Content Owner:
Investigational Drug Services

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02/22/2024

Standard Operating Procedure		
Procedure for out-of-range temperatures for Investigational Drugs		
Scope: ☐Dept./Unit/Clinic_____ ☒Service Line Investigational Drug Services ☐Institutional	**Patient Population:** ☐Neonatal ☐Pediatric ☐Adult ☐Sub-population: _____	**Patient Level of Care:** ☐Ambulatory ☐Acute ☐Intermediate ☐Critical Care ☐Emergency Dept ☐Labor and Delivery ☐Diagnostic/Procedural ☐Peri-operative ☐Other_____
Purpose: The investigational pharmacy provides service for drug-related research protocols and is responsible for overseeing the proper storage of investigational products in accordance with the sponsor's protocol.		

Background/ Rationale: The investigational pharmacy staff is to utilize a standard procedure for handling and documenting out-of-range temperatures that affect the storage environment of investigational products. This procedure is to be conducted in accordance with applicable federal and state regulations, as well as good clinical practice guidelines.

Equipment/Supplies: Refrigerators, Freezers and Room Temp devices

Procedure:

A. Handling out-of-range temperatures in the Investigational pharmacies:

1. All room temperature supply areas, refrigerators and freezers that store investigational drug product are backed up to a Metasys server and are centrally monitored through UVA Systems Control.
2. If the temperature in any of these storage areas goes out of range (see below for ranges), Systems Control is to notify maintenance first and then call the affected pharmacy.
    i. Target temperature ranges:
        1. Room temperature range: 68°F – 77°F *(alarm limits set to ≤69°F and ≥76°F) Some drugs are acceptable between 59°F and 86°F as defined per protocol or product.*
        2. Refrigerated range: 2°C – 8°C *(alarm limits set to ≤3°C or ≥ 7°C)*
        3. -20C freezer range: -25°C – -15°C *(alarm limits set to ≤-24°C and ≥-16°C)*
        4. -80C freezer range: -90°C – -70°C *(alarm limits set to ≤-88°C and ≥-72°C)*
3. Systems Control is to follow the Emergency Callback Report procedure, document who they call in each instance and when the call was made. (*See Emergency Callback Report for details).*
4. During IDS working hours (800 - 1630), Systems Control must call the affected investigational pharmacy (Main Hospital 982-1048; Cancer Center 982-5385) and alert the IDS pharmacist on duty to the temperature alarm. Systems Control is to give a report of the situation.
5. During off-hours, Systems Control must call the inpatient pharmacy at 924-5255, option 7 and ask to speak to the Pharmacy Supervisor on duty.

6. The Pharmacist responding to the call must go to the affected storage area and inspect the area for any obvious abnormality (door left open on freezer or erratic reading on the temperature dial).
7. If the temperature goes out-of-range at any time, there must be action. For example, maintenance must be called by systems control and the affected area must be inspected for abnormalities.
8. The responding Pharmacist must monitor the storage area for return to normal temperature.
9. If the responding pharmacist determines drug must be moved, the responding pharmacist is to follow the procedure below:
    i. All drug is to be moved to a secure, stable, and appropriate storage area in the pharmacy for temporary storage until the original investigational drug storage area has been deemed acceptable for use. Every effort should be made to transport the drug under appropriate storage conditions (i.e. ice packs for refrigerated or frozen drug product). Possible storage locations below:
        1. Main IDS:
            a. Room temperature: Move drug to Cancer Center IDS temperature-monitored storage room.
            b. Refrigerator: May move drug to other Main IDS refrigerators as space is available. Pay attention to refrigerator temps when moving drug. Alternate refrigerator will warm up quickly. Make note of the drug being moved so IDS can have an accurate list of drugs affected. If there is inadequate space in the Main IDS refrigerators, move drug to inpatient walk-in refrigerator.
            c. -20C Freezer: Label as MAIN IDS Study Drug and move the drug(s) to one of the Cancer Center IDS -20C temperature-monitored freezers if space is available.
            d. -80C Freezer: Move to one of the Cancer Center IDS monitored -80C freezers, as available. Please follow standard biohazardous handling precautions including donning proper PPE prior to entering biohazardous buffer room.
        2. Cancer Center IDS:
            a. Room temperature: May move to other room temperature drug storage room in EC4 (room 4331 and 4332). If both rooms are out of range, move to Main IDS.
            b. Refrigerator: May move drug to other Cancer Center IDS refrigerators (must make note of the drug being moved so IDS can have an accurate list of drug affected). If there is not room, may move drug to infusion pharmacy refrigerators. If no room in these refrigerators, must move drug to main hospital pharmacy, which may include Main IDS refrigerators, inpatient walk in refrigerator, IV room refrigerators, etc.
            c. -20C Freezer: There is a -20C freezer in each drug storage room (room 4331 and 4332). Move drug to the unaffected freezer (must make note of the drug being moved so IDS can have an accurate list of drug affected). If both freezers affected, move to -20C freezer within Main IDS.
            d. -80C Freezer: May move drug to other -80C freezer within the biohazardous IV room or to Main IDS -80C, as available. Please follow standard biohazardous handling precautions including

donning proper PPE prior to entering biohazardous buffer room.

ii. If moving drug to a location that contains hospital or infusion stock, or other investigational stock from a different IDS location:
    1. Clearly segregate investigational product using storage bins (totes can be retrieved from Slab).
    2. Multiple studies may be stored in one bin if necessary. Drug may be stored in the totes in their original shelf bins, if possible, or place in plastic baggies with HSR # on baggy. Ensure these drugs are clearly labeled as different studies.
    3. Label bins with the HSR #s that stored inside.
    4. If being stored in the inpatient walk-in refrigerator, seal the bins with zip ties.
    5. If moving Room Temp drugs from Main IDS to Cancer Center IDS, please request a tall wire rack from the loading dock store room. They have let us borrow them before.
    6. If moving other drug from one IDS storage area to another, label as product from the appropriate IDS pharmacy to separate stock.

iii. Label the storage bins as *'For Investigational Use Only'.* For drugs with excursions include *'Quarantined – Do Not Use'.*

iv. A portable temperature monitor is to be placed with the investigational drugs or manual temperature recordings must be taken on a daily basis by inpatient pharmacy staff. Portable temperature monitors and instructions for use may be found on shelf G-16 in a yellow bin labeled 'Portable Temperature Monitors' in the Main IDS Pharmacy.

v. The responding pharmacist is to send out an email to all inpatient pharmacists and supervisors that investigational drug has been moved to a new specified location.

vi. The responding pharmacist should send a detailed email to the IDS team (CL Pharmacy IDS Services CLPharmacyIDSServices@hscmail.mcc.virginia.edu to include the date, time notified of excursion, temperature upon entering IDS to assess the problem, location drug was moved and time moved to different location at a minimum. Please include any detail that will provide a full description of events.

10. Within 24 hours of the move or the next business day, the IDS staff member is to run an inventory report in Vestigo for all drug stored in the affected storage area. IDS staff is to conduct a full inventory and verify all drug listed on the report has arrived at the temporary storage area.
11. If the drug has been exposed to temperature that is outside the normal range (defined below) for any amount of time, the drug must be quarantined in Vestigo as a temperature excursion. All dispensing on the studies affected must halt and study teams are to be immediately contacted of the situation through email.
    i. Normal range defined as temperature range listed on the package label, protocol, investigators brochure, or pharmacy manual.
12. In the event of a temperature excursion:
    i. The sponsor will be notified with a temperature excursion form generated from Vestigo . Sponsor-specific temperature excursion forms will not be completed by IDS. If a sponsor requires a specific form to be completed, the study representative (e.g. CRA) will need to complete the form using the information provided in the Vestigo excursion form, and IDS will review and sign.
    ii. IP will be quarantined at the appropriate storage temperature (see 9i above) until determined by the sponsor if the drug may be released or destroyed per policy. See IDS Drug Destruction Policy.

13. Using the Vestigo inventory report as a guide, the IDS Pharmacist(s) are to contact all sponsors of the affected drug to make them aware of the temperature excursion and seek guidance on continued use. The list should be triaged based on immediate patient need. Due to the nature of prioritizing trials with immediate patient need and the staffing resources required to contact sponsors, IDS will not guarantee all sponsors will be contacted within 24 hours or 1 business day. Affected IP will be quarantined and not used until approved for continued use. We will do our best to contact all sponsors as soon as we are able.
14. All communication received from the sponsor must be maintained in the trial's folder on the IDS shared drive, and appropriate action must be documented in Vestigo (i.e. remove from quarantine, destroy, maintain in quarantine until monitor reconciliation, etc).

External References:

Joint Commission Standard MM.06.01.05
ICH GCP 4.6.4
ICH GCP 5.14.2
ICH GCP 5.14.3
ASHP *Guidelines on Clinical Drug Research*
United States Pharmacopeia (USP) standards, (USP Standard 33-NF28, Sections 10.30.10, 10.30.40,10.30.60))

REVISION HISTORY				
Version	Reason (new, cyclical, external)	Relevant Reviewers	Approved By (Area leadership)	Date of Approval
2/2011	Original	IDS Pharmacy	IDS Manager	2/2011
2	9/2012	IDS Pharmacy	IDS Manager	9/2012
3	4/2013	IDS Pharmacy	IDS Manager	4/2013
4	4/2014	IDS Pharmacy	IDS Manager	4/2014
5	10/2015	IDS Pharmacy	IDS Manager	10/2015
6	12/2015	IDS Pharmacy	IDS Manager	12/2015
7	09/2017	IDS Pharmacy	IDS Manager	9/2017
8	07/2020	IDS Pharmacy	IDS Manager	7/2020
9	09/2021	IDS Pharmacy	IDS Manager	9/2021
10	02/2024	IDS Pharmacy	IDS Manager	03/2024