Research Article

Temperature Mapping Study of Walk-in incubator in a Pharma Industry

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ABSTRACT

The purpose of this study was to carry out temperature and relative humidity mapping of a walk-in incubator. The study was aimed to determine the temperature and relative humidity distribution were uniform and maintained within the acceptance criteria throughout the walk-in incubator. The temperature and relative humidity were maintained and controlled by a HVAC system. The study was carried out using fourtech temperature/humidity data loggers. A total of seventeen data loggers were used, which were kept at specific locations in the walk-in incubator throughout the study. Based on acceptance criteria of the study protocol the temperature was to be maintained between 23 ˚C to 27 ˚C and relative humidity not more than 65 % RH. The some of the parameters was carried in the study as fallows, loaded chamber heat distribution study, empty chamber heat distribution study, door open recovery study, power failure recovery study.

Keywords: Temperature mapping, relative humidity mapping.

INTRODUCTION

Temperature mapping

Temperature mapping study is the process of analysing the uniform distribution of temperature and humidity across the controlled area under various practical conditions. The study was carried out to check and that the entire area inside a thermally insulated chamber is at the specified temperature at all times. This was carried out mainly for the storage facilities such as cold rooms, ware house, refrigerator, and vans for storage and transportation of medicines, vaccines, foods etc [1].

Temperature qualification

Temperature qualification was bit elaborate process which also involves mapping study as one part of the process. These series of tests also needs to be done for any sensitive areas such as ware houses, refrigerators, freezers, medicine rooms, vehicles, reefers, boxes, containers etc. especially for the storage and transportation of medicines/food. The process of temperature qualification involves complete identification of entire equipment involved inside the enclosed area such as chillers, sensors, evaporators, cooling units, dehumidifiers etc. and study of the complete system under various conditions. Understand regulatory requirements and comprehend architectural constraints. Before begin to build the qualification plan, ensure to understand the following requirements and constraints.

Calibration

The calibration of temperature control devices and temperature monitoring devices should be evaluated. Calibration must be within a year's validity, traceable to a national / international standard and the devices must be calibrated to three points based on the temperature range required for product storage.

Environmental range and set point

The environmental range was specified in accordance with the range of the temperature-sensitive product stored in the storage area, as specified in the product specification. This may vary between products and the most critical range should be specified in this case. The set point can be a fixed value or a variable value based on different seasons, external climate conditions, and time. Considerations must be made during planning towards using a variable set point value, with additional or extended mapping periods being the most common approaches.

Develop the mapping strategy

Develop the mapping strategy detailing the following but not limited to,

- Number of sensors to be used
- Type of loggers to be used
- Sensor locations and distribution
- Set point value, data to be generated, and reporting requirements

Establish a periodic environmental mapping program to ensure continuous compliance. The program should also outline additional mapping requirements such as when

changes affect the airflow pattern. When determining the sensor locations, it is important to document a rationale for choosing the locations, as well as create a diagram that provides a visual map of the locations. It is essential that every sensor be accurately identified by a unique ID number and a defined location. With regards to determining the number of sensors appropriate for your temperature mapping effort, there is no set formula. Guidelines suggest placing sensors uniformly throughout all three dimensions of the storage area. The number of sensors used must be enough to provide an accurate assessment of the temperature distribution in the area.

MATERIALS AND METHODOLOGY

Material

Walk in incubator was designed for application of growth & storage of bacterial cultures, gentle incubation & conditioning and Media Preparation.

The incubator is having the following features:

- Double walled with insulated modular panels
- Stainless steel SS 304 interior and exterior
- Stainless steel trays
- Observation window
- Heating and cooling system (Heater and Compressor, Condenser)
- Control Panel
- In built Temperature sensors (RTD Pt 100)
- Temperature Cut off thermostats
- Audio Visual Alarms for deviations

The incubator is supported with the life cycle management procedures like Calibration, Cleaning, Annual Maintenance Plan, Alarm challenge test and requalification

Dimension

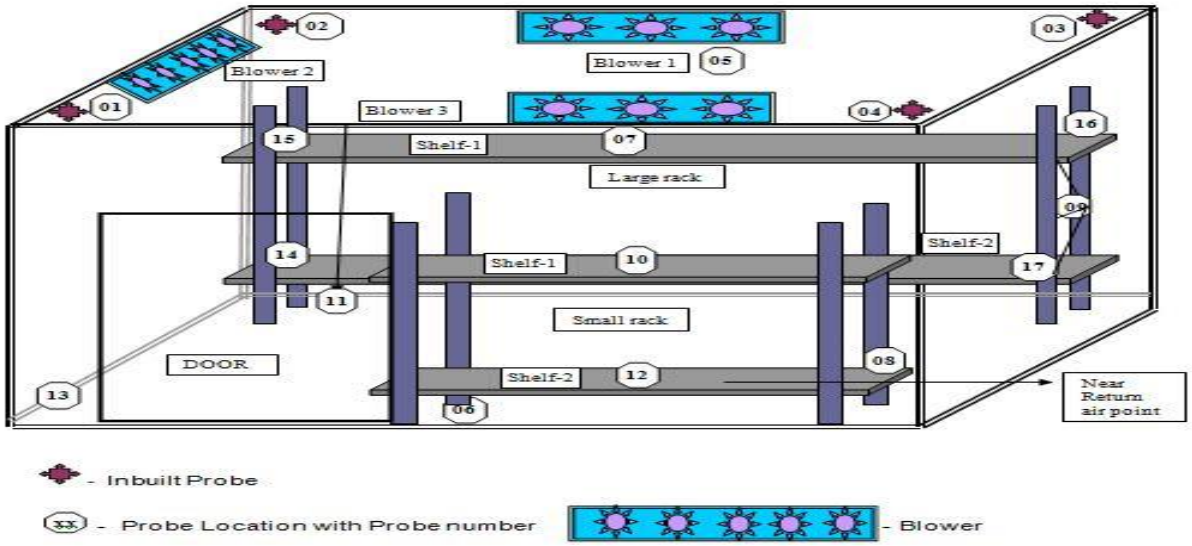

Figure 1: Schematic representation of data logger's location inside walk-in incubator

Number of sensor to be used

Table 1: Data logger location inside Walk-in incubator

Location No	Probe Location	Location Justification
1	Near the inbuilt sensor Top left corner of the room	Comparison of temperature profile of inbuilt sensor probe with external sensor
2	Near the inbuilt sensor Top left corner opposite entry	
3	Near the inbuilt sensor Top right corner opposite entry	
4	Near the inbuilt sensor Top right corner of the room	
5	Behind blower Near the air discharge	To study the impact of air discharge

6	Bottom back corner of the shelf-2 of small rack (door opening side)	Selected for temperature mapping to study the temperature distribution at corners of the rack and location is away from air currents & near to the door opening.
7	Behind Blower 3 Near the air discharge	To study the impact of air discharge
8	Bottom Front corner of shelf-2 of the small rack	Selected for temperature mapping to study the temperature distribution at corners of the rack & as location is near to the path of man & material moment.
9	Middle Between the of the large rack shelf-1 & shelf-2 away from door	selected for temperature mapping as location is Near Corner of the room, away from air currents, near to the material storage area
10	Middle of Shelf-1 of small rack	Selected for temperature mapping to study the temperature distribution at the middle of the rack which is Material storage area
11	Near to the door opening in hanging condition	Man & material moment area, near to the door opening
12	Middle of Shelf-2 of small rack	Selected for temperature mapping to study the temperature distribution at the middle of the rack which is Material storage area
13	Left side of the door	For evaluating temperature at the door (to study the effect of door opening)
14	Bottom back corner of the shelf-2 large rack (opposite to the door opening)	Selected for temperature mapping to study the temperature at the corners of the rack which is away from air currents
15	Front corner of the shelf-1 large rack(opposite to door opening)	selected for temperature mapping as location is at the Top of the rack, front corner & Exactly opposite to door opening, material storage area
16	Top Back corner of shelf-1 the large rack (away from the door)	Selected for temperature mapping to study the temperature at the corners of the rack which is away from air currents & near to material moment area
17	Bottom Front corner of the shelf-2 of large rack(away from door opening)	Selected for temperature mapping to study the temperature at the corners of the rack which is material storage area, near to the man & material moment

Select a type of EDLMs (Electronic Data Logging Monitor) to be used. Choose a device that has sufficient memory for the intended duration of the study. All data loggers must have an error of no more than ± 0.3 °C and ± 5 % RH at each calibration point. Valid calibration certificates for each of the data loggers used in the study must be included in the mapping report.[2] The Fourtec temperature/humidity data loggers which were used in the mapping study of the walk in incubator was shown in Figure 2. A total of 17 data loggers were used.

Execution team members

Identify a designated mapping team and list the team members. Record their signatures and initials so that signed records can be traced back to the person who prepared the document. Ensure that all team members receive the training needed to perform their assigned tasks.

Figure 2: Fourtec temperature/humidity data loggers

Temperature data loggers used

Table 2: Temperature data loggers used

SL. No	Model	Serial number of the data logger
1	LITE5032P-RH	9223935
2	LITE5032P-RH	9223965
3	LITE5032P-RH	9223976
4	LITE5032P-RH	9223981
5	LITE5032P-RH	9223983
6	LITE5032P-RH	9223991
7	LITE5032P-RH	9223996
8	LITE5032P-RH	9223997
9	LITE5032P-RH	9224001
10	LITE5032P-RH	9224002
11	LITE5032P-RH	9224003
12	LITE5032P-RH	9224004
13	LITE5032P-RH	9224017
14	LITE5032P-RH	9224019
15	LITE5032P-RH	9224028
16	LITE5032P-RH	9224030
17	LITE5032P-RH	9224036

Methods to map the walk in incubator

Empty chamber temperature mapping study was to analyse the uniform distribution mapping of loaded walk-in incubator. Power failure test was performed to determine the duration for which the temperature will be maintained if power fails. Temperature recovery test was performed to determine the time taken to reach the specified time limits after a power failure. Door opening test was performed to determine the duration for which a door can be kept opened without affecting the inside temperature.

Temperature Sensor Calibration Study

Methodology

Temperature sensors and data logger used for qualification studies shall be calibrated prior to the temperature mapping activity to ensure that the temperature measurement system is accurate and precise. Calibration temperature sensor shall cover the entire range of temperature set point, including operating temperatures which is subjected for the qualification of the equipment. The calibration reports were compliance with respect to the acceptance criteria and traceability of calibration standards.

Acceptance Criteria

The temperature sensors used for the study should be accurate to within ± 0.5°C up to 200°C and ± 1.0°C above 200°C.

Empty & Loaded chamber distribution studies

Methodology

Multi-channel Data logger(s) with RTD or T-type temperature sensors or wireless temperature loggers as applicable were used. One successful temperature distribution study was not less than 72 hours each for empty chamber and loaded chamber with login interval of NMT 5 minutes shall be performed during initial performance qualification[3]. During periodic re-qualification one distribution study of not less than 72 hours with loaded chamber was performed to confirm uniform temperature distribution in the chamber. Number of sensors for mapping was finalized based on the size of the chamber occupied by product.

Fix the sensors at the identified locations as per protocol. While placing the sensors, ensure that the sensor tip is not touching the walls of the chamber. Set the required temperature as applicable as per standard operating procedure of the equipment.

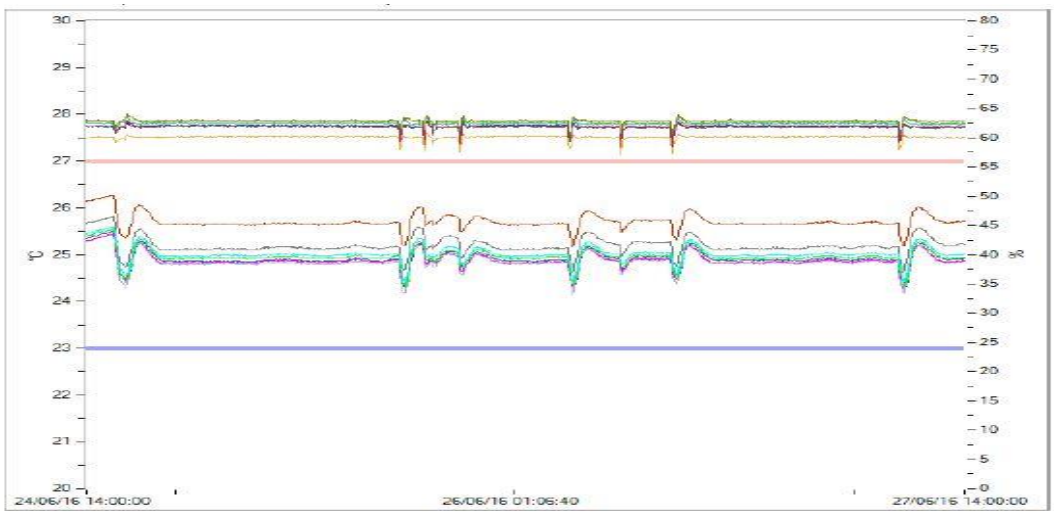

Figure 3: Loaded chamber distribution studies graph

Loaded chamber distribution studies

Table 3: Loaded chamber distribution studies result

Location ID of data logger	Temperature in °C			Relative humidity in % RH		
	Minimum	Maximum	Average	Minimum	Maximum	Average
T1	24.27	25.50	24.91	58.88	63.93	62.64
T2	25.16	**26.27**	**25.70**	**56.96**	60.83	**60.09**
T3	24.15	25.45	24.86	59.18	63.60	62.40
T4	24.31	25.45	24.89	58.48	62.72	61.88
T5	24.33	25.54	24.96	59.42	64.09	62.87
T6	24.63	25.81	25.19	58.50	62.92	61.98
T7	24.43	25.59	25.02	58.38	62.86	61.81
T8	23.95	25.52	24.85	59.88	**64.70**	62.66
T9	24.09	25.29	24.69	58.81	63.45	62.36
T10	24.27	25.48	24.89	59.29	63.84	62.67
T11	24.14	25.32	24.74	59.49	64.18	**63.02**
T12	24.37	25.55	24.97	58.99	63.34	62.34
T13	24.29	25.49	24.89	59.11	63.62	62.58
T14	24.17	25.34	24.76	58.41	62.72	61.77
T15	24.12	25.45	24.86	59.48	63.86	62.56
T16	**23.58**	25.19	**24.55**	60.30	63.92	62.34
T17	24.26	25.34	24.79	57.92	62.18	61.40

Loaded chamber heat distribution study was conducted for 72 Hrs. From Table 3 the study was observed and recorded that minimum and minimum average temperature at location T16 was found 23.58 ˚C and 24.55 ˚C respectively. Similarly maximum and maximum average temperature at location T2 was found 26.27 ˚C and 25.70 ˚C. Similarly minimum and minimum average relative humidity at location T2 was found 56.96 % and 60.09 % respectively. Similarly maximum and maximum average relative humidity at location T8 was found 64.70 % and 63.02 % respectively.

Empty chamber distribution studies

Table 4: Empty chamber distribution studies result

Location ID of data logger	Temperature in °C			Relative humidity in % RH		
	Minimum	Maximum	Average	Minimum	Maximum	Average
T1	24.27	25.50	24.91	58.88	63.93	62.64
T2	24.29	25.49	24.89	59.11	63.62	62.58
T3	24.15	25.45	24.86	59.18	63.60	62.40
T4	24.31	25.45	24.89	58.48	62.72	61.88
T5	24.33	25.54	24.96	**55.96**	60.83	**60.09**
T6	25.16	**26.37**	**25.70**	58.50	62.92	61.98
T7	24.43	25.59	25.02	58.38	62.86	61.81
T8	23.95	25.52	24.85	58.88	63.93	62.64
T9	24.09	25.29	24.69	59.88	**64.84**	62.56
T10	24.27	25.48	24.89	59.29	63.84	62.67
T11	24.14	25.32	24.74	59.42	64.09	62.87
T12	24.37	25.55	24.97	58.99	63.34	62.34
T13	**23.78**	25.19	**24.55**	59.11	63.62	62.58
T14	24.17	25.34	24.76	58.41	62.72	61.77
T15	24.12	25.45	24.86	59.49	64.18	**63.02**
T16	24.43	25.59	25.02	60.30	63.92	62.34
T17	24.26	25.34	24.79	57.92	62.18	61.40

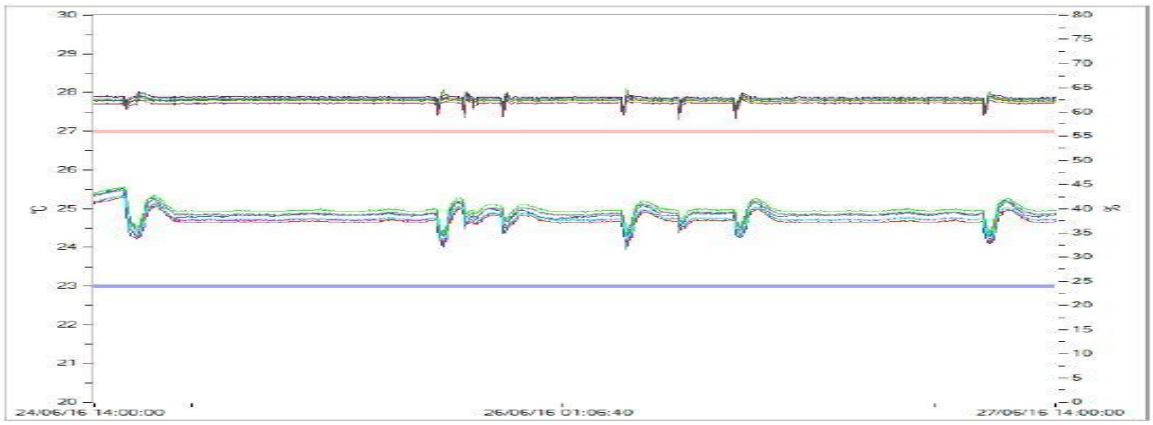

Figure 4: Empty chamber distribution studies graph

Empty chamber heat distribution study was conducted for 72 Hrs. From Table 4 the study was observed and recorded that minimum and minimum average temperature at location T13 was found 23.78 ˚C and 24.55 ˚C respectively. Similarly maximum and maximum average temperature at location T6 was found 26.37 ˚C and 25.70 ˚C. Similarly minimum and minimum average relative humidity at location T5 was found 55.96 % and 60.09 % respectively. Similarly maximum and maximum average relative humidity at location T9 was found 64.84 % and T15 63.02 % respectively.

Calculate the mean maximum temperature for each sensor

- Cold spot location and hot spot location shall be identified based on the minimum temperature, maximum temperature and mean of the temperature and calculate the mean maximum temperature. The data for mean maximum temperature calculation ware considered from the time when all the external probes reach the required set temperature.
- Data during the come up time were used for mean maximum temperature calculation. Evaluate and identify the hot spot based on the criteria given below. The location for which the mean maximum temperature was found to be highest.
- In the event of the mean maximum temperature calculated is found same for two or more different locations, then out them, the location at which the maximum temperature observed during mapping shall be considered for hot spot.
- Based on the evaluation of empty & loaded results hot spot & cold spot shall be recommended. If hot spot evaluated is not near the controlling /monitoring sensor of the chamber, the controlling / monitoring sensor shall be realigned / relocated to near the hot spot identified. In case if the alignment of the inbuilt probe to hot spot location is not possible, additional probe or data logger shall be placed for routine monitoring of the identified hot spot location and details shall be recorded in the qualification.

Acceptance Criteria:

The temperature observed for each probe throughout the 72 hours should be 25.5°C ± 2.5°C.

Door open recovery study

Methodology

The temperature recovery study (after door opening and closing) was performed during empty and loaded chamber condition. For this study, the same number of sensors and locations which are considered during empty and loaded chamber distribution study was considered including one sensor near to the controlling probe of the equipment. While placing the distribution sensors, ensure that the sensors tip shall not touch the wall of the chamber or the load. Note the respective sensor number on the sensor location diagram. Set the required temperature as applicable as per respective standard operating procedure of the equipment or approved protocol.

Procedure to be followed

While using wireless data loggers or other sensor for which the data cannot be monitored from outside of chamber then follow procedure. Set the required temperature as applicable as per respective standard operating procedure of the equipment and ensure the data logger date and time are matching with equipment set date and time. Set the data logging interval of not more than 30 seconds in data logger and start the study.

Wait approximately for 30 minutes for temperature stabilization or consider the stabilization time as per the information obtained during loaded chamber come up time. After stabilization note the time and then open the door for about 20 minutes.(20 minutes is considered as worst case scenario, since any of the storage equipment door will not be kept open for this much time period).After completion of 20 minutes, note the time of

the chamber at that moment and close the door and wait for about 30 minutes to one hour to ensure all the sensors achieved chamber condition. After completion of the study take out the temperature profile and evaluate & conclude the maximum time allowed for door open conditions, attach all report to qualification protocol.

Table 5: Door open recovery study

Location ID of data logger	Temperature in °C			Relative humidity in % RH		
	Minimum	Maximum	Average	Minimum	Maximum	Average
T1	24.13	29.28	26.75	59.88	65.93	**62.89**
T2	23.80	28.85	26.45	60.96	67.83	62.90
T3	24.63	**29.91**	**27.37**	60.28	67.60	64.95
T4	23.71	29.29	26.52	59.84	68.72	63.94
T5	24.49	28.94	26.75	60.46	69.09	64.86
T6	24.25	27.64	25.95	**59.58**	70.92	64.79
T7	24.55	27.79	26.47	61.45	**71.86**	65.56
T8	24.49	28.39	26.44	60.45	69.70	**66.75**
T9	**23.60**	28.70	26.65	59.85	66.45	65.95
T10	24.44	27.53	25.85	60.25	67.84	63.55
T11	24.27	28.14	26.58	61.85	68.18	64.65
T12	23.96	27.11	**25.65**	62.99	68.34	65.50
T13	24.78	29.09	26.95	60.11	66.62	65.65
T14	24.26	28.60	26.43	62.96	67.72	63.56
T15	24.32	27.55	25.95	60.48	67.86	65.34
T16	24.32	28.84	26.58	60.35	69.92	64.89
T17	24.11	28.68	26.95	59.95	68.18	65.56

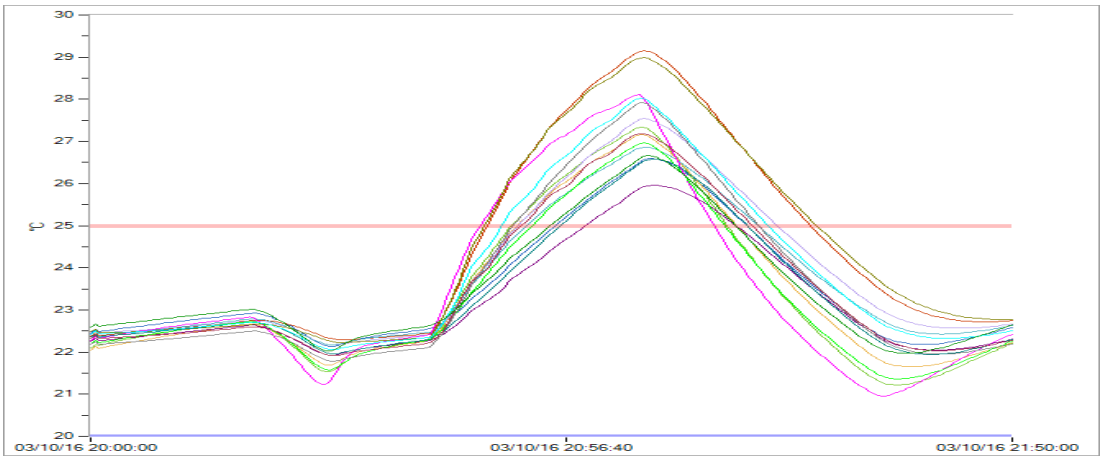

Figure 5: Door open recovery study

Door open recovery heat distribution study was conducted for 30 minutes. From Table 5 the study was observed and recorded that minimum and minimum average temperature at location T9 was found 23.60 ˚C and T12 25.65 ˚C respectively. Similarly maximum and maximum average temperature at location T3 was found 29.91 ˚C and 27.37 ˚C. Similarly minimum and minimum average relative humidity at location T6 was found 59.58 % and T1 62.89 % respectively. Similarly maximum and maximum average relative humidity at location T7 was found 71.86 % and T8 66.75 % respectively.

Power failure recovery study

Methodology

The power failure recovery study was performed with empty and loaded chamber with respective load photographs were attached to the qualification report. For this study, the same number of sensors which are considered during empty and loaded condition

distribution study was used (including one sensor near to the controlling probe of the equipment).While placing the sensors, ensure that the sensors tip were not touch the wall of the chamber or the load and note the respective sensor number on the sensor location diagram.

Set the required temperature as applicable as per respective standard operating procedure of the equipment. Ensure data logger date and time are matching with equipment, set the data logger logging interval of not more than 30 seconds in data logger and start the data logging.

Procedure to be followed

While using wireless data loggers or other sensor for which the data cannot be monitored from outside of chamber follow the below specified procedure.Set the required temperature as per respective standard operating procedure of the equipment or as per approved protocol.

Ensure data logger date and time are matching with equipment, set the data logger logging interval was not more than 30 seconds and place the loggers at identified locations and start the data logging.Allow the temperature in chamber to stabilize for about 30 minutes before start of the study.Record the time and switch "OFF" the power supply to the equipment.After about 4 to 5 hours note the time and switch "ON" the power supply to the equipment and wait for chamber stabilization for about 30 minutes to one hour or based on previous experience during temperature come up time.

Table 6: Power failure recovery study

Location ID of data logger	Temperature in °C			Relative humidity in % RH		
	Minimum	Maximum	Average	Minimum	Maximum	Average
T1	24.80	28.18	26.49	62.99	68.93	65.96
T2	24.87	27.48	26.75	60.11	65.83	62.97
T3	25.13	**28.31**	26.72	62.96	69.60	**66.28**
T4	24.83	27.42	26.53	60.48	70.72	65.98
T5	25.08	28.06	26.57	60.35	66.09	**63.22**
T6	24.76	27.16	25.96	59.88	69.92	64.97
T7	25.09	27.99	26.54	60.96	68.86	64.91
T8	25.05	27.12	26.85	60.28	**68.70**	64.49
T9	**24.51**	27.36	**25.93**	59.84	69.45	64.65
T10	24.93	28.02	26.75	60.46	68.84	64.65
T11	24.69	28.11	26.46	59.88	68.18	64.03
T12	24.63	28.05	26.34	**57.58**	69.34	63.46
T13	25.27	28.25	26.76	61.45	68.62	65.59
T14	24.78	28.00	26.39	60.45	67.72	64.85
T15	24.83	28.16	26.92	59.85	66.86	63.55
T16	24.90	28.29	**26.95**	60.25	69.92	65.85
T17	24.67	27.53	26.18	61.85	68.18	65.55

Power failure recovery study was conducted for 4 Hours. From Table 6 the study was observed and recorded that minimum and minimum average temperature at location T9 was found 24.51 ˚C and 25.93 ˚C respectively. Similarly maximum and maximum average temperature at location T3 was found 28.31 ˚C and T16 26.95 ˚C. Similarly minimum and minimum average relative humidity at location T12 was found 57.58 % and T5 63.22 % respectively. Similarly maximum and maximum average relative humidity at location T8 was found 68.70 % and T3 66.28 % respectively.

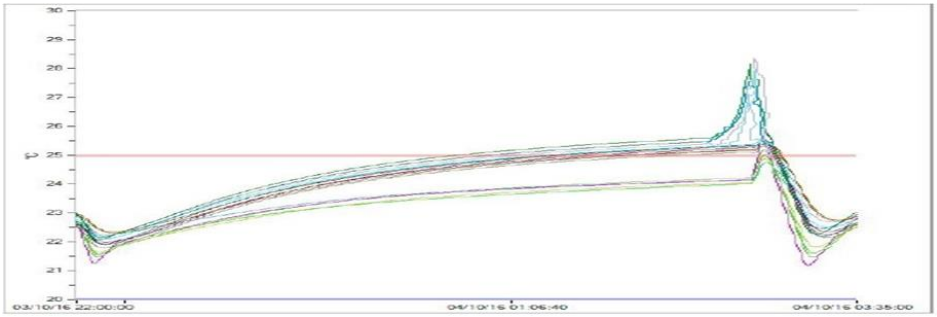

Figure 6: Power failure recovery study graph

CONCLUSION

Temperature and relative humidity mapping are essential studies were 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 Walk-in incubator for an Empty & Loaded Chamber, Door Open recovery Study,Power Failure Recovery Study. The results were found to be good and within the acceptance criteria.

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