



Temperature Mapping Study on Cold Room

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ABSTRACT

The purpose of the study was to carry out temperature mapping of a cold room. The study was aimed to determine the temperature distribution and the acceptance criteria throughout the cold room. The study was carried out using Kaye RF Val Probe temperature/humidity data loggers. A total of eighteen data loggers were used, which were kept at specific locations in the room throughout the study period. Based on the acceptance criteria of the study protocol, the temperature was to be maintained between 2°C to 8°C. Cold storage is a relatively simple cold room that is commonly used to store material between 2°C to 8°C. Such cold rooms are now available commercially as walk-in chambers and are used for the storage of critical pharmaceutical products, samples, and raw materials where excursions in temperature conditions may affect the quality of stored material(s) in terms of their appearance (color), consistency, potency, and impurity levels. Some of the parameters studied, External temperature conditions, Door opening time during handling of material in and /or out of the Cold Room, Power breakdown, Air flow velocity through fans (not less than 2400 CFM (cubic feet per minute), Too much material stored in the room (thermal load). Hence it is essential to qualify cold storage chambers under the worst-case scenarios.

Keywords: Temperature mapping, Cold room, Data loggers.

INTRODUCTION

Temperature mapping

Temperature mapping study and temperature qualification study are carried out generally in pharmaceutical industry. There are different kind of medicines and vaccines which need to be stored and transported at certain temperatures. Majority of these medicines and vaccines are under two categories viz. those to be stored between 2 to 8 °C and those to be stored between 15 to 25°C. It is important for the efficacy of the medicine that the same be stored and transported at the recommended temperature limits as above. If the medicine or vaccine goes above these temperature limits, the medicinal properties will be gradually lost and most importantly the products will not show any indication that it has been compromised. In such case the ultimate distributor and user will be unaware of the efficacy of the medicine. The storage is done in warehouses, cold rooms or refrigerators and transportation is carried out in boxes, vans, reefers and containers.¹

The temperature mapping is accomplished by using temperature indicating probes coupled with a data logger for data accusation. Questions may be asked regarding the number of probes to be utilized and their placement in the cold room for temperature mapping in the empty room and the loaded room. The basic consideration should be that the probes are distributed uniformly in the room and should cover all the vertical planes.

MATERIALS AND METHODS

Study parameters

The purpose of mapping the cold room is to establish sufficient data to ensure that the cold room is capable of:

- **Temperature:** Maintaining the desired temperature range throughout the cold room under extremes of external temperature.
- **Cold spot and hot spot:** Identifying potential hot spot(s) or cold spot(s) in the chamber.
- **Time:** Determining the time required for conditions to return to specified parameters (as desired) in case of excursions.
- **Effects:** Determining the effects of electrical or refrigeration source fluctuations or power failure.
- **Design** of the chamber is needed to decide on the number of probes and their locations for temperature monitoring. While designing the mapping study (protocol), understanding the design of the cold room is needed.

Design of the cold room

A cold room or chamber is a room in the shape of a cubical, made with prefabricated Polyurethane Foam (PUF) insulated panels or of brick and mortar with insulation to maintain the desired conditions of temperature and humidity within. Knowing that the seal between any two Panels are integral, and that there are no openings, other than the door, which may disturb the conditions of the chamber.²



Materials

Kaye data loggers

The Kaye RF Val probe system is a wireless thermal validation system that records temperature and humidity data. The Kaye RF Val probe system is designed for accurate, convenient, and reliable process validation of environmental chambers and storage areas. These applications include stability chambers, freezers, refrigerators and warehouses. A 2.4-GHz RF mesh network and multiple-redundant data storage support communications and storage of critical validation data, while safeguards guarantee data integrity, storage and compliance with regulatory requirements. The system consists of Kaye RF Val Probe Loggers, a Kaye RF Val Probe base station, and Windows-based software for programming and reading the loggers, calibrating loggers, verifying their calibration, and generating reports (see Figure 1 below). Data from multiple wireless loggers is combined in a single file from which reports are

generated. These reports are designed for implementation of 21 CFR Part 11 requirements for electronic records. Users can customize the reports by defining process cycles and specifying cycle-based calculations.



Figure 1: Kaye RF Val probe data loggers³

Table 1: Details of logger used and there locations

Sl. No.	Model	Sensor Serial Number	Location of Sensors
1.	Kaye Val probe	B08439	S1
2.	Kaye Val probe	B08461	S2
3.	Kaye Val probe	B08512	S3
4.	Kaye Val probe	B08615	S4
5.	Kaye Val probe	B08616	S5
6.	Kaye Val probe	B08627	S6
7.	Kaye Val probe	B08628	S7
8.	Kaye Val probe	B08631	S8
9.	Kaye Val probe	B08659	S9
10.	Kaye Val probe	B08668	S10
11.	Kaye Val probe	B08670	S11
12.	Kaye Val probe	B08683	S12
13.	Kaye Val probe	B08758	S13
14.	Kaye Val probe	B08767	S14
15.	Kaye Val probe	B08771	S15
16.	Kaye Val probe	B08776	S16
17.	Kaye Val probe	B08795	S17
18.	Kaye Val probe	B08788	S18

Methodology

Parameters that may affect the condition of the cold room

It is desired that the cold room chamber provide controlled temperature conditions. There are several

parameters that may have an impact on the condition of the cold room. These include:

- External temperature conditions
- Door opening time during handling of material in and /or out of the cold room
- Power breakdown

- Air flow velocity through fans (not less than 2400 CFM (cubic feet per minute))
- Too much material stored in the room (thermal load)

Therefore, during the mapping study the above listed parameters should be subjected as simulated worst-case conditions because these parameters may have an impact on the performance of the cold room.

Studies

1. Empty chamber temperature mapping
 - a. Door open and recovery study
 - b. Power failure and recover study
2. Loaded chamber temperature mapping
 - a. Door open and recovery study
 - b. Power failure and recover study
 - c. Come up study

Empty chamber temperature mapping

Door open and recovery study

To verify the room was capable of recover to the acceptable limit after the keeping the door of room for 10 min and find out recovery time.

- Ensure that the room was in empty condition
- Ensure the room was switched ON and in running condition. The temperatures of all sensors were within limit.
- Room door was for a period of 10 min.
- Temperature was logged in the data logger for every 10 seconds, during the door opening study period.
- The door was closed after 10 min.
- The temperature was maintained until all the sensors at various locations achieve the acceptance range.
- The temperature data was analysed and find out the recovery time.
- The details of the study were recorded in report.

Power failure and recovery study

- Power failure tests were carried out to check the duration for which temperature remains within the limits after a power failure. This study was for information only and not for qualification. This particular cold room lasted for 5 hours before temperature reached 8°C. Thereafter temperature recovery test was carried out to understand the duration taken to attain the desired level of 4°C. This test also was carried for information so that customer will aware of the duration in cases of emergency. As the cold room was already loaded with medicine, could not be carried out the tests beyond 8°C, however various other tests were carried out evaluate the entire cold room. The whole tests temperature and humidity mapping lasted for around 36 hours. During the recording of temperature and humidity, all other normal

activities were taking place such as loading, unloading, opening of doors etc. and were recorded for analysis. Temperature mapping study was the major part of the entire process identifying the hot and cold spots of the entire room. The hot and cold spots occur for various reasons and can be eliminated or reduced by various means. Potential reasons for the same will be identified during the process.

Loaded chamber temperature mapping

Door open and recovery study

To verify the room was capable of recovery to the acceptable limit after the keeping the door of room for 10 min and find out recovery time.

- Ensured that the room is in loaded condition
- Ensured the room was switched ON and in running condition. The temperatures of all sensors are within limit.
- The room door was opened for a period of 10 min.
- The temperature in the data logger was logged for every 10 seconds, during the door opening study period.
- The door was closed after 10 min.
- The temperature was monitored until all the sensors at various locations achieve the acceptance range.
- The temperature data was analysed and found out the recovery time.
- The details of the study were recorded in report.

Power failure and recover study

- Ensured that the instrument is ON condition and the temperature display readings are in 2-8°C.
- The sampling interval kept 01 minute in the data logger.
- The power supplies were switched off to the instrument, and Open the Door of the Cold room.
- The details were recorded in the report.
- Temperature mapping was performed till the any one external sensors temperature goes beyond 25°C. Record the time taken by the sensor to reach 25°C.
- The doors were closed and turn ON the power supply of the instrument and ensured that all the sensors temperature reaches its acceptance criteria 2-8°C.
- The Recovery time were documented for each sensor from the time of door closing.

Come up study

- The data loggers were switched ON for recording at an interval of 10 seconds.
- The Cold room was loaded with the necessary materials as per the client requirements. Do not overload the materials.
- The temperature was set of required range and switch on the instrument.



- The temperature was monitored for the required period till all the sensors reach acceptance criteria.
- Once the required temperature is attained, proceed to the next study
- The details of the study were recorded in report.⁴

Justification for probe locations

Probe location should be decided logically, strategically, and scientifically. The following locations cover the entire room. See the (figure 2)

RESULTS AND DISCUSSION

Performance qualification studies

Two separate studies are required to be performed for PQ. One study should be completed for the temperature distribution in an empty room or chamber running continually for 24 h. The second would be a temperature distribution study in a loaded room or chamber. Load the boxes with material that simulates a thermal load, such as starch, lactose, or water in bottles (in case liquid is to be stored in the chamber) record the temperature intermittently for 72 h. each, for three seasons (i.e., peak Summer, Monsoon (as applicable), and winter) to demonstrate that there is no effect of seasonal variations on the temperature controls in the cold room.

Sampling interval

10 Min (For 24 h static condition and 48 h. dynamic condition) 10 seconds (For 10 M power failure study, 90 sec door opening study, 10 minutes door opening study, hold over study)

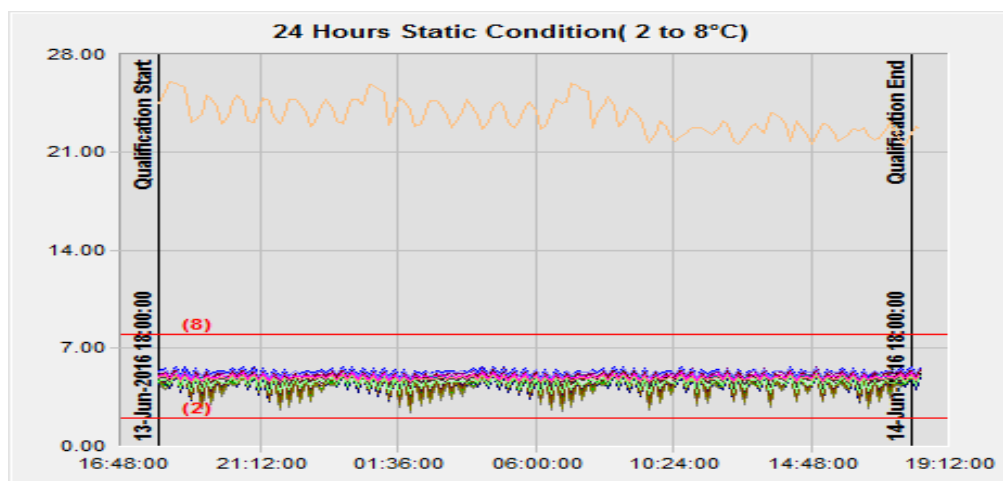


Figure 2: schematic representation of data loggers inside cold room.

Table 2: Data loggers' locations inside cold room⁵

Sl.No.	Temperature Sensors	Location	Justification
1.	S1	Left back corner top	Selected for temperature mapping to study the temperature distribution at left corners of the rack and location is away from air currents.
2.	S2	Left back corner bottom	
3.	S3	Left front corner top	
4.	S4	Left front corner bottom	
5.	S5	Right front corner top	Selected for temperature mapping to study the temperature distribution at right corners of the rack and location is away from air currents.
6.	S6	Right front corner bottom	
7.	S7	Right back corner top	
8.	S8	Right back corner bottom	
9.	S9	Middle of the left wall	selected for temperature mapping as location is Near Corner of the room, away from air currents, near to the material storage area
10.	S10	Middle of the back wall	Selected for temperature mapping to study the temperature distribution at the middle of the rack which is Material storage area
11.	S11	Middle of the right wall	
12.	S12	Near the door-01	Man& material moment area.
13.	S13	Near the door-02	
14.	S14	Middle of the right rack	Selected for temperature mapping to study the temperature distribution at the middle of the rack which is Material storage area
15.	S15	Near controlling probe	Comparison of temperature profile of inbuilt sensor probe with external sensor
16.	S16	Middle of the left rack	Selected for temperature mapping to study the temperature distribution at the middle of the rack which is Material storage area
17.	S17	Centre of the room	Selected for temperature mapping to study the temperature distribution at the middle of the room which is Material storage area
18.	S18	Kept outside the cold room for ambient temperature	Room temperature.

24 Hours static study



Graph 1: A graph of temperature distribution of the cold room 24 h.

Table 3: Study summary 24 Hours static condition.

Senor/logger Sl.	Min	Max	Avg	Max-Min
B08439 (C)	3.31	5.36	4.54	2.05
B08461 (C)	4.93	5.74	5.35	0.81
B08512 (C)	2.70	5.38	4.39	2.68
B08615 (C)	4.14	5.43	4.85	1.29
B08616 (C)	2.44	5.14	4.15	2.70
B08627 (C)	4.48	5.65	5.15	1.17
B08628 (C)	2.99	5.12	4.26	2.13
B08631 (C)	4.78	5.20	4.98	0.42
B08659 (C)	3.23	5.17	4.38	1.94
B08668 (C)	2.63	5.26	4.28	2.63
B08670 (C)	3.03	5.31	4.42	2.28
B08683 (C)	4.10	5.62	5.00	1.52
B08758 (C)	4.21	5.22	4.77	1.01
B08767 (C)	4.68	5.31	5.00	0.63
B08771 (C)	3.76	5.18	4.56	1.42
B08776 (C)	4.59	5.13	4.86	0.54
B08795 (C)	4.85	5.59	5.28	0.74
B08788 (C)	21.56	26.08	23.60	4.52

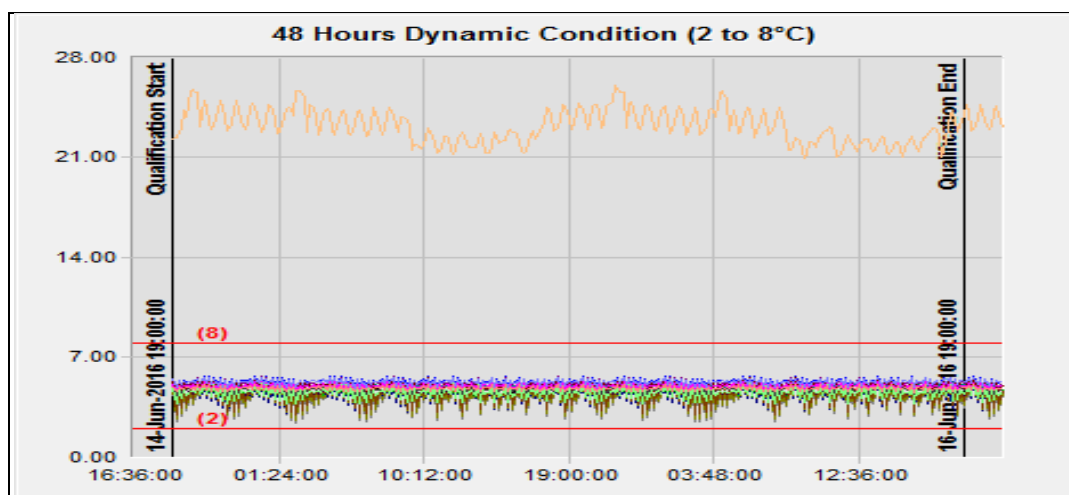
Static Study

Static study was conducted for 24 Hrs. From Table no 3 and graph no 1, shows the study was observed and recorded that minimum and minimum average temperature at location S5 was found 2.44°C and 4.15°C respectively. Similarly maximum and maximum average temperature at location S2 was found 5.74°C and 5.35°C respectively.

Dynamic Study

Dynamic study was conducted for 48 Hrs. From Table no 4 and graph no 2, shows the study was observed and recorded that minimum and minimum average temperature at location S5 was found 2.43°C and 4.15°C respectively. Similarly maximum and maximum average temperature at location S2 was found 5.71°C and 5.32°C respectively.

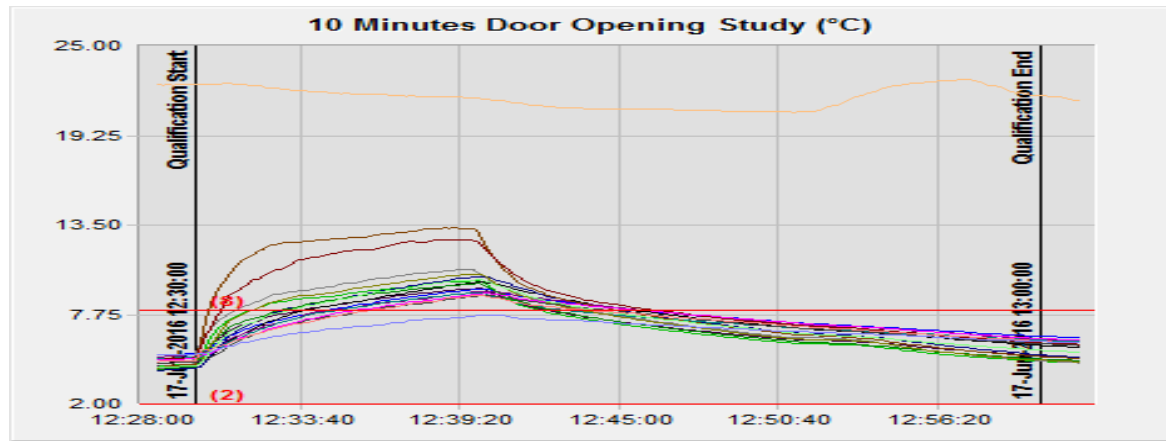


48 Hours Dynamic study**Graph 2:** A graph of temperature distribution of the cold room 48 h.**Table 4:** Study summary 48 hours dynamic condition.

Senor/logger SI.	Min	Max	Avg	Max-Min
B08439 (C)	3.28	5.36	4.54	2.08
B08461 (C)	4.86	5.71	5.32	0.85
B08512 (C)	2.71	5.38	4.38	2.67
B08615 (C)	4.04	5.41	4.83	1.37
B08616 (C)	2.43	5.15	4.15	2.72
B08627 (C)	4.49	5.67	5.18	1.18
B08628 (C)	2.94	5.11	4.26	2.17
B08631 (C)	4.81	5.21	5.00	0.40
B08659 (C)	3.19	5.16	4.37	1.97
B08668 (C)	2.63	5.26	4.28	2.63
B08670 (C)	3.01	5.32	4.42	2.31
B08683 (C)	4.04	5.61	4.98	1.57
B08758 (C)	4.15	5.24	4.77	1.09
B08767 (C)	4.67	5.32	5.00	0.65
B08771 (C)	3.74	5.17	4.55	1.43
B08776 (C)	4.58	5.11	4.85	0.53
B08795 (C)	4.87	5.60	5.28	0.73
B08788 (C)	20.95	26.03	23.20	5.08

Worst case study

10 minutes Door open study



Graph 3: A graph of temperature distribution of the 10 min door opening study.

Table 5: Study summary 10 min door open study.

Senor/logger Sl.	Min	Max	Avg	Max-Min
B08439 (C)	4.59	9.43	7.10	4.84
B08461 (C)	5.23	9.40	7.66	4.17
B08512 (C)	4.59	9.92	7.16	5.33
B08615 (C)	4.74	9.86	7.57	5.12
B08616 (C)	4.79	10.66	7.62	5.87
B08627 (C)	5.16	9.24	7.57	4.08
B08628 (C)	4.32	10.19	7.52	5.87
B08631 (C)	5.00	9.17	7.35	4.17
B08659 (C)	4.40	9.74	7.13	5.34
B08668 (C)	4.49	10.35	7.44	5.86
B08670 (C)	4.56	13.31	8.77	8.75
B08683 (C)	5.06	12.56	8.77	7.50
B08758 (C)	4.70	8.97	7.28	4.27
B08767 (C)	4.92	9.12	7.49	4.20
B08771 (C)	4.48	9.98	7.47	5.50
B08776 (C)	4.78	8.97	7.32	4.19
B08795 (C)	5.20	7.75	6.77	2.55
B08788 (C)	20.74	22.89	21.67	2.15

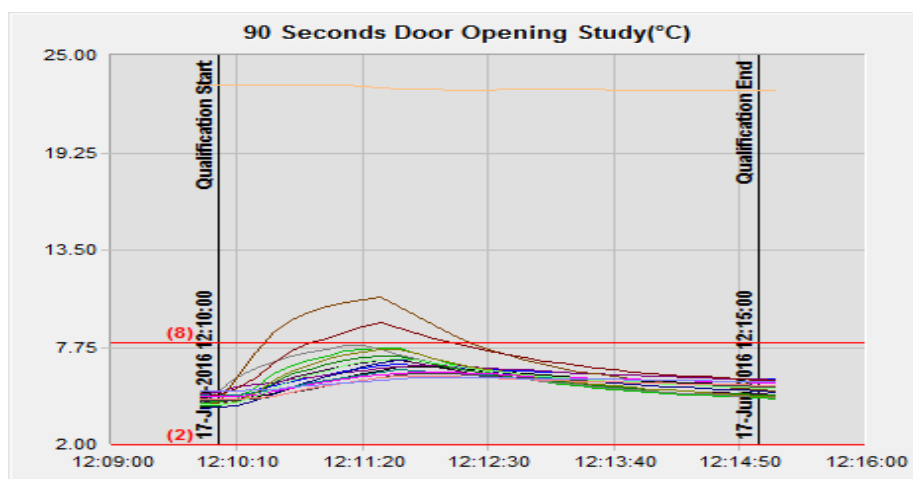
Door Opening Study for 10 Min

Door opening study was conducted for 10 min. From Table no 5 and graph no 3, shows the study was observed and recorded that minimum and minimum Average

temperature at location S7 was found 4.32°C and S17 6.77°C respectively. Similarly maximum and maximum average temperature at location S11 was found 13.31°C and S12 8.77°C respectively. Recovery time was observed 06 min 30 Sec.



90 seconds Door open study



Graph 4: A graph of temperature distribution of the 90 seconds door opening study.

Table 6: Study summary 90 seconds door opening study.

Senor/logger SI.	Min	Max	Avg	Max-Min
B08439 (C)	4.51	7.01	5.77	2.50
B08461 (C)	5.17	6.73	6.12	1.56
B08512 (C)	4.50	7.71	5.98	3.21
B08615 (C)	4.65	6.62	5.84	1.97
B08616 (C)	4.83	7.86	6.14	3.03
B08627 (C)	5.06	6.70	6.15	1.64
B08628 (C)	4.21	6.97	5.80	2.76
B08631 (C)	4.95	6.41	5.84	1.46
B08659 (C)	4.31	7.26	5.86	2.95
B08668 (C)	4.37	7.64	6.00	3.27
B08670 (C)	4.43	10.76	7.46	6.33
B08683 (C)	4.92	9.21	7.06	4.29
B08758 (C)	4.60	6.23	5.63	1.63
B08767 (C)	4.82	6.27	5.80	1.45
B08771 (C)	4.38	7.10	5.95	2.72
B08776 (C)	4.69	6.07	5.60	1.38
B08795 (C)	5.17	5.98	5.73	0.81
B08788 (C)	22.90	23.27	23.06	0.37

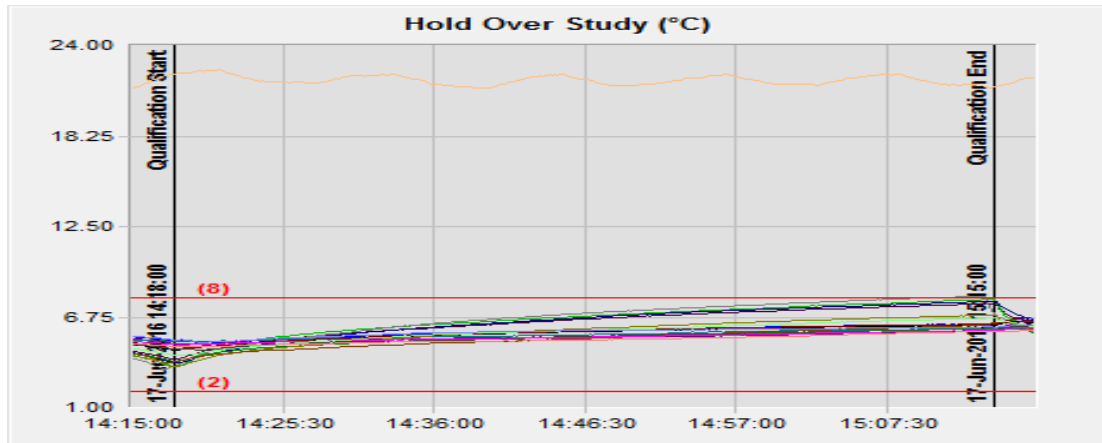
Door Opening Study for 90 sec

Door opening study was conducted for 90 sec. From Table no 6 and graph no 4, shows the study was observed and recorded that minimum and minimum Average

temperature at location S7 was found 4.21°C and S16 5.60°C respectively. Similarly maximum and maximum average temperature at location S11 was found 10.76°C and 7.46°C respectively. Recovery Time was observed 01 Min.



Hold over study



Graph 5: A graph of temperature distribution of the hold over study.

Table 7: Study summary Hold over study.

Senor/logger SI	Min	Max	Avg	Max-Min
B08439 (C)	4.05	7.60	6.44	3.55
B08461 (C)	5.08	6.30	5.84	1.22
B08512 (C)	3.64	7.89	6.61	4.25
B08615 (C)	4.66	6.25	5.74	1.59
B08616 (C)	3.64	8.07	6.72	4.43
B08627 (C)	5.00	5.89	5.50	0.89
B08628 (C)	3.85	7.75	6.48	3.90
B08631 (C)	5.20	5.98	5.64	0.78
B08659 (C)	3.93	6.06	5.41	2.13
B08668 (C)	3.58	6.88	5.84	3.30
B08670 (C)	3.90	6.40	5.37	2.50
B08683 (C)	4.69	6.30	5.77	1.61
B08758 (C)	4.67	5.90	5.45	1.23
B08767 (C)	4.98	5.92	5.48	0.94
B08771 (C)	4.35	6.70	5.82	2.35
B08776 (C)	4.85	5.85	5.34	1.00
B08795 (C)	5.14	6.12	5.80	0.98
B08788 (C)	21.29	22.46	21.81	1.17

Hold over study

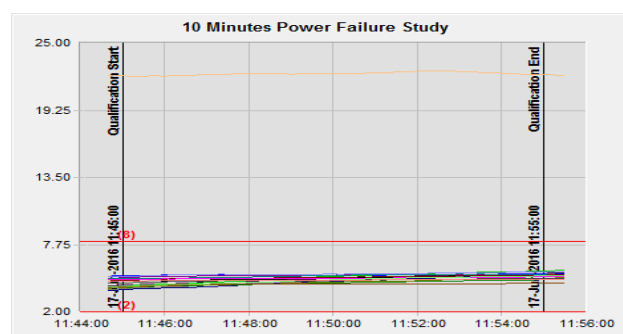
Hold over study was conducted. From Table no7 and graph no 5, shows the study was observed and recorded that minimum and minimum Average temperature at location S10 was found 3.58°C and S16 5.34°C respectively. Similarly maximum and maximum average temperature at location S5 was found 8.01°C and 6.72°C respectively. The hold over time was observed to be 53 min and 50 sec.

Power Failure Study

Power failure study was conducted for 10min. From Table no8 and graph no 6, shows the study was observed and recorded that minimum and minimum Average temperature at location S7 was found 3.90°C and S11 4.35°C respectively. Similarly maximum and maximum average temperature at location S3 was found 5.50°C and

S17 5.23°C respectively. Temperature excursions were not observed beyond acceptance criteria during the study.

10 minutes power failure study



Graph 6: A graph of temperature distribution of the 10 min power failure study.



Table 8: Study summary 10 min power failure study

Senor/logger SI	Min	Max	Avg	Max-Min
B08439 (C)	4.27	5.29	4.83	1.02
B08461 (C)	5.06	5.26	5.15	0.20
B08512 (C)	4.21	5.50	4.95	1.29
B08615 (C)	4.46	5.13	4.87	0.67
B08616 (C)	3.97	5.21	4.64	1.24
B08627 (C)	4.91	5.21	5.12	0.30
B08628 (C)	3.90	5.17	4.57	1.27
B08631 (C)	4.85	5.22	5.07	0.37
B08659 (C)	4.08	4.74	4.46	0.66
B08668 (C)	4.10	4.86	4.52	0.76
B08670 (C)	4.16	4.45	4.35	0.29
B08683 (C)	4.69	5.13	4.96	0.44
B08758 (C)	4.48	4.86	4.70	0.38
B08767 (C)	4.80	4.99	4.87	0.19
B08771 (C)	4.20	5.06	4.70	0.86
B08776 (C)	4.63	4.81	4.72	0.18
B08795 (C)	5.04	5.41	5.23	0.37
B08788 (C)	22.17	22.62	22.38	0.45

CONCLUSION

Temperature and relative humidity mapping are the essential studies to be carried out in pharmaceutical industries for the maintenance of drug stability and safety during storage and transport until when the product reaches the customer. This study was carried out to map temperature and relative humidity of a cold room for a period of 72 h. The results were found to be good and within the acceptance criteria.

CFR: Code of Federal Regulations

GDP: Good Distribution Practice

PQ: Performance Qualification

PUF: Polyurethane Foam

SOP: Standard Operating Procedure

USP: United States Pharmacopeia

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