



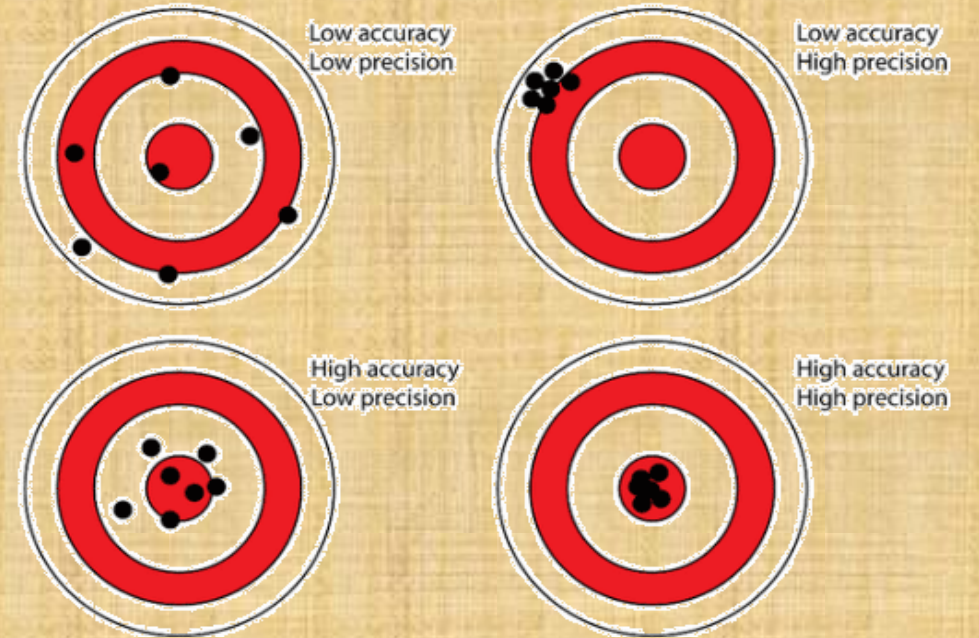
دورة تدريبية حول :

التوزيع الحراري للأحجام المغلقة الحرارية

Thermal Mapping for Closed Volumes

Definition

- * Metrology
- * Mapping
- * Measurement method
- * Measurement procedure
- * True value
- * Accuracy
- * Precision



Definition

- * Error
- * Correction
- * Repeatability
- * Reproducibility
- * Verification
- * Validation
- * Uncertainty
- * Traceability

Definition

- **EDLM** electronic data logging monitor
- **TTSP** time- and temperature-sensitive pharmaceutical product
- **GMP** good manufacturing practice
- **3PL** third-party logistics (provider)

Calibration Conditions

- 1- Staff (Training-Experience)
- 2- Equipment (Specifications-Calibration ..)
- 3- Standard (International-In House Method)
- 4- Environmental Conditions (Temp.-Hum.)



Requirements for Closed Volume

- Availability of sensors for air temperature with the associated indicators as components of the closed volume.
- Availability of control systems for the quantities to be calibrated as components of the closed volume.
- Availability of the manufacturer's technical specifications.
- Availability of technical documents on the sensor category

Equipment

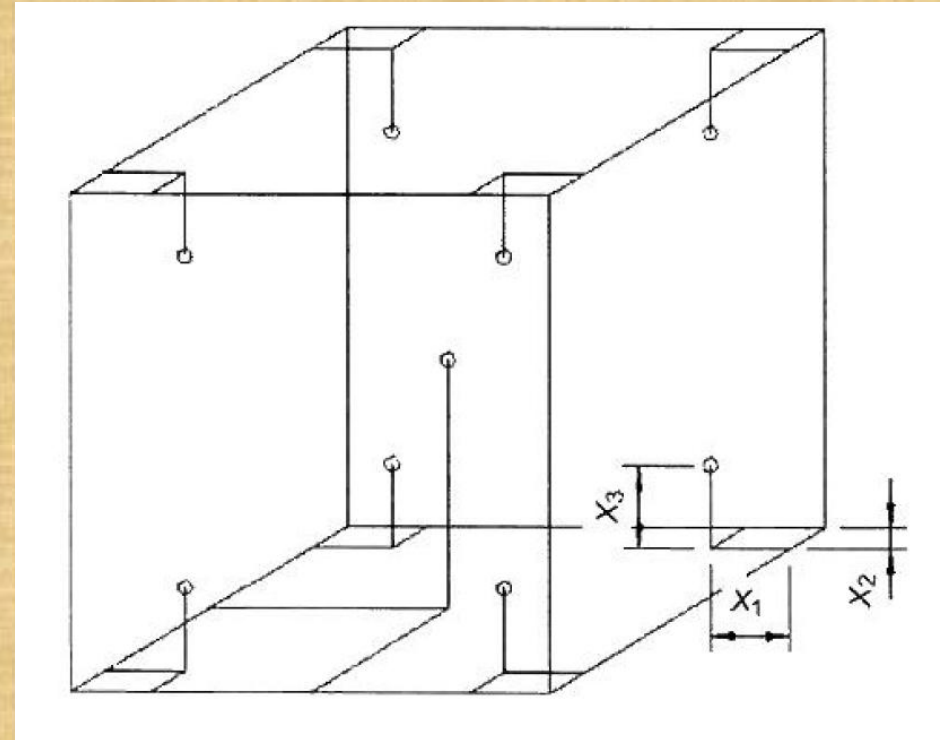


Thermal Mapping for Closed Volume



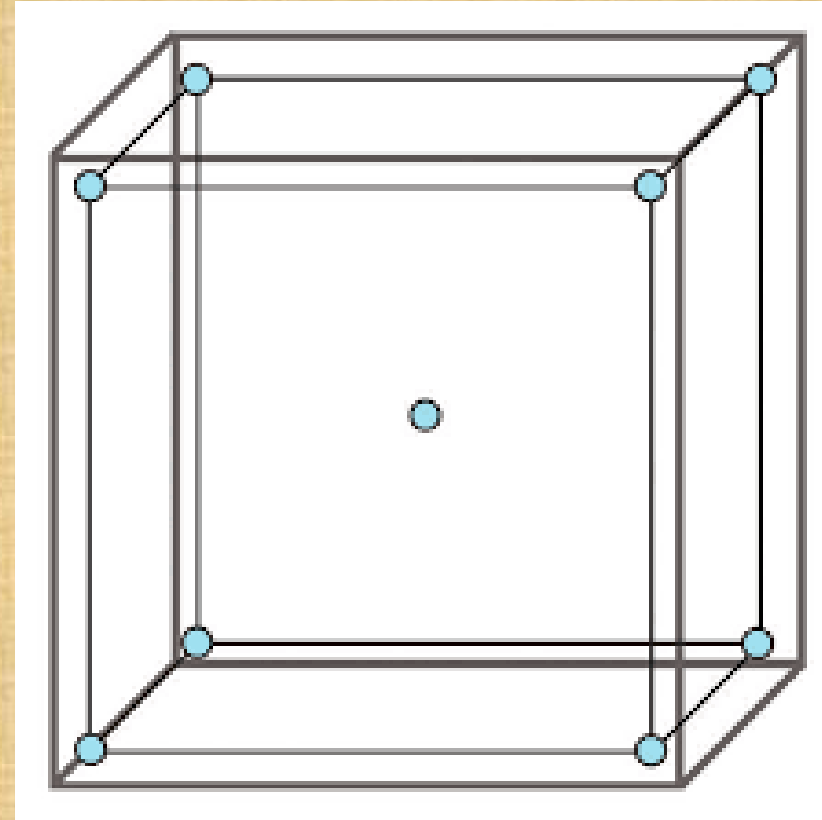
Thermal Mapping for Closed Volume

- Closed Volume



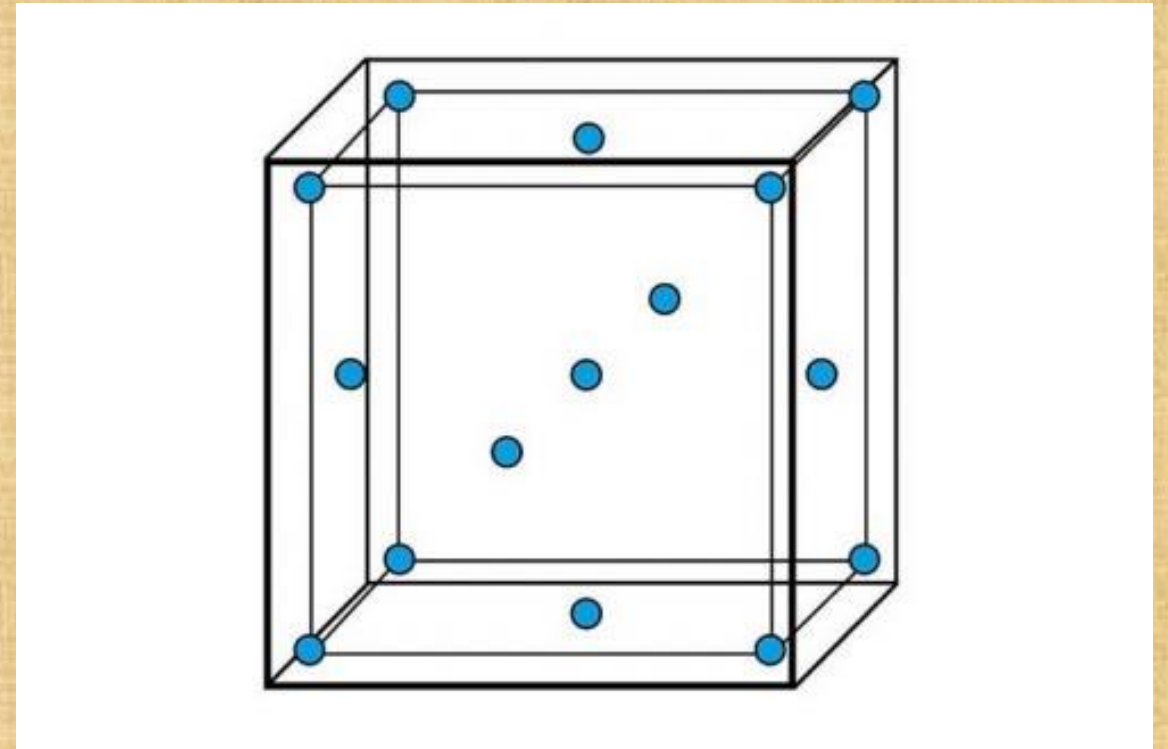
Thermal Mapping for Closed Volume

- 9 sensors were distributed
Inside Volume < 2000 L



Thermal Mapping for Closed Volume

Inside Volume > 2000 L
15 sensors were distributed



Thermal Mapping for Closed Volume

Distribute the sensors as customer request



Thermal Mapping for Closed Volume

- At 2 location beside closed volume sensor
- Fluctuation
- Stability
- Homogeneity
- Correction



- **Temperature Homogeneity**

- the maximum deviation of the temperature of a corner or wall measuring location , from the reference location

- **Temperature Fluctuation**

- the maximum deviation of the temperature from all sensors

- **Determination of temporal Stability**
- The temporal stability for air temperature and air humidity is determined from the registration of the temporal variation of temperature or relative humidity, respectively, over a period of time of at least 30 min after steady-state conditions have been reached

Analysis of Data

[illegible]

Analysis of Data

- Stability
- Homogeneity
- Fluctuation
- Correction

Uncertainty

Symbol	Source of Uncertainty	Value $\pm$ oC	Probability Distribution	Divisor	Sensitivity Coefficient	Method of estimation
t_s	Uncertainty of standard		Normal	1	1	Calibration certificate
t_d	Drift of standard		Rectangular	$\sqrt{3}$	1	Max. Difference between two successive calibrations of the standard
t_{uut}	resolution of UUT		Rectangular	$\sqrt{3}$	1	digital indicator = 0.5 of resolution
t_{hom}	Temperature homogeneity		Rectangular	$\sqrt{3}$	1	max difference between sensors
T_{stab}	Temporal stability		Rectangular	$2\sqrt{3}$	1	Difference between maximum and minimum value of measurements
t_{rep}	Repeatability of UUT		Normal	1	1	Standard deviation of measurements
	Combined Un.					
	Expanded Un.					

WHO Guide



Equipment

Typical Mapping Duration

Fridge, Freezer, Incubator

24 to 72 Hours

Cold Store

24 Hours to 7 Days

Warehouse

7 Days

- Temperature Distribution Test (Empty)
- Temperature Distribution Test (Loaded)
- Door Open Test
- Power Off Test



The temperature-mapping process has four stages

- a. Prepare a mapping protocol.
 - b. Carry out the mapping exercise.
 - c. Prepare a mapping report.
 - d. Implement the recommendations by carrying out the remedial and other actions identified in the mapping report. A follow-up mapping exercise may then be needed to verify the effectiveness of the remedial actions.
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- The permitted temperature ranges in these areas will vary – for example: $-25.0\text{ }^{\circ}\text{C}$ to $-10.0\text{ }^{\circ}\text{C}$, $2.0\text{ }^{\circ}\text{C}$ to $8.0\text{ }^{\circ}\text{C}$, or $15.0\text{ }^{\circ}\text{C}$ to $25.0\text{ }^{\circ}\text{C}$. Temperature-mapping may also need to be carried out in spaces without active temperature control.
 - calibration certificate with a guaranteed error of no more than $\pm 0.5\text{ }^{\circ}\text{C}$ at each calibration point;

The mapping protocol

- a. Approval page and change control history
- b. Acronyms and glossary
- c. Description and rationale
- d. Scope
- e. Objectives
- f. Methodology
- g. Mapping report template

Objectives

- Measuring temperature variations at each location within the chosen area, by day of the week and time of day.
- ■ Documenting **high and low temperature fluctuations** caused by the environmental control systems operating at the time of the study – for example, heating, cooling and ventilation.
- ■ Identifying potential **airflow** issues that may be the cause of temperature variations.
- ■ Recommending where time & temperature can **safely be stored** in the mapped area and where they must not be stored. These recommendations should take account of any temperature deviations identified during the study as well as the approved temperature range(s) for the products being stored in the area.

Objectives

- ■ **Identifying the best places** to locate temperature sensors for routine monitoring in circumstances in which a monitoring system is to be installed. If a monitoring system is already installed, identify the best places to relocate temperature sensors (if necessary).
- ■ **Making recommendations for any remedial actions** needed to overcome the problems identified in the study.

Methodology

- **Step 1** – select Data Loggers; error of no more than ± 0.5 °C at each calibration point
- **Step 2** – designate the mapping team
- **Step 3** – survey the site
 - length, width and height;
- ■ **drawing of each area**, showing elements, such as shelving or pallet racking, that may have an effect on the even heating or cooling of the space and which may affect its temperature stability. The shelving or pallet racking will be used to place the EDLMs, so it is important to record these components accurately;
- ■ **the location of heating and cooling components**, including air distribution outlets and/or ceiling fans;
- ■ **the location of existing temperature** recording sensors and temperature controlling sensors.

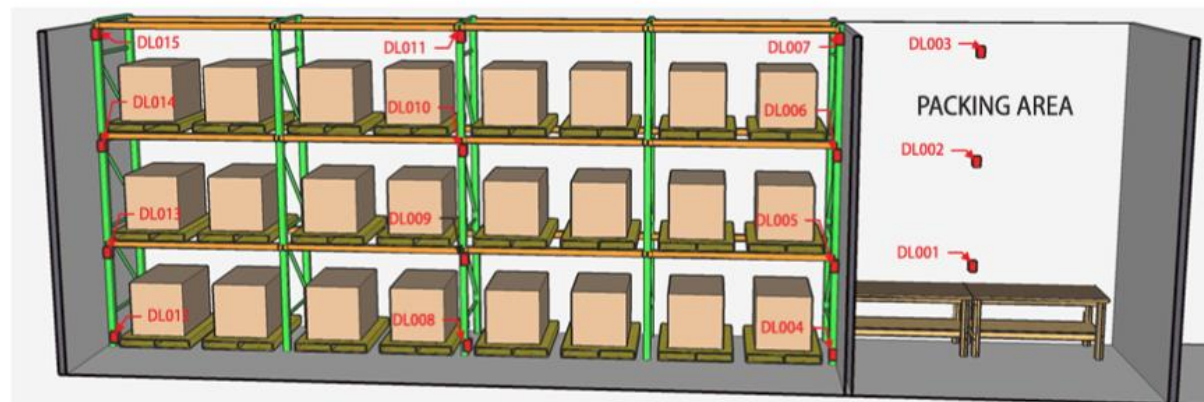
Methodology

- **Step 4** – establish acceptance criteria:
- The protocol should define the required acceptance criteria, based on the type of TTSPPs being stored (+ 2.0 °C to + 8.0 °C or + 15.0 °C to + 25.0 °C)
- temperature-mapping study is designed to include door opening 30 minutes

Methodology

- **Step 5** – determine data loggers locations
- **Length** and **width** (every 5–10 metres)
- **Height** (3.6 metres or less normal height of warehouses) one level at 1.2 metres and second level at 3.0 metres.
- (4-6 metres in height, EDLMs can be positioned at heights of 0.3 metres, 1.8 metres, 3.6 metres and 5.4 metres)

Typical location of data loggers in a pallet racking storage area



9 sensors were distributed
Inside Volume < 2000 L

- inside Volume < 2000 L
15 sensors were distributed



Methodology

- **Step 6** – record data loggers, monitoring sensors and thermostat locations
- **Step 7** – label and program the data loggers
- **Step 8** – fix data loggers in position
- **Step 9** – conduct the mapping exercise
- **Step 10** – download and consolidate the data

Mapping report template

- The mapping report should include the following sections:
- **a. Introduction:** a description of the objectives of the mapping study.
- **b. Summary:** a summary and discussion of the results organized in the sequence set out in the mapping protocol, including a summary of deviations (if any).
- **c. Conclusions and recommendations:** a general conclusion for all verifications and observations indicating the acceptability of the equipment for operation. Recommendations and remarks can be incorporated in this section.

Conducting the mapping exercise

- * Conduct the mapping exercise
 - Ensure that all relevant personnel in the store are fully briefed
 - At the end of the study period, collect all the devices, deactivate them, and download the data for analysis.
 - Power outages should similarly be recorded.

Analysing the data and preparing the mapping report

- Minimum and maximum temperatures and hot and cold spots
- Mean temperatures
- Interpreting the results and making recommendations

Analysing the data and preparing the mapping report

- **Determination of temporal instability**

- The temporal instability for air temperature and air humidity is determined from the registration of the temporal variation of temperature or relative humidity, respectively, over a period of time of at least 30 min after steady-state conditions have been reached

$$\text{Satability} = \text{Max. T} - \text{Min T}$$

at 30 minutes after stability

at all points in the closed volume

Analysing the data and preparing the mapping report

- **Determination of temporal inhomogeneity**
- Homogeneity= $\text{Max. } T - \text{Min } T$
- at all corners
- **Determination of temporal fluctuation**
- Fluctuation= $\text{Max. } T - \text{Min } T$
- at specified points

Uncertainty budget:

Source of Uncertainty	Value	Divisor	Sensitivity Coeff	Standard Uncertainty
Combined Uncertainty of standards		1	1	=(Value*Sensitivity Coeff)/Divisor
Drift of standards		$\sqrt{3}$	1	
Resolution of UUT		$\sqrt{3}$	1	
homogeneity		$\sqrt{3}$	1	
stability		$\sqrt{3}$	1	
Repeatability		1	1	
Combined uncertainty				
Expanded uncertainty				

Implementing the mapping report recommendations

- A drawing or diagram showing where time- and temperature-sensitive pharmaceutical product (TTSPPs) can safely be stored in the space that has been mapped: It is possible that there may be some zoning involved. For example, products that are not affected by freezing could be allocated to parts of a cold room where the mapping study has shown some freezing risk.

Implementing the mapping report recommendations

- ■ **Allocation** of pallet bays to specific categories of TTSP on the warehouse management system in order to control where stocks are positioned.
- ■ **Repositioning** of temperature monitoring sensors and/or environmental control sensors.
- ■ **Adjustment of air outlets** to reduce temperature stratification and/ or minimize cold and hot spots.
- ■ **Upgrading of mechanical systems** to improve temperature control and performance.
- ■ A **decision** to use the space for other purposes because it is unsuitable for storage of TTSPs.

QUESTIONS?



Thank you