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Reducing the Number of Temperature Sensing Devices during Performance of Temperature Mapping

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Abstract

Temperature mapping of drug storage facilities is a time-consuming procedure. At the same time, the procedure for its implementation is not strictly regulated by normative legal documentation. One of the main issues that arise during preparation for the temperature mapping is the choice of the required number of temperature sensing devices or electronic data logging monitors (EDLMs). The number of devices used for measurements during temperature mapping affects the resource intensity of the event both economically and organizationally. With this in mind, the authors propose an approach to determining the accuracy of temperature prediction while reducing the number of control devices. The aim of the study is to substantiate the possibility of reducing the number of temperature sensing devices based on the data of the formed temperature field. Advantages of the proposed approach are: reduction of material costs and working time, reduction of the total amount of data to be analyzed, which will facilitate processing and reduce the time of preparation of reporting documents.

Keywords: temperature mapping, temperature field, temperature control for storage of pharmaceutical products.

Introduction

The study of the temperature distribution (temperature mapping) in the premises for storing medicinal products is an important measure that allows to ensure stable quality of products at all stages of drug circulation: during production, manufacture, storage and transportation. The transition to temperature mapping is primarily due to the variety of layouts of modern premises, their technological equipment and the complexity of organization of production processes in storage areas.

Temperature mapping of drug storage facilities is a labour intensive procedure. At the same time, the procedure for its implementation is not strictly regulated by normative legal documentation.

One of the non-regulatory sources that can guide the conduct of temperature mapping is Technical supplement to WHO Technical Report Series, No. 961, “Temperature mapping of storage areas” [1]. It provides a description of the activities carried out in the course of temperature mapping, its objective, handling procedures and content of the protocol and the report on temperature mapping, provides recommendations for annexes to these documents. The activities described in WHO guideline relate more to the preparatory actions and the process of temperature mapping. Methods for analyzing data, obtained during temperature mapping, are not addressed in WHO guideline.

One of the main issues that arise during preparation for the temperature mapping is the choice of the required number of temperature sensing devices. The number of EDLMs used for measurements during temperature mapping affects the resource intensity of the event both economically and organizationally.

For example:

To study temperature distribution in the storage room for drug products, which is 7 meters in height, 25 meters in width and 40 meters in length, will require up to 270 EDLMs (!) according to existing recommendations [1, 2].

Reducing the number of EDLMs on the one hand reduces the cost of equipment for temperature mapping, but, on the other hand, increases the risk of temperature abuse during storage of drugs.

An essential component of temperature mapping in a storage room for drug products is developing a temperature field [3], which is determined by measuring temperature at certain points in the investigated room with a specified periodicity. The results of these measurements are the basis for the prediction of temperature at any point in the investigated environment/room/area. Recommendations for the placement of EDLMs in the storage room are limited to arrangement of EDLMs on horizontal levels (height between levels of 1.2 - 1.8 m) and determining control points at each level with a minimum distance between devices (5-10 m). At each of these levels it is possible to construct (with the forecast of the remaining temperature values) temperature cross-sections (Figure 1). Temperature cross-sections are illustrative of the temperature field of the room under study, on the basis of which we will be able to substantiate the conclusions and recommendations of the report, thereby fulfilling the goals of temperature mapping, among which the main are:

- determination of cold and hot temperature spots in the room under study;
- determination of the maximum temperature fluctuations in the room under study;
- identification of storage locations with a risk of temperature abuse;
- determination of periodicity in daily (routine) room temperature control (temperature monitoring system settings).

Temperature field of the storage room volume is characterized by temperature cross-sections, the accuracy of which directly depends on the number of control points in the plane of the temperature cross-section. The more temperature cross-sections we can build, the better (more accurately) we can characterize temperature change in the room. Therefore, if we arrange EDLMs in the studied room in a grid fashion (Figure 2, variant 2), so that the area is reasonably covered, then we will be able to construct a greater number of temperature cross-sections. This will not only increase accuracy of temperature field, but will also simplify prediction of temperature outside the points of EDLMs placement.

Accuracy of the temperature field is influenced by: the error of temperature monitoring devices, the precision of EDLMs location and the methods for predicting temperature outside the control points.

Requirements for monitoring devices for temperature mapping (EDLMs) are described in detail in [1].

The selected EDLMs must:

- be technically suitable for the specific mapping task and for the intended operating environment;
- provide a reliable and continuous reliable 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, with time intervals ranging from one minute to 15 minutes or more
- have sufficient memory for the intended length of the study and the chosen recording interval;
- have a NIST-traceable 3-point calibration certificate with a guaranteed error of no more than ± 0.5°C at each calibration point;
- allow the recorded time-temperature data to be downloaded to a computer system for subsequent analysis;
- allow 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 [1, 4].

Under the *precision of EDLMs location* in the investigated volume of the room, we understand correspondence of the spatial arrangement of each device to its intended location in accordance with the *EDLMs arrangement diagram* (it is a mandatory annex to the temperature mapping protocol). In addition, during the installation of devices, it is possible to confuse ID numbers associated with specific control points. These errors in most cases are associated with "human factor" and can be eliminated by mandatory control during the installation and dismantling of EDLMs.

The accuracy of the data obtained by prediction directly depends on the number of EDLMs used for temperature mapping in a specific volume of the storage facility. This is due to the fact, that the decrease in control points in the investigated storage volume increases the probability of temperature prediction error outside the control points and depends primarily on the accuracy of EDLMs and the selected trend for prediction.

As an example, we consider the measurement of temperature at three points (Figure 3).

Assume that the axis OX_n is on the temperature cross-section of the temperature field. Temperature is measured in points x_1, x_2, x_3 and equals to t_1, t_2, t_3 respectively.

The essence of temperature field plotting reduces to prediction of temperature at any point on the intervals [X_1; X_2] and [X_2; X_3]. Due to the uniform temperature change, a small difference in the temperature values at the measurement points compared with the accuracy of EDLM, we can assume that a linear trend can be used for prediction of temperature values in these intervals, as shown in Figure 3.

Our objective is to reduce the number of EDLMs used. Let's assume that the control device at point x_2 should be removed. In this case it is necessary to determine how accuracy of the temperature values prediction will change on the interval [X_1; X_3], if measurements are made only in points x_1 and x_3, that is, not with three but with two control devices.

To quantify the temperature measurement error with two devices, instead of three, we use the deviation of the obtained temperature value from the predicted value (value A in Figure 4).

By comparing the value A with the known instrument error of EDLMs used Δt_{EDLM}, it is possible to characterize the accuracy of temperature prediction while reducing the number of control devices. With a large number of consecutive measurements N at t_2 point, the ratio of the number of cases, for which the value A is less than Δt_{EDLM}, to the total number of measurements N will characterize the accuracy of temperature prediction with a decrease in the number of control devices.

MATERIALS AND METHODS

The data was obtained during temperature mapping, which we made for the company "A+LOGISTICS". Temperature mapping was done in refrigeration chamber # 13/2 for storage of drugs at a temperature of +8°C - + 15°C.

The measurements were made with measuring complex iButton Data Logger Revisor type iBDLR-L (type of measurement, approved by the order of Federal Agency of the Russian Federation on technical regulation and metrology, certificate of verification No. 5545/2018 valid until 15.02.2022).

Main settings of control devices.

Measurement start date	11:00 05.05.2018
Delayed start	11:00 05.05.2018
Measurement interval	1 minute
Measurement accuracy	0,5 °C
Measurement period	2 days, 20 hours, 8 minutes
Number of measurements at each control point	4096 measurements
Number of control points	12
Total measurements	49152

The diagram of EDLMs arrangement during temperature mapping is shown in Figure 5a.

Based on the analysis of the data obtained, it is necessary to estimate the error of the predicted temperature in the entire investigated storage volume, if the number of devices is reduced by one third. (Figure 5b).

RESULTS

Using the summary table of temperature values at each measurement point during the period of this study (Table 1), we can determine, when the deviation of the true value of the temperature reading of EDLMs (which we want to exclude during in future) exceeds the predicted temperature value by an amount greater than the error of EDLM used.

For illustrative purposes we take the results of the measured temperature at points 7, 8, 9 (Figure 5a) on May 05, 2018 at 11:02:01. According to the summary table (Table 1), the temperature at these points was 11.69 °C, 10.96 °C, and 11.38 °C, respectively. For point 8, along with the measured temperature value, we can calculate the predicted temperature value from the data of points 7 and 9. The difference between the measured value and the predicted value will be 0.57 °C, which is greater than the error of the monitoring device used (0.5 °C). This means that at this moment the monitoring device at point 8 (Figure 5a) would record a temperature deviation.

If we take the following results of the measured temperature on May 5, 2018 at 11:03:01 at points 7, 8, 9 (Table 1), then the temperature at these points was 11.69 °C, 11.16 °C, 11.38 °C respectively. The difference between the measured value and the predicted value at point 8 in this case will be 0.22 °C, which is less than the error of the monitoring device used (0.5 °C). This means that at this moment the monitoring device at point 8 (Figure 5a) would not record a temperature deviation.

DISCUSSION

Thus, using all 4096 temperature measurements at this point, it is possible to compose the frequency of deviation of the obtained temperature values at point 8 from the predicted values in each measurement and compare them with the error of the monitoring device (Figure 6).

The ratio of the number of cases, in which deviations of the obtained temperature values at point 8 from the predicted values do not exceed the error value of EDLM used, to the total number of measurements is 0.932 (93%). This value shows that absence of monitoring device at point 8 during the next temperature mapping in this room will decrease the prediction accuracy by 7% (Figure 6).

sequence number of measurement	Device serial number		4157E75000000002	417C405600000027	4184F55600000069	41020057000000CA	418602570000007F	4174FD5600000025	41EE0357000000D0	410CF856000000CE	413303570000005E	41A10057000000CF	413C0157000000F9	41F5F956000000E7
	Device number on the diagram		*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*
	Date	Time	*Temperature, °C*											
1	*05/05/2018*	*11:00:01*	11,50	11,75	11,63	11,56	11,63	11,75	11,69	11,56	11,44	11,63	11,44	11,63
2	*05/05/2018*	*11:01:01*	11,50	11,75	11,63	11,56	11,63	11,75	11,69	11,26	11,44	11,63	11,44	11,56
3	*05/05/2018*	*11:02:01*	11,50	11,75	11,63	11,56	11,63	11,75	11,69	10,96	11,38	11,63	11,44	11,56
4	*05/05/2018*	*11:03:01*	11,50	11,75	11,69	11,56	11,63	11,75	11,69	11,16	11,38	11,63	11,44	11,56
5	*05/05/2018*	*11:04:01*	11,50	11,75	11,63	11,56	11,63	11,75	11,69	11,36	11,38	11,63	11,44	11,56
…	…	…	…	…	…	…	…	…	…	…	…	…	…	…
4096	*08/05/2018*	*07:08:01*	11,50	11,75	11,69	11,56	11,63	11,75	11,75	11,63	11,44	11,63	11,44	11,63

Table 1. Summary table of temperature values at each measurement point during the study period (EDLMs with device numbers 2, 5, 8 and 11 are planned to be removed)

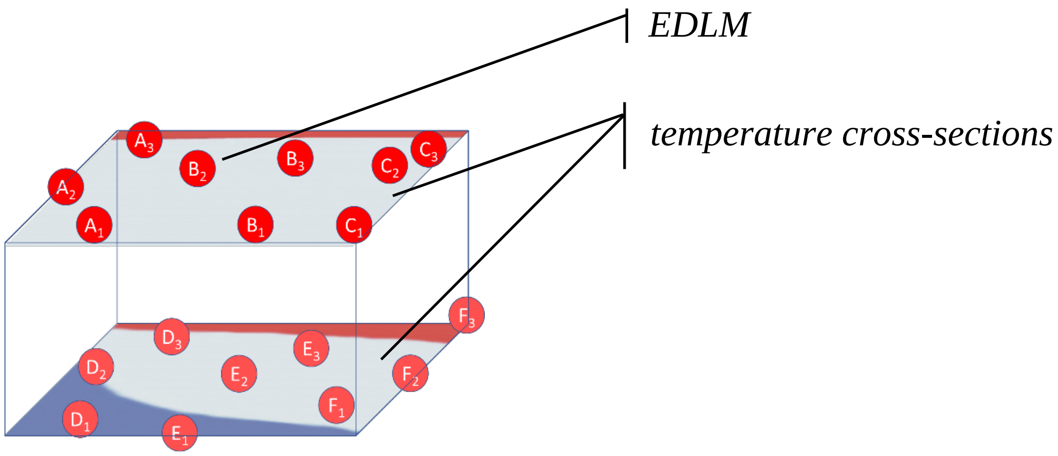
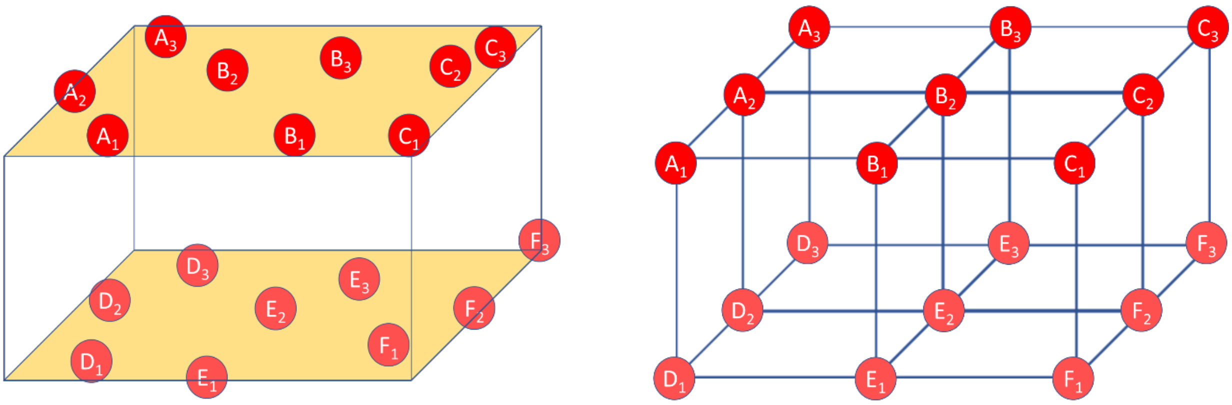


Figure 1. Temperature field of the room under study



(1) *(2)*

Figure 2. Variants of EDLMs placement: 1 – randomly, 2 – in a grid fashion

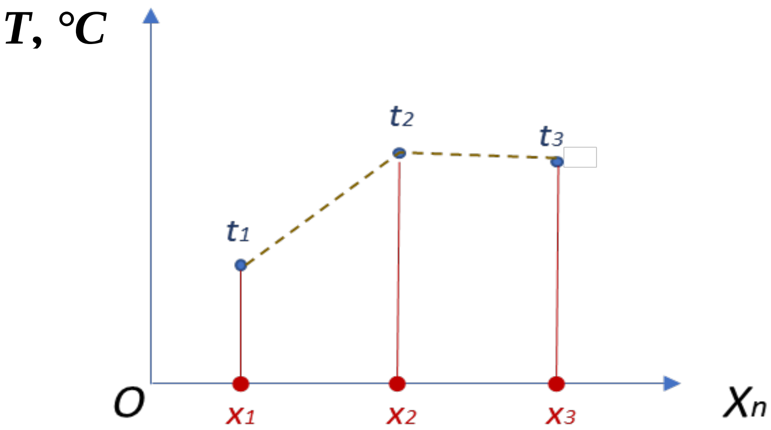


Figure 3. Measured temperature values in three points

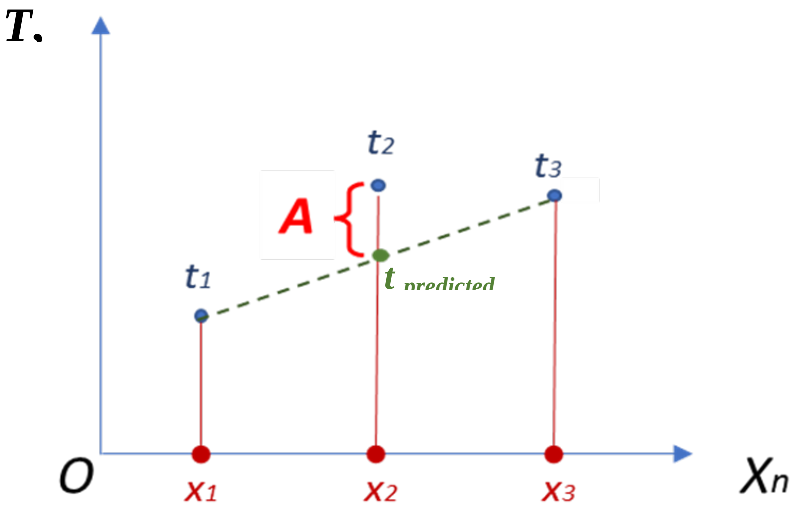
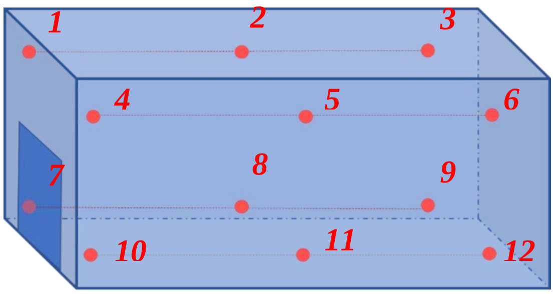
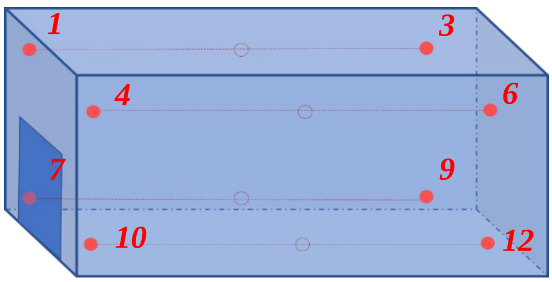


Figure 4. Deviation of the predicted temperature from the measured value during the study



a)



b)

Figure 5. The diagram of EDLMs arrangement during temperature mapping: a) before quantity reduction of EDLMs; b) after quantity reduction of EDLMs

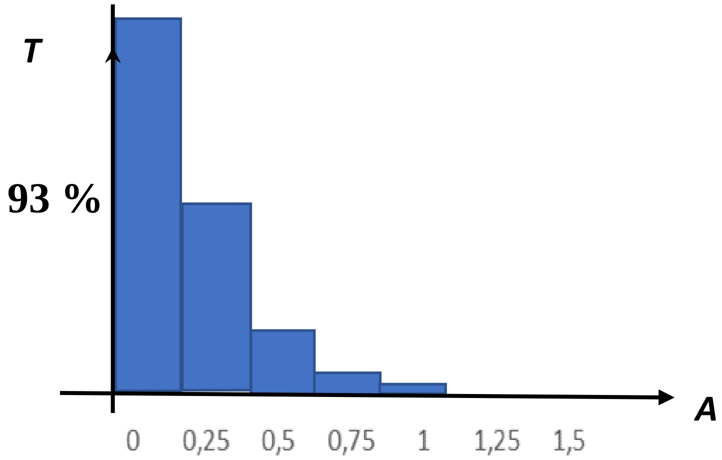


Figure 6. The frequency of deviations of the obtained temperature values from the predicted

Conclusions

When applying the proposed method for determining the accuracy of the temperature field, associated with quantity reduction of EDLMs during temperature mapping of storage facilities for medicinal products, a number of features should be taken into account. Before making a decision to reduce the number of control devices, it is necessary to make measurements at this point, i.e. carry out the initial temperature mapping. Quantity reduction of EDLMs should be carried out only for those conditions for which temperature mapping was performed. For example, if the heating system is changed (switched on), the quantity reduction of EDLMs according to the procedure described above should be repeated.

The calculated value, which characterizes the accuracy of determining the temperature in the room, can serve as a justification for quantity reduction of EDLMs during next temperature mapping. Advantages of the proposed approach are: reduction of material costs and working time, reduction of the total amount of data to be analyzed, which will facilitate processing and reduce the time of preparation of reporting documents.

References

1. Temperature mapping of storage areas, *Technical supplement to WHO Technical Report Series* 2011, *961*.
2. "MUK 4.3.2756-10 4.3 Control methods. Physical factors. Methodical guidelines for measuring and evaluating the climate of industrial premises. Methodical guidelines" (approved by the Chief State Sanitary Doctor of the Russian Federation on 12.11.2010).
3. Pyatigorskaya, N.V., Beregovykh, V.V., Belyaev, V.V., Greibo, S.V., Pyatigorskiy, A.M., Necessity of Temperature Mapping of Storage Areas for Pharmaceutical Products, *Journal of Pharmaceutical Sciences and Research* 2018, *10(3)*, 662-664.
4. Title 21 of the Code of Federal Regulations that establishes the United States Food and Drug Administration (FDA) regulations on electronic records and electronic signatures (ERES).