



Session 4 GLP – engineering



Estimation of potential risks resulting from temperature shifts in laboratory animals (mice, rats, guinea pigs) beyond the recommended ranges

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The main prerequisite for researching

For preclinical studies in vivo, the recommended environmental conditions of the laboratory animals must be observed in order to obtain reliable results.

Emergency situations that may also affect the microclimate of the laboratory animals should not be excluded. This can lead to serious misrepresentation of the test results.

No literature has been found to describe the effect of minor (not extreme) temperature variations beyond the recommended ranges on clinical and physiological parameters of laboratory animals. This study, aimed at assessing the potential risks of temperature changes in laboratory animals (mice, rats, guinea pigs) outside the recommended ranges of influence on the basic parameters is necessary for further application in the current work.



Recommended ranges for keeping laboratory animals

Guidelines/recommendations for the keeping of laboratory animals	Type of animal / keeping temperature, °C		
	Mice	Rats	Guinea pigs
Guide for the care and use laboratory animals [1, 2]	20 – 26	20 – 26	20 – 26
Guidelines on care of laboratory animals and their use for scientific purposes [3]	19 – 23	19 – 23	16 – 23
Code of practice for the housing and care of animals bred, supplied or used for scientific purposes [4]	20 – 24	20 – 24	15 – 21
Guidelines for the maintenance and care of laboratory animals [5].	20 – 24	20 – 24	20 – 24

The devil is in the details



Declared error
 $\pm 1^{\circ}\text{C}$

How do you evaluate?
Is that a deviation?

Purpose of work

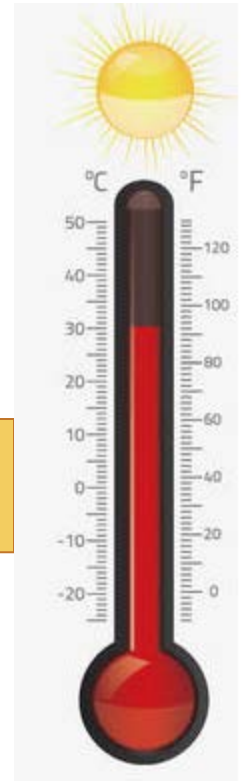
The purpose of the study was to assess potential risks arising from temperature shifts in laboratory animals (mice, rats, guinea pigs) beyond the recommended ranges of influence on key indicators.



And what happens if?

The temperature will be lower.

The temperature will be higher.



Is the temperature change going to affect hematological and biochemical blood parameters?



The main objectives of the study:

1. Creation of the required temperature level in the laboratory animal housing for each group of animals according to the research plan design;
2. Evaluation of the impact of temperature shift in the laboratory animals housing outside the recommended ranges on the general condition of laboratory animals;
3. Evaluation of the impact of temperature shift in the laboratory animals housing outside the recommended ranges on hematological and biochemical blood tests in laboratory animals;
4. Evaluation of the impact of temperature shift in the laboratory animals beyond the recommended ranges on the mass factors of the laboratory animals organs.



Characteristics of experimental groups of outbred mice, rats and guinea pigs that were kept at temperatures above recommended ranges

№ groups	Number of animals		Temperature and duration of maintenance
	male	female	
1	5	5	From +20°C to 26°C for 4 weeks (control for group 3)
2	5	5	From +20°C to 26°C for 1 week (control for groups 4,5,6,7)
3	5	5	From +27°C to +30°C for 4 weeks (each week the temperature was raised by 1°C)
4	5	5	+27°C for 1 week
5	5	5	+28°C for 1 week
6	5	5	+29°C for 1 week
7	5	5	+30°C for 1 week



Complete set of devices for precise temperature maintenance:

- 1. Meter-regulator microprocessor single-channel AWEN TRM1 (thermoregulatory microprocessor 1 channel)**
- 2. Temperature sensor - sensor element of sensitive copper technical HEMT-13.**
- 3. Control thermometer - data logger TESTO 174H4.**
- 4. executive device - 2 electric heaters 1.5 kW each**
 - oil - provides long-term temperature maintenance through thermal inertia
 - ceramic with air fan - provides fast reaction to temperature changes

The temperature sensor is mounted at the same point as the control logger and the temperature sensor of the individual ventilated S8 cells to ensure equal readings. In this case, a correction is introduced in TRM1 based on the comparison of the logger TESTO174H and TRM1. The required temperature and its differential, taken equal to 0.1°C, are set in TRM1, which gives a control signal to the executive devices when the temperature exceeds the set limits.

Characteristics of experimental groups of outbred mice, rats and guinea pigs contained at temperatures below recommended ranges

№ groups	Number of animals		Temperature and duration of maintenance
	male	female	
2	5	5	From +20°C to 26°C for 1 week (control for groups 10,11,12)
8	5	5	From +20°C to 26°C for 3 weeks (control for group 9)
9	5	5	From +19°C to +17°C for 3 weeks (each week the temperature was reduced by 1°C)
10	5	5	+19°C for 1 week
11	5	5	+18°C for 1 week
12	5	5	+17°C for 1 week



Composition of a set of devices to keep the temperature precisely low:

1. Split-system LESSAR LS-H07KPA2/LU-H07KPA2 with cooling capacity of 2.19 kW, designed for a room area up to 22 sq.m. with actual area of 12.2 sq.m. and working for cooling at outdoor air temperature from +18 to +43 degrees C. The set includes a remote control LZ-KNP, which is used to select the set temperature at a discrete rate of 1 degree C. The indoor air conditioner unit is equipped with a display on which temperature settings are displayed in the operating mode.

2. Control thermometer - verified data logger TESTO 174H

The control logger is installed at the same point as a temperature sensor individual ventilated S8 cells to ensure equal readings.

The required temperature is set in the indoor unit of the air conditioner, which gives the control signal to the external unit when the temperature goes out of established limits.

Monitoring of mice, rats and guinea pigs did not show any signs of deterioration in the general condition of the animals when the temperature increased from 27°C to 30°C.

Animal species	when the temperature rises from 27 ° C to 30 ° C for 4 weeks (increase by 1 ° C / week)			when the temperature rises to 27 ° C , 28 ° C, 29 ° C and 30 ° C for 1 week		
	General state	Biochemistry and Hematology	Organ mass ratios	General state	Biochemistry and Hematology	Organ mass ratios
Mouse	WITHOUT CHANGES			WITHOUT CHANGES		
Rat						
The guinea pig						

Monitoring of mice, rats and guinea pigs did not show any signs of deterioration of the general condition in animals when the temperature decreased from 19°C to 17°C.

Animal species	when the temperature drops from 19 ° C to 17 ° C for 3 weeks (decrease by 1 ° C / week)			when the temperature drops to 19 ° C , 18 ° C and 17 ° C for 1 week		
	General state	Biochemistry and Hematology	Organ mass ratios	General state	Biochemistry and Hematology	Organ mass ratios
Mouse	WITHOUT CHANGES			WITHOUT CHANGES		
Rat						
The guinea pig						

Risk analysis

Degree of harm (consequences of danger) - S

Probability of danger – O

Relevance	Points
Catastrophic	5
Critical	4
Serious	3
Low (not serious)	2
Very low (not significant)	1

Probability of occurrence	%	Points
Often	51-100	5
Often	21-50	4
Occasionally	11-20	3
Seldom	3-10	2
Almost impossible	Up to 2	1

Probability of hazard identification – D

Detection probability	%	Points
High	More than 98	1
Satisfactory	96-98	2
Average	85-95	3
Low	80-85	4
Very low	Less than 80	5

Risk category

Priority risk score	Risk category
Below 10	Insignificant risk
11-40	Acceptable risk
41-70	Significant risk, immediate solutions
71 and higher	Unacceptable risk

Risk analysis

№	Reason	Potential Waiver (Source of Harm)	Consequences (Harm)	Consequences (Harm)	Chance of Hazard - O	Probability of hazard identification - D	Risk Priority Number(S*O* D)
1	Non-standard situations related to the violation of the necessary conditions for the maintenance of laboratory animals	Deviation of the temperature of laboratory animals from the recommended ranges upwards or downwards	Impact on animal health, which may subsequently affect research results	3	3	1	9

Immaterial risk does not affect the performance of the Organization or the reliability of data obtained

The maintenance of sexually mature animals for one and four weeks at the temperature from 27°C to 30°C (which is 4°C above the recommended range) and for one and three weeks at the temperature from 19°C to 17°C (which is 3°C below the recommended range), does not have a clinically significant impact on the vital signs of animals and the risk of emergency situations related to the maintenance of the recommended temperature is insignificant

Thank you for your attention!

