York and Scarborough Teaching Hospitals NHS Foundation Trust R&D Unit
Standard Operating Procedure
Pharm/S48

Temperature Monitoring (Clinical Trials)

IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED

All staff should regularly check the R&D Unit's website and/or Q-Pulse for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

The definitive versions of all R&D Unit SOPs appear online. If you are reading this in printed form check that the version number and date below is the most recent one as shown on the R&D Unit website: https://www.research.yorkhospitals.nhs.uk/sops-and-guidance-/ and/or Q-Pulse

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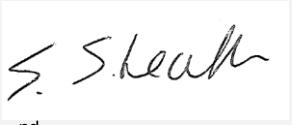
	Signature:	
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This SOP will normally be reviewed every 3 years unless changes to the legislation require otherwise

Version History Log

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date Implemented	Details of significant changes
1.0	16th March 2009	
2.0	27th July 2009	
3.0	1st January 2010	Pharmacy SOP put into revised template, temperature excursion section added
4.0	2nd July 2012	Change of SOP Controller. Removal of references to the North and East Yorkshire Alliance. Updated to reflect addition of freezer temperature monitoring form, addition of temperature excursion notification form
5.0	24th February 2014	Inclusion of Scarborough Hospital as a site working to this SOP. Removal of guidance relating to Comark temperature loggers. Addition of central Temperature excursion record file.
6.0	19th October 2015	Inclusion of new forms. Change of author. Process of cold chain transport to offsite units and other minor changes.
7.0	5th February 2018	Change of author. Reference to the devices in use and changes to reflect and standardise practice across both sites. New location for NotionPro validation certificates.
8.0	22nd February 2021	Change of link to R&D website. Change of author. Addition of instructions on how to monitor IMP storage locations off-site.
9.0	29th March 2021	Minor changes only
10.0	23rd February 2022	Changes to reflect software update from NotionPro to Hanwell EMS system. Change of author. Change of author.

Contents

1 Introduction, Background and Purpose

Correct storage of Investigational Medicinal products (IMP) is vital to assure the integrity and quality of the medicinal products used in clinical trials. Routine temperature monitoring forms an integral part of that assurance, ensures that a continuous record of storage temperature is available for all IMPs and allows production of temperature records for the Sponsor or MHRA if requested.

Where IMP is stored outside Pharmacy, temperature monitoring will be undertaken as described in study specific trial instructions.

2 Who Should Use This SOP

This SOP should be followed by all members of the pharmacy clinical trials team within Pharmacy at York and Scarborough Teaching Hospitals NHS Foundation Trust.

3 When this SOP Should be Used

This SOP should be used by the pharmacy clinical trials team when monitoring and reviewing storage temperatures in areas where IMP is stored.

This SOP should be used in conjunction with the general pharmacy SOP for temperature monitoring.

4 Procedure(s)

A member of the pharmacy clinical trials team should be assigned to monitor and/or review the temperature of IMP storage areas daily on Monday to Friday (with the exception of bank holidays).

5 Temperature Monitoring Systems and Devices

The pharmacy temperature monitoring system (Hanwell EMS) is in routine use within clinical trials and Denward temperature loggers are used to provide back-up monitoring should Hanwell EMS fail.

Temperature logging systems or devices used for temperature monitoring IMPs should be UKAS certified where possible. Annual calibration of the Hanwell EMS system is arranged by the pharmacy quality assurance team and the calibration certificate stored on QPulse.

The location of all Denward loggers should be tracked using the ‘Clinical Trials Temperature Logger Sign-Out Form’ (Pharm/F109) in the Temperature Monitoring file in the Clinical Trials office.

Loggers should be retrieved and sent to Denward for recalibration prior to the expiry of the current calibration certificates. The recalibration date for each of the loggers is also recorded on the ‘Clinical Trials Temperature Logger Sign-Out Form’.

Denward loggers are externally calibrated. A purchase order must be raised for recalibration requests and the order number quoted on the request to the manufacturer. Examples of letters that can be amended and used to send to Denward with the loggers requiring calibration can be found on the X:Drive. To access these letters, go to the 'Admin' file, 'Denward loggers', and then they are in the 'Letters' section.

All areas where IMP or Pharmacy-controlled trial products are stored will be monitored. This includes:

- The clinical trials dispensary (York & Scarborough)
- All clinical trials fridges (York & Scarborough)
- All clinical trials freezers (York & Scarborough)
- Any clinical trials Ultra-Low freezers (York & Scarborough)
- The pharmacy Cold Store (York)

All refrigerators must be continually monitored to ensure that the temperature remains within the range 2°C to 8°C.

Ambient temperatures must also be continually monitored to ensure that temperatures remain within the range 15°C to 25°C.

Freezers, including Ultra-Low freezers, require continuous temperature monitoring when used to ensure that the temperature is maintained between -15°C and -25°C or another suitable range as defined in the clinical trial protocol.

In addition to the calibration of Hanwell EMS and the Denward loggers, all IMP storage locations are required to be validated annually. The process of validation and fridge/freezer mapping can be found in the SOPs provided by the Quality Assurance team on Pharmacy QPulse. The validation form on QPulse should be used to record this validation process, and once completed, the Quality Assurance team will confirm if the storage location has been validated successfully.

6 Daily Temperature Recording

Temperature records for all areas within pharmacy where IMP is stored should be checked each weekday (with the exception of bank holidays) via the Hanwell EMS temperature monitoring system. Use Pharm/F108 to record these checks.

At the start of each working day a member of the pharmacy clinical trials team should:

- Log on to svsnotion1/EMS/ username: pharmacy password: view1234
- The Home screen will show both Scarborough and York hospital locations, the following steps apply to whichever hospital site needs to be accessed.
- Hover over the middle icon that shows 'View Reports' and select this option
- This brings you to the 'Scheduled Reports' screen.
- There will be a report titled 'CT Daily', select the option to 'Edit settings'

- Select date of last check as the start date
- Select the current date as the end date
- Once the date range is set, select 'Run Now'
- A green banner will show on the 'Scheduled Reports' Screen stating that the report is being generated.
- Hover over the 'Reports' heading and select 'Reports Folder'
- Select the most recent 'CT Daily' report, paying attention to the date and time of the report. Click the PDF link for this report.
- Document the results from the PDF report on form Pharm/F108 in the central temperature monitoring folder in the clinical trials office
- Inform a senior staff member of any temperature deviations.
- Repeat these steps for any other sites as required

The Clinical Trials Manager should review and sign each completed form at the end of each month and take action as appropriate.

Completed forms should be stored in the 'Archived ward list checks and daily temperature readings' folder located in the clinical trials dispensary at the York site.

7 Creating Monthly Temperature Graphs

7.1 At the end of each month, generate a Hanwell EMS cumulative graph for each storage location as follows:

- Log on to svsnotion1/EMS/ using 'pharmacy' as the username and 'view1234' as the password
- Select the required site (York or Scarborough)
- Select the graph symbol for 'View Live Data'
- Hover over the 'View Data' heading and select 'Live View' from the list, then select the relevant sensor location.
- Select the graph symbol for the sensor required, this will bring up the current graph
- Enter the start date, select 'month' as the interval period and select 'Submit' to generate the monthly graph
- Select the icon for 'Save as PDF' and open the download link, then print the graph.
- File the printed graph in the appropriate section of the 'Monthly Temperature Graphs' folder located in the clinical trials office.
- Paper copies of graphs should be retained for 10 years. Monthly graphs can be sent to R&D as part of the Monthly Audit, can be requested by sponsors, and should be included in Pharmacy site files upon close-out unless instructed otherwise.
- Save the opened graph file on the X-Drive in the relevant year folder within the Hanwell EMS Monthly Graphs section. This can be found in the

temperature folder in the 'Admin' part of the X:Drive. The file name should follow the format location, month and year e.g. Dispensary January 2020

- Once all the required temperature graphs have been printed and filed, with electronic copies stored on the X:Drive, exit Hanwell EMS.

8 Back-up Temperature Monitoring Devices

To ensure that temperatures are continuously monitored even in the event of a Hanwell EMS failure, Denward loggers should be activated and placed in each area where temperature recording is deemed necessary.

Denward loggers should run throughout the week and be reset every Monday morning (or the next working day in the case of bank holidays). They can be reset as follows:

- Click on the EasyLog icon on the PC desktop
- Insert the logger in to a USB port on the PC
- Click on Set up and start the USB data logger icon.
- Follow the instructions displayed on the screen ensuring that the correct units and parameters are set (remember to delay the start by a minimum of twenty minutes for any logger going in to a fridge, or one hour going in to a freezer). The logger should also be set to read at 5 minute intervals.
- Ensure that the process has been completed - this will be indicated by a tick and a notification to remove the logger.
- Remove the logger
- Place the logger in to the correct location straightaway.

Before removing the Denward logger from any freezer, a new logger should be set up using the procedure above and placed in to the freezer. The logger should have a delay of one hour before it starts recording so that it is allowed to get down to the correct temperature first. Only when this logger has started recording, can the original logger be removed from the freezer and stopped. Ensure that any loggers placed in/removed from different storage areas are recorded on the logger accountability sheets.

Note that logger data will only be saved and graphs printed in the event of a Hanwell EMS failure or excursion.

Ultra-low freezers may only have one form of temperature monitoring device due to the access port in the back of the appliance only allowing for one port to be inserted. This may be Hanwell EMS, Denward or another provided device which can be calibrated or replaced. Ultra-low freezers will have their own operating SOPs.

9 Temperature Excursions

A temperature excursion is deemed to have occurred if the recorded temperature for a given storage location falls outside its pre-defined limits.

If a temperature excursion occurs, quarantine the affected IMP at the correct temperature immediately as outlined in Pharm/S59.

Move the IMP supplies to an area which is within normal range. The IMP must be clearly marked as quarantined and for clinical trials use only and a record of the temperature in the new storage area must be kept.

If the ultra-low freezer has a temperature excursion it may not be possible to place the stock inside the appliance into another location with the same temperature requirements. The stock may need to be left inside the freezer and the door kept closed to prevent the temperature falling too quickly and speak to the sponsor urgently.

Notify all members of the pharmacy clinical trials team so that they are aware that the stock cannot be used.

Inform all the relevant sponsors whose stock is stored within the area where the temperature excursion occurred. This should be done in writing via email and a copy of the temperature graph included with the email. Request that the sponsor confirms in writing whether the IMP is suitable to use following the excursion.

Inform the relevant Research Nurse(s) for the affected clinical trials as soon as possible as they may have to re-arrange patient visits if the Sponsor has not confirmed that the affected IMP is still suitable for use.

Further information on reporting temperature excursions can be found in individual study pharmacy site files.

If the reason for the excursion has not been identified, or has not been corrected, contact the Facilities department to check the air conditioning system/refrigerator/freezer as applicable. Record the job reference number and any actions taken on the temperature monitoring form (Pharm/F54).

If the temperature excursion has been resolved and the trial sponsor has confirmed that the product is safe for use, remove the IMP from quarantine and return it to the designated storage area for that trial.

Document all actions taken in the ‘Temperature Excursion Record Form’ (Clinical Trials Pharm/F79) using one form per trial affected and file the completed form(s) in the Temperature Monitoring Folder. Some sponsors may provide their own temperature excursion forms and may request further information about the excursion.

Write a file note for each affected trial and attach all correspondence relating to the affected IMP and a copy of the temperature graph. The file note should be filed within the temperature section of the pharmacy site file and a copy placed in the relevant study file.

Update the file note log so that it reflects all temperature excursions which may have occurred.

10 Fridge and Freezer Alarm Fault Reporting

Move any IMP stored in the affected fridge or freezer to a suitable alternative temperature controlled location ensuring that the temperature is still continually monitored.

Report suspected fridge or freezer alarm faults to the pharmacy quality assurance department. If they are unable to determine the cause, escalate the report to the facilities department.

11 Hanwell EMS Alarm Activation

Hanwell EMS will send an alarm notification by email when temperatures fall outside the permitted temperature range. These alarms should be actioned in accordance with the general pharmacy SOP for temperature monitoring.

12 In the Event of Hanwell EMS failure

If Hanwell EMS fails or elapses then:

- Obtain daily temperature readings from the digital display on the individual Denward loggers. Record these readings as noted for Hanwell EMS above.
- Download data from the Denward loggers and save it on the x-drive each Monday morning (or next working day) as previously.
- Print weekly graphs as follows:
    - Click on the EasyLog icon on the PC desktop
    - Insert the logger in to a USB port on the PC
    - Click on Stop the USB Data Logger and download data icon.
    - Enter the current date after the logger location e.g. CTAmbient01.12.20 and save the data on the X-Drive in the Denward logger section of the electronic ‘Temperatures’ file.
    - Follow the instructions displayed on the screen ensuring that the correct units and parameters are set (remember to delay the start by a minimum of 20 minutes for any logger going in to a fridge, and one hour for a freezer)
    - Ensure that the process has been completed before removing the logger.

13 Cold Chain Transport to off-site units

To avoid temperature excursions when transporting cold chain items to off-site units, a validated process must be followed.

Temperature loggers will be used to ensure that no temperature excursions have occurred during transport or packaging.

Trial specific instructions contain information on the correct method of packing each shipment or carrier.

14 Temperature monitoring IMP at off-site units or out of the Pharmacy Department

IMP and Pharmacy-related trial products that are stored off-site at other clinics or hospitals for example, or are stored out of the Pharmacy department, i.e on wards, must be temperature monitored.

Outside of the Pharmacy department, Hanwell EMS is out of signal range and is therefore unable to be used. Denward loggers should be used instead in order to accurately monitor the temperature where the stock is stored. Upon set up of the study or the addition of a new ward/off-site clinic, a Denward logger should be set up (as explained in section 8) with the correct temperature parameters and at an interval of 5 minutes, and placed in the IMP storage location. Due to the Denward logger only storing data for 56 days when set at an interval of 5 minutes, the storage location will need to be monitored monthly and the logger changed over for one that is newly set up. This process of changing over the Denward logger is detailed below:

- For Ambient stock: Set up a Denward logger as detailed in Section 8 of this SOP ensuring that the correct parameters are entered, the logger is set to read at an interval of 5 minutes, and the 'Push to start' option is selected. Once the trials member arrives at the site/location, they should place the logger in the storage location and push the button to start the logger recording. The previous logger can then be removed from the location and downloaded.
- For Fridge and Freezer stock: A member of the trials team should attend the location with a laptop and Denward logger. When they arrive at the site/location, they should set up the Denward logger as described above, but they should set up a delay of one hour before the logger starts recording. They should then put the logger in the fridge/freezer and wait until it starts recording before taking out the previous logger. The previous logger can then be stopped and downloaded.

If no temperature excursions have occurred, then the graph should be saved on the X:Drive and printed and placed in the Pharmacy file.

If a temperature excursion has occurred, then the stock should be quarantined immediately and the sponsor should be contacted for further instructions.

Study specific SOP/instructions

For studies where IMP is kept outside of Pharmacy, study specific monitoring instructions (including how temperature monitoring is to be conducted) should be created depending on the individual requirements of the study, this should be stored in section 1 of the Pharmacy site file when finalised.

Denward loggers need to be manually checked to determine if a storage location has gone out of range. Research team members may have to check this daily/or before issuing IMP to patients by scrolling through the temperature reading screens on the logger by pressing the button on the front of the logger. How and when this procedure is to be carried out should be documented in the study specific SOP and circulated with the relevant members of the research team.

15 Validation of off-site transfer using a shipping container

Prior to sending IMP to an offsite location the process must be validated to ensure that there are no temperature excursions and that the process can be replicated without issue.

16 Related SOPs and Documents

Pharm/F79	Temperature Excursion Record Form (Clinical Trials)
Pharm/S59	Quarantine of IMP
Pharm/F42	Quarantine Notice
Pharm/F43	Quarantine Log
Pharm/F108	Daily Clinical Trials Temperature Checks
Pharm/S76	Storage and dispensing of Investigational Medicinal Products outside of Pharmacy
Pharm/F109	Clinical Trials Temperature Logger Sign-Out Form