

Title: Temperature Recording and Required Labeling for Refrigerators, Freezers, and Controlled Temperature Areas.

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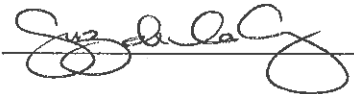
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References: USP <1150>: Pharmaceutical Stability
USP <1079>: Good Storage and Shipping Practices
USP General Notices 10.30: Storage Temperature and Humidity
SOP 270: Non-Conformance Reports and Corrective/Preventative Actions
SOP 2140: Thermometer Calibration
NIST GMP-11 (Revision March 2003) 'Good Measurement Practice for Assignment and Adjustment of Calibration Intervals for Laboratory Standards' EviSense Manual

<u>Rev. No.</u>	<u>Effective Date</u>	<u>Revision Summary</u>
1.	11-15-91	Original Version
2.	07-27-92	EPA/SAS Format
3.	05-02-94	Update Format for GLP
4.	09-05-95	Minor Revisions in Section 2
5.	12-17-97	Added form for Freezer
6.	10-06-98	Converted to LWP format. 2. Procedure Changed: min/max thermometers, Sample Refrig.2-6°C, Freezers less than -10°C, Extracts less than 10°C
7.	09-03-99	Include refrigerator labeling requirements. Minor wording changes Sections 1.0, 2.0 and 3.0. Extract storage changed to extract and standard storage.
8.	08-08-01	2.0: Removed time reference. 2.1: Added container label contents. 3.0: Removed italics.
9.	02-01-02	Added: deviation/corrective action form, updated label in Appendix I, and reviewed by and date sections to logsheets.
10.	02-19-02	Sections 1.0, 2.0: Minor wording changes. Referenced sample storageroom temperature throughout and created logsheet. Section 3.0: Added min/max temperature deviations allowed before corrective action, corrective action steps.
11.	02-14-03	Added reference to lab standard storage rooms throughout. Added logsheets for extract and standard storage room and freezer, and lab standard storage room. Added min/max allowable temperatures to logsheets.

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12.	02-17-09	Change to Bodycote name and organization structure. Reformatted Attachments I-V. Changed freezer specs to correspond with USP. Added reference to NCR SOP 270. Removed references to laboratory areas and testing areas and defined critical laboratory areas.
13.	08-03-09	Sec. 2.0: added. Sec. 3.1: Corrected freezer specification to -25°C to -10°C per USP; changed alarm and action points. Sec. 3.5: added. Sec. 4.2.2: expanded. Appendix Attachment V: Added for Ultra-Low Freezer.
14.	JUN 01 2011	Revised throughout to reflect transition to the EviSense system.

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<u>Prepared by</u>	<u>Date</u>	<u>Technical Review</u>	<u>Date</u>
	05/25/11	Mary Hammons	5/26/11
QA Approval/Date:			06/01/11

1.0 SCOPE AND APPLICATION

To establish guidelines for recording the temperature of laboratory refrigerators, freezers, and areas used for the storage and testing of samples, extracts, or standards. To act as a reference and training guide for use by employees responsible for monitoring temperature in the laboratory. To assure that all refrigerators and freezers are properly labeled appropriate to their intended use.

2.0 INTRODUCTION

Temperature is monitored in the laboratory through the use of calibrated probes and thermometers. Storage of test articles in the laboratory prior to analysis is short-term, typically 10-14 days. No stability study storage is performed in this laboratory. In the case of a significant temperature excursion, the client is notified and a replacement sample may be sent if the client does not have stability data to support the excursion. Maintaining retain samples for this purpose is the responsibility of the client.

3.0 PROCEDURE

3.1 Critical laboratory areas are continuously monitored with a calibrated probe connected to wireless monitoring system (EviSense). A temperature excursion beyond the control limits results in automatic notification of the QA Officer or their designee. This notification occurs 24 hours a day, seven days a week.

3.1.1 GMP sample, standard, and reagent storage refrigerators, freezers, and controlled room temperature areas required for GMP testing are designated critical laboratory areas.

3.1.2 Excursions will be annotated by QA in the EviSense system with corrective actions taken or a justification of why the excursion is acceptable. (Refer to Sec. 3.4).

3.2 Non-critical refrigerators and freezers may be alternately configured with a min/max thermometer with an audible alarm for the continuous monitoring of temperature. The current, minimum, and maximum temperature of each refrigerator and freezer is recorded once each business day on the appropriate form (Attachments I, II, III, IV, and V).

3.2.1 If the audible alarm sounds, the employee who notes the condition will document the issue on the Deviation/Corrective Action form, attached to the logsheet (Attachment V), and notify the QA Unit.

3.2.2 QA will document corrective actions on the Deviation/Corrective action form, attached to the logsheet (Attachment VI).

- 3.3 Temperature probes are placed in a liquid container (water for refrigerators and laboratory areas, isopropyl alcohol or polyethylene glycol for freezers). Each container is labeled with its contents and associated area, refrigerator, or freezer number. Some probes are permanently attached to a sealed container of glycol. These containers are not refillable and do not need to be labelled.
- 3.4 At a minimum of once each business day, the Quality Assurance Unit (QAU) will log into the temperature monitoring system to note whether any temperature excursions have occurred. Each excursion event will be annotated in EviSense with a statement indicating the potential impact of the excursion.
- 3.3.1 In the case of a temperature excursion for more than 45 minutes in a GMP sample storage area (or any temperature excursion of over 30°C in a controlled room temperature area, below 0°C for a refrigerator, or above 0°C for a freezer), a Non-Conformance Report will be opened per SOP 270 and clients whose samples or analyses are impacted will be notified within one business day. The responsibility for determining the impact of the temperature excursion and authorizing the use of the sample, submitting a new sample, or retesting lies with the client.
- 3.3.2 In the case of a temperature excursion for more than 45 minutes in a non-GMP sample storage area or in a reagent or extract storage area, a Non-Conformance Report will be opened and the client will be notified only if the average temperature for the past 24 hours has exceeded the control limits. If a sample is no longer suitable for analysis or an analysis has been impacted, alert the client and determine the need for retesting or obtaining a new sample for analysis.
- 3.3.3 A mean kinetic temperature analysis per USP <1150> may be used to determine the significance of the temperature excursion. Note that the USP definition of "Controlled cold temperature" is as follows: "temperature maintained thermostatically between 2° C and 8° C that allows for excursions in temperature between 0° C and 15° C that may be experienced during storage, shipping, and distribution such that the allowable calculated mean kinetic temperature is not more than 8° C". Transient spikes outside of these limits may be permitted provided that the client indicates in writing that the excursion is supported by stability data.
- 3.3.4 Because increased sample degradation is associated with an increase in mean kinetic temperature, excursions below -25°C in freezers, below -90°C in the ultra-low freezer, and below 15° C in controlled room temperature areas used for sample, extract, or reagent storage is permitted without further investigation.

3.4 Corrective actions following an NCR investigation may include:

- 3.4.1 Checking the thermostat for blockage.
- 3.4.2 Adjusting the thermostat.
- 3.4.3 Tagging the unit “Out-of-Service” and repairing or replacing the unit.
- 3.4.4 Moving samples or reagents to a different, appropriate area.
- 3.4.5 Incorporating fans to adjust the room temperature.
- 3.4.6 Use of a data logger in systems not monitored with EviSense to record the extent of temperature fluctuations.

3.5 Generate a monthly printout for each critical laboratory area from EviSense and submit for review, approval, and filing.

3.6 For systems not monitored by EviSense, change the temperature log sheet forms at the end of each month and submit the completed forms to the QA Unit for review, approval, and filing.

3.7 At the time the temperature log sheet forms are replaced, observe the liquid containers for all probes and add liquid if necessary. Check the alarm set points on the min/max thermometers to ensure that they are accurately set.

4.0 QUALITY CONTROL

4.1 Specified conditions and control limits:

Location	Average	Min. Temp	Max. Temp
Refrigerators (Sample Storage)	2-6 °C	2°C	8°C
Freezers (Samples and Standards)	-10 to -25°C	None	-10°C
Refrigerators (Extract/Standard Storage)	2-8°C	2°C	8°C
Ultra-Low Freezer (Samples and Standards)	-70 to -90°C	None	-70°C
Ambient Temperature Areas	68-77°F (20-25°C)	59°F (15 °C)	86°F (30°C)

- 4.2 Refrigerators for the storage of chemicals or samples must be labeled, “This is not an explosion proof refrigerator. Do not store flammables,” unless that refrigerator is specifically designed for the storage of flammable materials. Laboratory refrigerators must also be labeled, “No food or drink should be stored in this refrigerator.” Any equivalent wording is acceptable. An example of this label may be found as Appendix I.
- 4.3 Annually, all GMP sample storage refrigerators and freezers will be temperature mapped according to a pre-approved protocol to determine the extent of normal temperature fluctuations at the above setpoints. Remapping must occur after repair or other significant change in the equipment.
- 4.4 Temperature measuring devices will be calibrated following SOP 2140: Thermometer Calibration.

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Attachment I
NON-GMP
REFRIGERATOR TEMPERATURE LOG SHEET

Month/Year _____

Fridge # _____

Day	N/A	Current	Min	Max	Initials	Day	N/A	Current	Min	Max	Initials
1	<input type="checkbox"/>					17	<input type="checkbox"/>				
2	<input type="checkbox"/>					18	<input type="checkbox"/>				
3	<input type="checkbox"/>					19	<input type="checkbox"/>				
4	<input type="checkbox"/>					20	<input type="checkbox"/>				
5	<input type="checkbox"/>					21	<input type="checkbox"/>				
6	<input type="checkbox"/>					22	<input type="checkbox"/>				
7	<input type="checkbox"/>					23	<input type="checkbox"/>				
8	<input type="checkbox"/>					24	<input type="checkbox"/>				
9	<input type="checkbox"/>					25	<input type="checkbox"/>				
10	<input type="checkbox"/>					26	<input type="checkbox"/>				
11	<input type="checkbox"/>					27	<input type="checkbox"/>				
12	<input type="checkbox"/>					28	<input type="checkbox"/>				
13	<input type="checkbox"/>					29	<input type="checkbox"/>				
14	<input type="checkbox"/>					30	<input type="checkbox"/>				
15	<input type="checkbox"/>			31			<input type="checkbox"/>				
16	<input type="checkbox"/>										

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Temperature is to be maintained at an average of 2-6°C (35-43 °F). If < 1 °C or > 8 °C , notify QA.
N/A: Weekend, Holiday, or date not applicable.

QA Review: _____

Date: _____

Attachment II

**NON-GMP
FREEZER TEMPERATURE LOG SHEET**

Month/Year _____

Freezer # _____

Day	N/A	Current	Min	Max	Initials	Day	N/A	Current	Min	Max	Initials
1	<input type="checkbox"/>					17	<input type="checkbox"/>				
2	<input type="checkbox"/>					18	<input type="checkbox"/>				
3	<input type="checkbox"/>					19	<input type="checkbox"/>				
4	<input type="checkbox"/>					20	<input type="checkbox"/>				
5	<input type="checkbox"/>					21	<input type="checkbox"/>				
6	<input type="checkbox"/>					22	<input type="checkbox"/>				
7	<input type="checkbox"/>					23	<input type="checkbox"/>				
8	<input type="checkbox"/>					24	<input type="checkbox"/>				
9	<input type="checkbox"/>					25	<input type="checkbox"/>				
10	<input type="checkbox"/>					26	<input type="checkbox"/>				
11	<input type="checkbox"/>					27	<input type="checkbox"/>				
12	<input type="checkbox"/>					28	<input type="checkbox"/>				
13	<input type="checkbox"/>					29	<input type="checkbox"/>				
14	<input type="checkbox"/>					30	<input type="checkbox"/>				
15	<input type="checkbox"/>			31			<input type="checkbox"/>				
16	<input type="checkbox"/>										

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Temperature is to be maintained at an average of -10 - -25 °C. If > -5 °C, notify QA.

N/A: Weekend, Holiday, or date not applicable.

QA Review: _____

Date: _____

APPENDIX I

SAMPLE REFRIGERATOR LABEL

Refrigerator

1

Jobs 10 to 19 only

CAUTION

This is NOT an explosion proof freezer.
Do NOT store
FLAMMABLES.

NO food or drink to be stored in this freezer.