

STANDARD OPERATIONAL PROCEDURE (SOP)
MEDICATION TEMPERATURE MANAGEMENT FOR INVESTIGATIONAL PRODUCT

Purpose

This procedure describes the specific procedures relating to medication temperature management processes for investigational product (IP) for the Investigational Drug Service (IDS) Program at University of Utah Health

Definitions

A. **Acceptable Temperature Ranges for Devices Used for Storage of Investigational Product:**

Storage Device	Celsius	Fahrenheit
Controlled room temperature	15° to 25°	59° to 77°
Refrigerator	2° to 8°	35.6° to 46.4°
-20°C Freezer	-25° to -10°	-13° to 14°
-80°C Freezer	-84.4° to -70°	-120° to -94°

- B. **Investigational drug:** A new drug or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms "investigational drug" and "investigational new drug" are deemed to be synonymous for purposes of this part. Any drug which has not received FDA approval for use in humans. Also refers to any drug, which is FDA approved and is being used under protocol for human research, possibly outside of FDA approved labeling.
- C. **Investigational drug service:** A function of the Department of Pharmacy and provides support to ensure the safety and efficiency of trials at University of Utah Health that use investigational product(s)/investigational drug(s). Pharmacy personnel that perform investigational drug accountability at UUH satellite locations approved for conducting research protocols are considered an extension of the IDS.
- D. **Investigational product (IP):** A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.
- E. **Principal investigator:** The principal investigator or medical researcher in charge of carrying out a clinical trial's protocol. This includes obtaining IRB approval as well as informed consent of participating individuals, patient evaluation and monitoring and provision of medication and medication orders valid under the protocol.
- F. **Temperature Variance:** a temperature reading outside of the acceptable temperature ranges and outside of the acceptable storage temperatures defined per individual protocol BUT NOT considered a temperature excursion AFTER rounding rules are applied
- G. **Temperature Excursion:** a temperature reading outside of the acceptable temperature ranges and outside of the acceptable storage temperatures as defined per individual protocol AFTER rounding rules are applied. See below for further information regarding temperature excursions.

- H. **Temperature Monitoring Hardware Device:** a fully automated temperature monitoring system that provides continuous temperature monitoring. Temperature monitoring hardware monitors accurately measure temperature and continually send information to a web-based software system, which is accessible by IDS pharmacy personnel. Temperature records can be produced by authorized users for investigational refrigerator, freezer, or ambient temperature sensor by logging into the temperature monitoring software system.
- I. **Vestigo®:** A 21 CFR Part 11 compliant electronic accountability software application designed specifically for investigational pharmacy use and utilized by University of Utah Health IDS. Refer to www.mccreadiegrou.com/vestigo/ for additional information.

Description

- A. Investigational product will be maintained within the recommended temperature ranges above to ensure integrity and potency of the product.
- B. Temperature monitoring hardware devices are installed on all Investigational Pharmacy refrigerators, freezers, and ambient storage locations. The devices monitor and record temperatures every 5 minutes. Temperature records can be produced by Investigational Drug Service (IDS) staff for any investigational refrigerator, freezer, or ambient temperature monitoring hardware device by IDS staff logging into the temperature monitoring software system.
- C. All Investigational refrigerator, freezer, and ambient temperature monitoring hardware devices monitors are set to alert IDS staff before a temperature excursion occurs.
- D. For approved, commercially available medications, which are not repackaged/re-labeled by sponsor for investigational use, the IDS will use USP 659 guidelines for allowable temperature range(s).
- E. For temperature measurements that are reported and recorded, temperatures will be interpreted using the following rounding rules:
 - 1. For temperatures that are recorded and reported temperatures in tenth degrees (i.e. – 22.4 degrees or 3.8 degrees), these tenths will be rounded to the closest degree in Celsius
 - a. If a temperature is equal to or greater than xx.5, then it will be rounded up to the nearest whole degree.
 - b. If it is equal to or less than xx.4, then it will be rounded down to the nearest whole degree

Implementation

- A. Record Keeping
 - 1. Each IDS refrigerator, freezer, and ambient temperature storage location containing IP will only have temperature monitored and recorded through use of the institutional standard temperature monitoring hardware devices.
 - 2. At the beginning of each calendar month, IDS staff will generate a report from the temperature monitoring software system for the previous calendar month that outlines a graph the minimum and maximum temperatures for each storage device.
 - a. This report will saved and filed electronically in a secure, shared folder
 - b. This report may be provided to monitors upon request for any specific month and hardware device associated with IP storage.

B. Calibration

1. Temperature monitoring hardware devices, refrigerators, and freezers will be calibrated on an annual basis by the biomedical department or other designated party.
2. Documentation of calibration shall be filed electronically in a secure, shared folder.
3. Last date of calibration of temperature monitoring hardware devices will be maintained electronically in a secure, shared folder.

C. Temperature Variances and Excursions

1. If the temperature measured by any investigational product refrigerator, freezer, or ambient device begins to go out of range, then the temperature monitoring software system will send a message to the on-call IDS pharmacist
2. Definition of a temperature excursion
 - a. Defined as a temperature deviation from the acceptable temperature ranges as defined above and sustained for a contiguous time period of greater than 30 minutes
3. The IDS pharmacist on-call is responsible for managing the alert. Managing the alert includes the following:
 - a. Checking the device in question and confirming that the temperature is in fact beginning to go outside of, or is outside of the appropriate range by
 - i. either having other pharmacy personnel on-site checking the location in question or
 - b. personally coming on-site to check the location in question
 - c. Determining if the temperature that is out of range is considered a temperature excursion per definitions and rounding rules provided above.
 - d. Contacting HCH Facilities & Engineering at (801) 587-4444 to make ambient air temperature adjustments to thermostats if needed
 - e. Determining and documenting the root cause of the temperature variance/excursion within 24 hours of the temperature variance/excursion occurring
4. IDS pharmacist on-call is expected to act on the temperature alert notification within 15-30 minutes of receiving the alert.
5. In the event that the temperature meets definition of a temperature excursion, all IP that was involved will be immediately quarantined. See Procedure: IDS Quarantine Processes for more information

D. Notification of Study Sponsor of Temperature Excursion

1. The responding pharmacist and/or IDS personnel should research acceptable temperature allowances using the study protocol, investigator's brochure, pharmacy manual, and IP labeling.
2. The IDS personnel will notify the study monitor or designee within 48 hours of the temperature excursion occurring if required after conducting research into the temperature excursion.
3. If the sponsor/study monitor does not respond within 48 hours of being notified of the temperature excursion, the IDS personnel shall refer to the study protocol, Investigator's Brochure and IP labeling for specific instructions on temperature excursions and appropriate actions
 - a. If there are NO instructions on temperature excursions in the study protocol, Investigator's Brochure and IP label, then the IP shall continue to be quarantined and removed from available inventory until receiving further instruction from the sponsor/study monitor.

4. IDS pharmacy staff should keep a record of all e-mails and communications with the study monitor regarding the temperature excursion. E-mails should be added to the correspondence folder within the folder for each protocol located on an electronic, secure share drive.
- E. Movement of investigational product
1. If the responding pharmacist determines that the refrigerator or freezer is non-operational, or the ambient air temperature will not be returned within range quickly, then the on-call IDS pharmacist shall ensure that IP is moved to a temporary location with the same storage conditions. This may be done by the following:
 - a. Transferring IP to other refrigerators, freezers, central pharmacies, or coolers as appropriate per storage requirements of each IP.
 - b. Setting up portable fans, air conditioning units or heaters in the IDS pharmacy for ambient temperature management if needed
 - i. Portable air conditioning units are located on-site at Huntsman Cancer Hospital.
 - ii. If portable fans or heaters are needed, UUH facilities should be contacted at (801) 581-2424 or (801) 581-2781.
 - c. Following sponsor-required notification and documentation for temperature excursions, if required by protocol.
 - i. IP shall remain at this temporary location until the issue has been resolved (eg, device has been fixed, new device acquired).
 2. If IP must be moved to another location outside of the IDS Pharmacy, then the IDS pharmacist shall ensure that an inventory of IP is taken by the next business day.
 3. If the IDS pharmacist determines that IP must be moved to a central pharmacy location, then he or she will ensure that IP segregated from hospital inventory and labeled "For Investigational Use Only" or some similar wording.
 4. IDS personnel will make every effort to ensure that IP is transferred under appropriate conditions (eg, ice packs for cold storage IP).
 5. IDS personnel shall notify all inpatient pharmacists and pharmacy management of the movement of IP as necessary.

Owner: IDS Manager

Last updated: 04/30/2021

Previous updates: 5/11/2020, 10/21/2019; 2/19/2018

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