STANDARD OPERATIONAL PROCEDURE (SOP)
AUDITOR AND MONITOR VISITS

Purpose

The purpose of this standard operational procedure is to outline and enforce a standardized process for clinical trial monitor visits within the Investigational Drug Service (IDS) at University of Utah Health (UUH).

Definitions

A. Auditor or Monitor: an individual who observes each trial site to ensure that the standardized operation procedures for the trial are being followed, reporting and managing any deviations from the investigation plan as they occur. An auditor/monitor may work directly with the sponsor company of a clinical trial, as an independent freelancer or for a contract research organization. Auditors/monitors may also do the following functions related to clinical research studies; ensure compliance with the clinical trial protocol, check clinical site activities, make on-site or remote monitoring visits, review case report forms and communicate with clinical research coordinators.

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. Vestigo®: A 21 CFR Part 11 compliant electronic accountability software application designed specifically for investigational pharmacy use and utilized by University of Utah Heath IDS. Refer to www.mccreadiegroup.com/vestigo/ for additional information.
Description

A. Scheduling a visit for an audit
   1. Auditor visits are to be scheduled by either the monitor or the study coordinator by using the appointment calendar on external IDS webpage. The webpage collects the information needed to schedule the auditor prior to their visit and notifies IDS pharmacy personnel once the appointment has been scheduled by the auditor. The auditor is also responsible for notifying the research team of their intended visit to the IDS pharmacy.
   2. It is the responsibility of the auditor or the research coordinator to schedule an auditor visit using the IDS auditor scheduling webpage. Auditor visits must be scheduled a minimum of 8 weeks in advance. Shorter notice may be allowed if approved by the IDS manager prior to scheduling. However, auditing space and resources are limited within the IDS-designated area and shorter notice may not be feasible.
   3. Visits are to be limited to a maximum of 2 business days; however, visits can be extended if the IDS can accommodate, with prior approval at time of scheduling.
   4. Frequency and number of auditor visits per study is specific to each protocol (no defined maximum per year per the IDS).
   5. Visits must be completed during regular IDS business hours
   6. Only unblinded auditors are allowed to schedule visits with the IDS
   7. Auditor visits may need to be scheduled in an off-site location to accommodate the time and space needed by the auditor in conjunction with other IDS activities. The IDS will coordinate this with the research team to ensure that research documents are kept in the appropriate chain of custody at all times during the audit visit.

B. Remote and On-Site Monitoring
   1. The IDS supports remote and on-site monitoring for research protocols.
   2. Remote and on-site monitoring visits must be scheduled using the scheduling webpage as described below (Section C.).

C. An additional fee for special monitoring requests (eg, Vestigo® access or accountability logs outside of a scheduled appointment) may be charged per the amount provided in the IDS pharmacy estimate.

D. Scheduling a Monitor Appointment
   1. Remote and on-site monitor visits are to be scheduled by either the monitor or the study coordinator by using the appointment calendar on external IDS webpage. The webpage collects the information needed to schedule the monitor prior to their visit and notifies IDS pharmacy personnel once the appointment has been scheduled by the auditor. The monitor is also responsible for notifying the research team of their intended remote or on-site visit to the IDS pharmacy.
   2. It is the responsibility of the monitor or the research coordinator to schedule a monitor visit using the IDS monitor scheduling webpage. Monitor visits must be scheduled a minimum of 4 weeks in advance. Shorter notice may be allowed if approved by the IDS manager prior to scheduling. However, monitoring space and resources are limited within the IDS-designated area and shorter notice may not be feasible.
   3. Remote and on-site visits are to be limited to a maximum of 1 hour; however, visits can be extended if the IDS can accommodate, with prior approval at time of scheduling.
4. The IDS can accommodate no more than 2 monitors (1 remote and 1 on-site) during any given time frame, and no more than 8 hours of monitor visits per business day.
5. Frequency and number of monitor visits per study is specific to each protocol (no defined maximum per year per the IDS).
6. Remote and on-site visits must be completed during regular IDS business hours
7. On-site monitors are not permitted to enter the IDS pharmacy, which is located within the central pharmacy of the Huntsman Cancer Hospital.
   a. Restrictions to visualizing and/or handling investigational product and related-items may apply.
8. Only unblinded monitors are allowed to schedule monitoring visits with the IDS pharmacy.

E. Preparation for Monitor Visit completed by the IDS
1. After a monitor visit has been confirmed using the IDS monitor scheduling webpage, IDS personnel will send a standardized e-mail to the monitor, including the monitor SOP and Vestigo® access information.
2. Confirm that Vestigo® is complete and up-to-date for the specific studied being monitored.
3. Address and resolve any outstanding issues or data queries from prior monitoring visits.
4. Provide Vestigo® access day of the scheduled visit. Vestigo® access will expire by 1600 on the day of the visit.

F. Monitor Expectations
1. Upon arrival to the IDS-designated area, monitors will fill out and sign the Monitoring Visit Log if conducting an on-site monitor visit. For remote monitoring visits, monitors are required to enter a visit summary note within Vestigo®. This will document that the remote visit occurred.
2. Vestigo® access will be provided by the site.
3. All monitors will utilize and document within Vestigo® to perform drug returns/destruction, and perform all accountability. No additional drug accountability forms or documents provided by the monitor will be used for drug accountability.
4. Monitors must mark “returns” to be destroyed or to be sent back to the sponsor during the visit within Vestigo®. No additional drug accountability forms or documents provided by the monitor will be used for drug accountability.
   a. a. It is the responsibility of the monitor to send a packing box to the IDS pharmacy prior to the visit, provide a shipping label, count inventory. The drug will be packaged before the end of the visit.
5. Monitors will provide a summary of their review and findings at the conclusion of the monitoring visit within Vestigo®. Any additional reviews that are provided post-monitor visit will be filed electronically within Vestigo®.

G. Access to Study Information
1. Copies of study information may be provided to monitors in the following ways:
   a. Monitors may generate accountability logs (or any other electronic documents made available to them in Vestigo®) and save them to the IDS desktop or secured laptop, and send to sponsor e-mail.
      i. After the conclusion of a monitor visit, accountability logs are ONLY available via e-mail request. Printed accountability logs will be provided with an additional charge of special monitor fees to the study.
ii. The monitor must not send accountability records via personal e-mail in any circumstance due to noncompliance with HIPPA.

iii. Research records must only be sent to a sponsor e-mail address. It is the responsibility of the monitor to ensure the correct e-mail address is being used. If an inappropriate e-mail is used for sending research documents from Vestigo® then future monitoring visits may be revoked or refused.

b. Temperature monitoring logs will provide the monthly minimum/maximum temperatures and are ONLY available via e-mail after the conclusion of the monitor visit. Printed temperature monitoring logs will be provided with an additional charge of special monitor fees to the study.

c. All study documents and materials provided to the auditor/monitor for review must be secured at all times with pharmacy personnel or a member of the research team present (auditors or monitors may not be left alone with research documents).

H. Viewing Study Drug

1. The IDS pharmacy is located in the central pharmacy of Huntsman Cancer Hospital.

2. Monitors and auditors are not permitted in the central pharmacy per Utah state pharmacy law and senior pharmacy leadership except in the rare circumstance related to a for-cause situation.
   a. A request to access the pharmacy will be submitted to the Chief Pharmacy Officer who will review the request and decide if access is required.
   b. If approved, the monitor or auditor shall be accompanied 100% of the time by a member of the IDS staff while in the pharmacy.
   c. IDS staff will track these requests.

3. For on-site visits, please check in at suite 2110. A pharmacy technician will be dedicated to helping during the monitor visits (ie, on-site and remote).

4. Virtual viewing of investigational product stored under refrigeration, in the freezer, or at ambient temperature is available.
   a. IDS is able to take pictures of investigational product or participate in video calling service (eg, FaceTime) so the monitor may visualize the product.
   b. IDS is open to other ideas to visualize investigational product.
      i. Additional options will need to be approved by the IDS pharmacy manager.
      ii. The monitor should describe the option via e-mail to the IDS pharmacy at least one week prior to the scheduled visit.

5. Current inventory on-hand can also be accounted for within Vestigo® without direct visualization per monitor discretion.

I. Monitor/Audit Visit Follow-Up

1. All communication between monitor and IDS will be done through Vestigo® for items to be destroyed or returned.

2. All communication between monitor and IDS will be done through e-mail for any additional document procurement requested by the monitor post-monitor visit.

3. Communicate to the project pharmacist and IDS manager any issues that were discussed during the monitor visit.
   a. Ensure any issues or follow-up discussed during the visit are followed up on and/or completed that day or passed along to another technician/pharmacist.
4. Any potential issues identified at a monitoring visit or audit (including temperature excursions) should be provided to the PI, primary CRC, and the associated program manager.

J. Technician Responsibilities Related to Monitor/Audit Visit
   1. Prepare for monitor/audit visit (see above).
   2. Facilitate monitor visit.
      a. Refer the monitor or auditor to the virtual IDS pharmacy tour at first visit and upon request.
      b. Virtually escort the monitor throughout the pharmacy when needed (eg, to view IP when stored in fridge or freezer).

K. Pharmacist Responsibilities Related to Monitor/Audit Visit
   1. Mitigate any issues during the monitor/audit visit as identified by technician.
   2. Follow up on any outstanding issues prior to and after the monitoring/auditing visit as identified by technician.

Addendum

A. Letter to clinical drug study monitors and auditors (2019-09-24)

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Memorandum

TO: Clinical drug study monitors and auditors

FROM: Linda S. Tyler, PharmD
       Chief Pharmacy Officer

DATE: September 24, 2019

RE: Remote monitoring and decreased direct access to investigational drugs by study monitors and auditors

University of Utah Investigational Drug Service (IDS) currently uses remote study monitor visits. In this case, remote means not directly in the pharmacy—many monitors are on site for these visits. These remote visits use time-date-stamped pictures of the investigational product or live viewing through a video calling service. We implemented this to meet some regulatory and space constraints, however, we believe it offers increased options and flexibility for study monitors and auditors. It also provides an additional layer of documentation that we believe will be useful for study monitoring.

As part of implementing the remote study visits, we are also asking study monitors and auditors to decrease their need to have direct access to the study drug material. We need to make this request because of a recent change in the drug storage location for investigational drugs and the regulatory implications. I have included the details in the Appendix. Several things you can do to reduce your need for direct access to study drugs would include:

- Where possible, decrease the frequency that you need direct access to every 3-6 months or less and supplement with remote visits in between.
- If you have several studies at University of Utah, batch the study monitoring where possible and conduct the direct monitoring at one time.
- Decrease the amount of time you need to be in the drug storage area during your visit through careful planning with our IDS team.

When direct access is needed, you need to make this request in writing (by email) at least 4 weeks prior to the visit. As part of the request you need to be clear which studies will be reviewed and the purpose of the direct access. The purpose is necessary so we can appropriately plan for your visit. We recognize that access is required from time to time to meet FDA regulatory requirements as well as specific company policies related to drug study monitoring. All requests need to be approved by myself as the Chief Pharmacy officer or my designee, which in this case will be any of the 3 senior directors in our department. We know that in some cases 4 weeks’ notice will not be possible, but as much advance notice as possible is helpful to help prevent on-site delays and to ensure that the appropriate IDS staff is available for your visit.

Thank you in advance for your cooperation making this change. Direct questions or concerns regarding this policy to Elyse MacDonald, IDS Pharmacy Manager, Elyse.MacDonald@hsc.utah.edu, or Kavish Choudhary, Senior Director of Inpatient and Infusion Pharmacy Services, Kavish.Choudhary@hsc.utah.edu. Please see the SOP for Auditor and Monitor Visits (https://pharmacist.utah.edu/investigational-drug-service/pdf/sop-ids-auditor-monitor-visits.pdf) for additional information related to the new process. Please know that we are your partners in clinical research and want to do our very best to support you and to meet the regulatory requirements for pharmacy and clinical trials. We appreciate all your support as we work together through this new process.
Appendix: Background on implementing remote monitoring and decreased direct access to investigational drugs by study monitors and auditors

The IDS operations and investigational drug storage location has relocated to the central pharmacy at the Huntsman Cancer Hospital. This relocation was necessary so that we could remodel and update the facilities to meet regulatory compliance. Rest assured, all investigational drug study product is segregated from all other drug supplies. The following outlines the relevant regulations and standards that are pertinent in our desire to decrease the direct access to drug product in the pharmacy.

1. The remodel was conducted to meet USP <797> and USP <800> requirements.
   - USP <797> addresses the standards for pharmacy clean rooms and is a requirement of the Utah State Board of Pharmacy and our hospital accreditation standards.
     - The negative pressure area that we are storing some investigational drugs is adjacent to the entrance to the clean rooms.
     - We need to be cognizant of clean room dress code that specifies no jewelry and no make-up may be worn while in the area. Monitors and auditors entering the drug storage area will need to adhere to these standards. Feel free to clarify with the IDS staff if this requirement is needed for your visit prior to the visit.
   - USP <800> addresses the requirements we need to follow both in facilities and operations to protect employees from harm when handling hazardous substances. At University of Utah Health, as part of our risk assessment, we consider all investigational drugs as hazardous drugs.
     - It is very important to us that we keep our staff as safe as possible. As such, these safety measures would apply to anyone in the drug storage area.
     - These standards as well as USP <797> require Personal Protective Equipment (PPE) when you enter the area to prevent harm to personnel and maintain the clean room environment. We will provide you with any PPE that you may require for your visit (usually this would be gowns and gloves, but could include mask, booties or head covering.)

2. The Utah State Board of Pharmacy regulations do not allow for unauthorized people to be in the pharmacy. Unauthorized people in this context would be anyone who does not have a pharmacy license. Pharmacists and pharmacy technicians licensed in the State of Utah who are employees by University of Utah Health would be authorized personnel.
   - We need to balance the regulatory requirements with wanting to meet the study monitoring needs. We feel we can do this by decreasing the time that monitors spend in the pharmacy and specifically the drug storage area. We can do this by using remote monitoring, consolidating visits, and planning visits carefully to minimize the time in the pharmacy.
   - The State Board does not want unauthorized people to disrupt the pharmacy operations.
   - Study monitors and auditors are unauthorized people in this context. They can only be in the pharmacy if they are escorted, do not interfere with normal operations, and do not take staff away from patient care activities. When we can plan for visits, we are not interrupting staff to allow them to support monitors and auditors.
   - For reference, the following summarizes the specific citation from the Utah Pharmacy Practice Act and associated Rule.
     - Anyone not participating in the operations of the pharmacy thereby interrupting pharmaceutical care is considered unauthorized personnel according to the Utah Pharmacy Practice Act.
     - Utah Administrative Code R156-17b, states that allowing unauthorized personnel into a pharmacy is unprofessional conduct.
     - Permitting unauthorized personnel into the pharmacy may result in a fine and risks the licenses of the pharmacists and the pharmacy. Permitting a study monitor or auditor in central pharmacy pulls a pharmacist or pharmacy technician from normal pharmacy functions, interrupting patient care.