another copy will be made available for working purposes.
- This copy, in which data gathered and recorded during qualification, and to which documents (such as layout, printouts, etc.) are attached, becomes the Qualification Report for the examined system.
- Once Performance Qualification Protocol is completed, any changes shall have to be checked, planned, and approved by DR REDA PHARMACY STORE and mentioned in the change history table.
- Any non-conformities encountered and any other discrepancies from acceptability criteria of this Protocol shall be recorded in the "Deviation Report" attached Data Sheet Number (Data Sheet Number 01.01.03.01 in Annex 01.01 (PQ Results Data Sheets)).

### 3.2 Key Concepts

- **Mean Kinetic Temperature:**

  Mean kinetic temperature (MKT) is defined by the ICH as 'A single derived temperature that, if maintained over a defined period of time, affords the same thermal challenge to a drug substance or drug product as would be experienced over a range of both higher and lower temperatures for an equivalent defined period. The mean kinetic temperature is higher than the arithmetic mean temperature and takes into account the Arrhenius equation.' The Haynes formula can be used to calculate the MKT. It is higher than the arithmetic mean and takes into account the Arrhenius equation from which Haynes derived his formula. Thus, MKT is the single calculated temperature that stimulates the non-isothermal effects of storage temperature variations.

$$T_k = \frac{\Delta H / R}{-\ln \frac{e^{-\Delta H/RT}{}_{(1)} + e^{-\Delta H/RT}{}_{(2)} + \ldots + e^{-\Delta H/RT}{}_{(n)}}{n}}$$

Where:

$T_k$ = MKT in °K
$\Delta H$ = Heat of activation/activation energy
$R$ = Universal gas constant ($8.3144 \times 10^{-3}$ kJ.Mole$^{-1}$. °K$^{-1}$)
$T$ = Temperature in °K
$n$ = Total number of equal time periods over which data are collected

### 3.3 Associated Material and Equipment Description

To ensure that the temperature distribution in the space to be mapped is adequately characterized, we should use a sufficient number of electronic data logging monitors (EDLMs) along with suitable computer equipment and software to store and analyze the data. The selected EDLMs will:

- be technically suitable for the specific mapping task and for the intended operating environment.
- provide a reliable and continuous record of time-temperature data.
- have an appropriate temperature range so that all anticipated temperature extremes can be recorded.
- have a user-programmable data sampling period, allowing time intervals to be set in the range from 1 minute to 15 minutes (maximum) and sufficient memory for the intended length of the study and the chosen recording interval.
- have a US National Institute of Standards and Technology (NIST)- traceable 3-point calibration certificate with a guaranteed error of no more than ± 0.5 °C at each calibration point.
- enable the recorded time-temperature data to be downloaded to a computer system for subsequent analysis.
- have data storage and analytical software that complies with applicable regulatory requirements (for example: 21 CFR part 11).

| Used Reference Equipment Description | | | | | | |
|---|---|---|---|---|---|---|
| Description | No. of EDLMs | Location | Accuracy | Manufacturer | Model | Calibration Due Date |
| Data Logger | 12 | Inside Cold Room | ± 0.5 °C | Will be determined at the execution phase | | |
| The exact location of each data logger in Cold Room is specified in the layout, see point 3.7 in this protocol. | | | | | | |

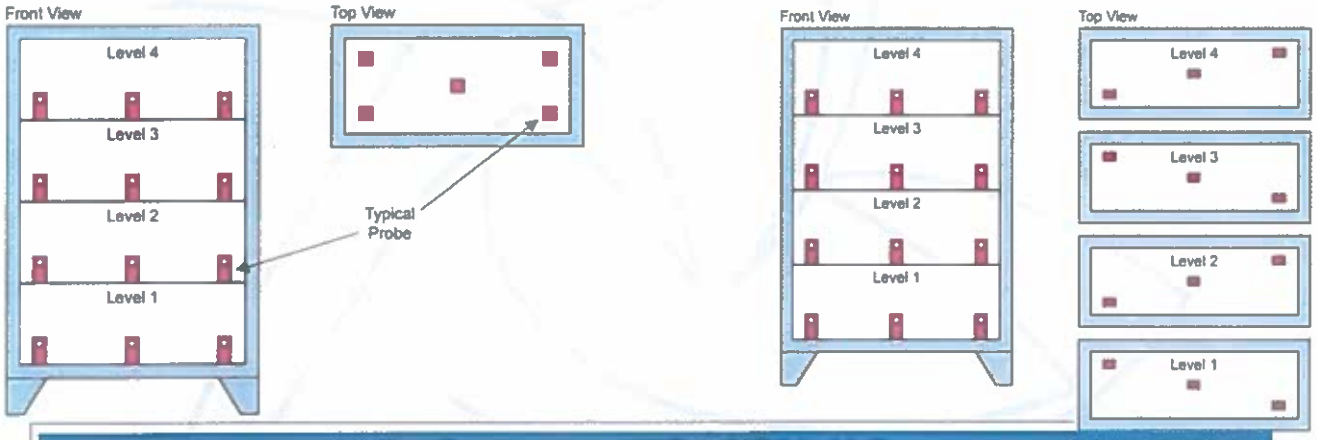
### 3.4 Data Loggers Quantity and Distribution Locations Rationale

By distributing data loggers at various locations within the Cold Room , we can ensure that temperature remain consistent throughout it, minimizing the risk of temperature differentials that could affect products integrity.

#### 3.4.1 Chambers/Equipment Qualification:

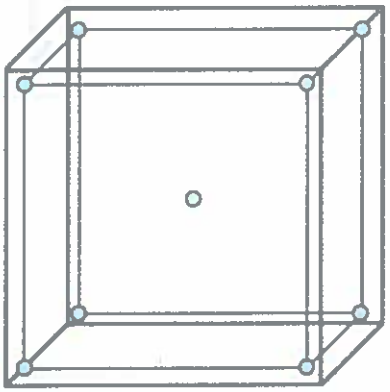
As the heat goes up and cold down the data loggers shall be placed on top and bottom shelves of the equipment. Shelving and loads may create 'hot spots' by obstructing air circulation. Due to less circulation of air in corners the data loggers shall be placed near to each corner of the equipment (As illustrated in the below figures).

- **Top Shelf:** Placing a data logger on the top shelf enables monitoring of temperature variations at the highest point within the system, where heat distribution may differ from lower levels.
- **Bottom Shelf:** Monitoring temperature at the bottom shelf helps assess heat circulation and ensures uniformity throughout the entire system space.
- **Near the Door:** Positioning a data logger near the door provides insights into temperature stability and potential impacts of external factors on the internal environment.
- **Center:** Placing a data logger in the center of the system helps evaluate overall temperature uniformity and ensures that critical samples receive consistent heat exposure.
- **Adjacent to the Heating Source:** Monitoring temperature close to the heating source allows for assessing the efficiency of heat distribution and the impact on temperature fluctuations.

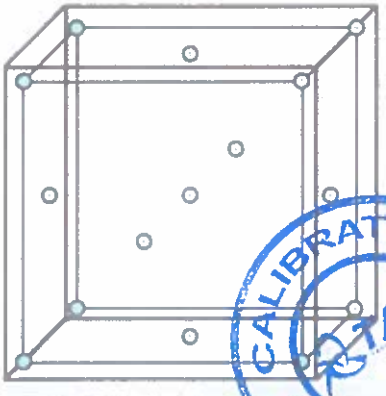



**Best Practice as per ISPE and IEC Guidelines:**

**For Chambers up to 2 m³ (2000 L):**
use 9 EDLMs (corners + center) within the usable volume of the chamber.



**For Chambers up to 20 m³ ( more than 2000 L):**
use 15 EDLMs (corners, center, wall centers) within the usable volume of the chamber.



### 3.5 Procedure Description

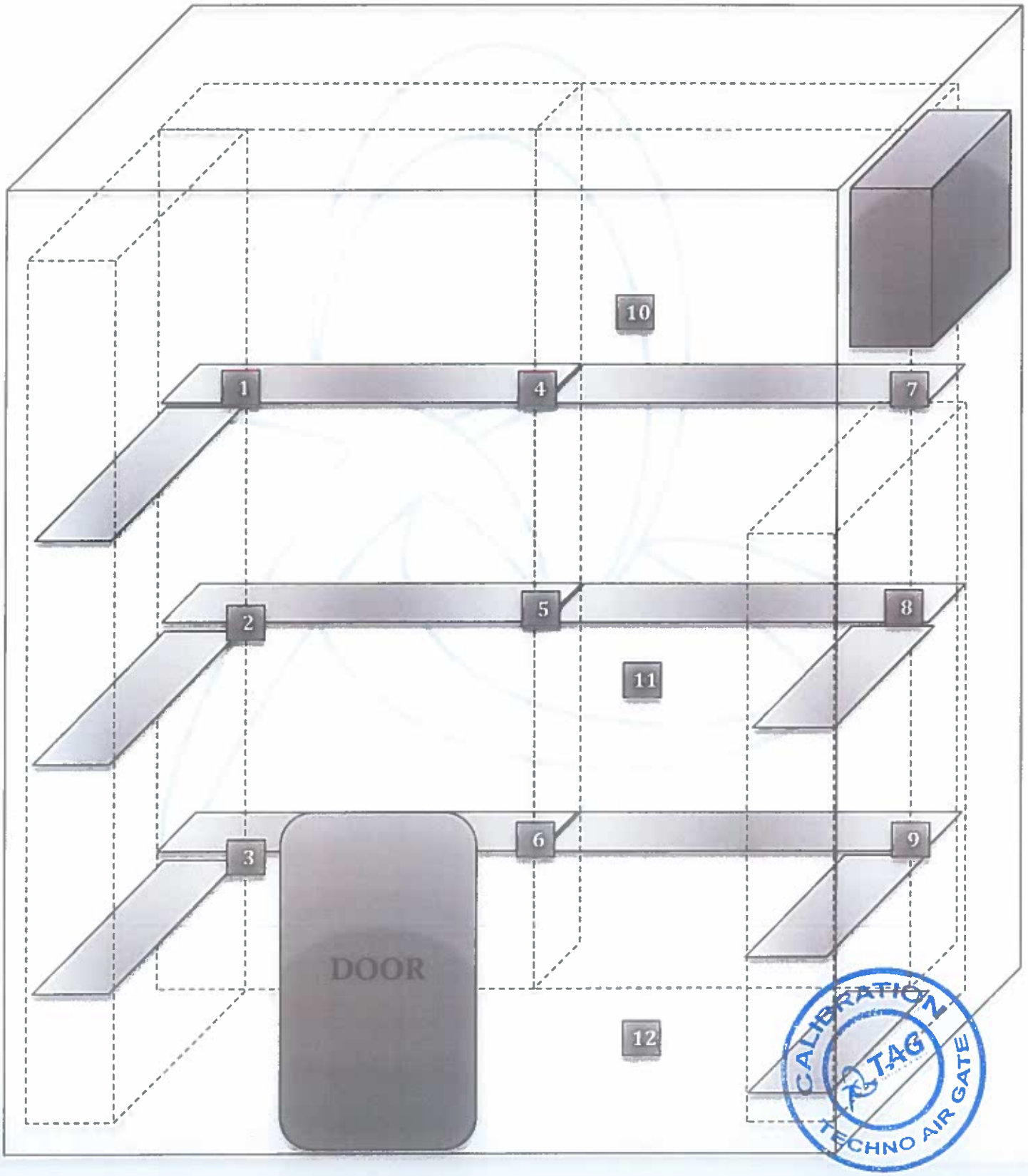
The following steps outline the methodology for conducting the performance qualification study.

| Methodology | |
|---|---|
| **Pre-requisite** | Steps 1 to 5 must be completed before the mapping protocol can finally be approved. |
| **Step (1)** | **Selecting Data Logger:**<br>- The selected data loggers have been previously calibrated (on annual basis) at points covering the study range. For their specification, see point 2.3 in Annex 01.01 (PQ Results Data Sheets) and their calibration certificates are attached in the turn over package (Annex 01.02). |
| **Step (2)** | **Designating the Technical Team:**<br>- See point "5. SIGNATURE LOG" including the list of the team members with their signatures/initials for traceability. |
| **Step (3)** | **Determining the system under qualification specifications:**<br>- Document volume, drawings, and heating/cooling component locations. |
| **Step (4)** | **Defining Acceptance Criteria:**<br>- Base criteria on product/equipment requirements and/or according to the customer requirement (or omit for exploratory studies). |
| **Step (5)** | **Determination of EDLM Locations:**<br>- As explained in point 3.3, we will need 20 EDLMS to perform accurate qualification for this Cold Room . |
| **Step (6)** | **Recording EDLM and thermostat Locations:**<br>- The exact location of each data logger in Cold Room is specified in the layout, see point 3.7 in this protocol.<br>- For the table of EDLM locations and the controller set point, see data sheet no. (01.01.01) in Annex 01.01 (PQ Results Data Sheets). |
| **Step (7)** | **Labelling and Programming EDLMs:**<br>- Assign unique IDs and record serial numbers of each EDLM.<br>- Program each EDLM with the same sampling interval which should be set between 1 and 15 minutes. Set the same start time for all units.<br>- For the exact study design, see point 2.4 in Annex 01.01 (PQ Results Data Sheets). |
| **Step (8)** | **Fixing EDLMs in Position:**<br>- Position and fasten the EDLMs so that they cannot be damaged or displaced during the course of routine operations.<br>- Ensure that sufficient time is allowed for the EDLMs to be conditioned to the ambient temperature before the mapping exercise begins. |
| **Step (9)** | **Conducting Mapping Exercise:**<br>- For the exact study design including study period details, see point 2.4 in Annex 01.01 (PQ Results Data Sheets) |
| **Step (10)** | **Performing Intervention Tests:**<br>- Power Failure (Blackout): For the exact test design see point 2.3 in Annex 01.01 (PQ Results Data Sheets).<br>- Door Opening: For the exact test design, see point 2.3 in Annex 01.01 (PQ Results Data Sheets). |
| **Step (11)** | **Data Analysis:**<br>- Download the EDLM readings and consolidate the data for the study analysis.<br>- Issue the report and identify the hottest point, coldest point attained and calculation of mean kinetic temperature.<br>- Mark the area of hottest and coldest points.<br>- Review the report and note down the maximum, minimum temperature reached during the interventions (power failure, door opening) and the time required to regain the temperature. |

### 3.6 Study Design

| Heat Distribution Study Design | | | | | |
|---|---|---|---|---|---|
| **Controller Setting:** @ 4 °C (will be determined at the execution phase) | | | | | |
| **Acceptance Criteria:** (2 - 8) °C | | | | | |
| Cycle No. | Load Description | Start Date | Stop Date | Sampling Period | Sample Frequency |
| 1. | Full Load | dd/mm/yyyy hr:min AM/PM | dd/mm/yyyy hr:min AM/PM | 3 Day (72 hrs.) | 2 minutes |

### 3.7 Endorsed Layout and Data Loggers' Distribution



### 3.8 Acceptance Criteria

The general acceptance criteria for PQ stage specify that the results of all the locations envisaged in this Protocol, when correctly run and documented in the attached forms, confirm the expected result.

### 3.9 Results Evaluation

After conducting the performance qualification study, the results will be thoroughly evaluated to assess temperature distribution, uniformity, and stability within the storage environment. Key aspects to consider in the final report after the evaluation include:

- Comparison of measured temperatures against set criteria and industry standards.
- Analysis of data trends and patterns to understand the overall thermal performance of the facility.
- Identification of temperature variations, and hot/cold spots would be identified for future monitoring.

### 3.10 Deviation Report

Any observed deviations from acceptance criteria encountered while running the performance qualification shall be recorded in the specific form named "Deviation Report" enclosed in (Data Sheet Number 01.01.03.01 in Annex 01.01 (PQ Results Data Sheets)) to be reported to DR REDA PHARMACY STORE for taking and following up the corrective actions for those deviations.

### 3.11 Conclusion and Recommendations

- Based on the results of the performance qualification study, a conclusion will be drawn regarding the effectiveness of the temperature control system and the overall thermal stability of the system. The conclusion will summarize the key findings of the study and address whether the system meets the required temperature specifications for intended use.
- Following the evaluation and conclusion of the thermal mapping study, recommendations will be provided to improve temperature management and enhance the overall efficiency of the system. By incorporating the following recommendations, organizations can optimize temperature control, mitigate risks of product degradation, and ensure compliance with regulatory requirements. These recommendations may include:
  - Implementing adjustments to the temperature control system to address identified hot/cold spots.
  - Upgrading controlling systems to improve temperature stability.
  - Enhancing monitoring and alarm systems for better temperature control.
  - Establishing protocols for door opening/closing procedures to minimize temperature fluctuations.
  - Conducting regular maintenance and calibration of temperature monitoring devices.

## 5. SIGNATURE LOG

| Printed Name | Title | Company / Department | Initials | Signature |
|---|---|---|---|---|
| Bassant Waleed | Technical Office Team Leader | TAG | B.W | Bassant |
| Abdelrahman Ramadan | Site Engineer | TAG | A.R | A. Ramadan |
| Noha Essam | Technical Office Senior | TAG | N.E | Noha Essam |
| Ahmed Tarek | Technical Manager | TAG | A.T | |