

**VAMHCS R&D SERVICE
STANDARD OPERATING PROCEDURE**

SOP: HRP 02.05

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AUDITING THE INVESTIGATIONAL DRUG SERVICE (IDS)

OBJECTIVE:

- To ensure that the operations of the Investigational Drug Service comply with VA and other federal regulations as well as VAMHCS and other local standards.
- To ensure that the operations of the Investigational Drug Service are routinely monitored by R&D Service staff.
- To ensure that remedial action is taken for any shortfalls found or, if the error cannot be corrected, to make changes in procedures to prevent future problems.
- To document internal quality assurance activities regarding the Investigational Drug Service.

BACKGROUND / SCOPE:

The VAMHCS R&D Service and the VAMHCS Pharmacy Service have formal policies in place for receipt, security, dispensing, accountability, and disposal of investigational entities. The R&D Service has designated its Human and Animal Research Protections Officer (HAARPO) to oversee quality management activities of the VAMHCS Investigational Drug Service (IDS). A routine audit of the Investigational Drug Service will occur at least on a biannual basis. The HAARPO is not responsible for quality management activities of the Pharmacy Service as a whole.

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RESPONSIBILITIES:

The Investigational Drug Pharmacist (IDP) is responsible for:

- collaborating with the VA Pharmacy Service in establishing internal policies and procedures governing the Investigational Drug Service and for having the policies approved through normal VAMHCS channels;
- complying with institutional, state and federal policies and regulations regarding the handling of investigational entities;
- keeping accurate records of receipt, dispensing and disposal of study entities;
- ensuring that satellite sites for studies conducted through the Investigational Drug Service (IDS) comply with all applicable policies and procedures;
- complying with applicable policies when the IDS is itself a satellite site;
- ensuring that his/her staff complies with internal policies and procedures, VAMHCS SOPs, GCPs, and other applicable policies;
- facilitating the efforts of staff in this process.

The Human and Animal Research Protections Officer (HAARPO) is responsible for:

- auditing the activities of the VAMHCS Investigational Drug Service according to the procedures outlined in this SOP;
- discussing audit findings with the Investigational Pharmacist and collaborating on a resolution plan as needed;
- reporting her/his findings to the ACOS/R&D and the R&D Committee

ATTACHMENTS (Available on the R&D Service website):

http://www.maryland.research.va.gov/research/human/human_subject_forms.asp

- "Study Subject Worksheet"
- "Pharmacy Audit Form A: Investigational Drug Dispensing Tool"
- Companion Tool for Pharmacy Audit Form A
- "Pharmacy Audit Form B: Investigational Drug Log Tool"
- Companion Tool for Pharmacy Audit Form B
- "Pharmacy Audit Form C: Investigational Drug Service Audit Report"
- VAMHCS Investigational Drug Service Drug Log

PROCEDURE:

1. Routine (scheduled) spot audit

- 1.1. As time and staffing allows, the Human and Animal Research Protections Officer (HAARPO) or designee may perform one or more audits per year (but at least biannually) on the Investigational Drug Service.
- 1.2. The auditor will notify the Investigational Pharmacist that an audit is due and will arrange for a site visit. Although the auditor will work independently during the

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audit, it is essential for the Investigational Pharmacist to be available to answer questions during the audit and to attend the exit interview.

- 1.3. The auditor will obtain a list of active studies administered by the Investigational Drug Service. The auditor will randomly select 3-5 studies depending on the total number of studies, but will audit more if necessary. The auditor will try to include VA Cooperative Studies, industry studies, Greenebaum Cancer Center studies, and investigator-initiated studies in the sampling of studies to be audited.
 - 1.4. The R&D Service may adjust the audits based on the type & situation of audit being conducted.
 - 1.5. The auditor will use versions of the forms and procedures outlined in #3.3 below.
 - 1.6. At the conclusion of the audit, an exit interview will be held with the Investigational Pharmacist to review and clarify audit observations, answer questions, and collect feedback on the audit process.
 - 1.7. An audit report will be completed. If necessary, resolution plans will be negotiated with the Investigational Pharmacist and documented on the "Investigational Drug Service Audit Report".
 - 1.8. The resolution plan should be completed within the following two (2) weeks. The auditor will conduct follow-up assessments as needed until the plan is completed and signed off by the HAARPO.
 - 1.9. Final Reports (see #5 below) will go to the Investigational Pharmacist, the the ACOS/R&D, the R&D Committee, EPIC, the IRB, and regulatory agencies if necessary. The Chief, Pharmacy Service is also made aware of audit results. The Investigational Pharmacist and the Chief, Pharmacy Service will be notified in writing if there is a possibility of inspection by regulatory authorities. See item #4 below for details about the Final Audit Report.
 - 1.10. Original audit sheets, notes and reports are filed in the R&D Service.
2. For-cause audits
- 2.1. For-cause audits can be generated by the findings of routine audits (e.g. the audit finds cause for deeper scrutiny and problem-solving) or by complaints or allegations of noncompliance.
 - 2.2. The HAARPO or other appropriate person performs the audit.
 - 2.3. Little prior notice is given to the Investigational Pharmacist.
 - 2.4. Enrollment of new subjects to some or all studies administered by the Investigational Drug Service may be halted pending the conclusion of the audit.
 - 2.5. The auditor first assesses the basic problem/complaint. It is possible that an exhaustive root cause analysis will not be necessary if the Investigational Pharmacist has already identified and activated remedial actions, if the problem/complaint does not appear to be related to the Pharmacy Service itself, if the problem/complaint does not appear to be institutionally related, if the problem/complaint does not appear based in fact, or other reasons. The auditor must report to the ACOS/R&D and the RDC, the reasons why a full audit is not performed.
 - 2.6. If there appears to be reason for a thorough audit, an audit plan is specifically designed to examine the area of concern. This audit plan may necessitate the development of specific audit tools. VAMHCS Risk Management or

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- Performance Improvement may be included as an auditor or as a second prong in the audit approach.
- 2.7. Up to 100% of charts may be subject to audit.
 - 2.8. The HAARPO may conduct study audits, regulatory document audits, inspections of internal policies and procedures and SOPs, and audits of compliance with R&D Service/VAMHCS policies, procedures and SOPs. The R&D Service reserves the right to audit other documents as necessary for the type & situation of audit being conducted.
 - 2.9. At the conclusion of the audit, an exit interview will be held with the Investigational Pharmacist to review and clarify audit observations, answer questions, and collect feedback on the audit process. If necessary, resolution plans will be negotiated with the Investigational Pharmacist and documented on the "Investigational Drug Service Audit Report".
 - 2.10. An audit report will be completed. If necessary, resolution plans will be negotiated with the Investigational Pharmacist and documented on the "Investigational Drug Service Audit Report".
 - 2.11. The Resolution Plan should be completed within the following two (2) weeks. The HAARPO will conduct follow-up assessments as needed until the Plan is signed off.
 - 2.12. Final Reports (see #4 below) will go to the Investigational Pharmacist, the R&D Committee, the ACOS/R&D, EPIC, the IRB, and regulatory agencies if necessary. The Chief, Pharmacy Service is also made aware of audit results. The Investigational Pharmacist and the Chief, Pharmacy Service will be notified in writing if there is a possibility of inspection by regulatory authorities. See item #4 below for details about the Final Audit Report.
 - 2.13. Original audit sheets, notes and reports are filed in the R&D Service.
3. The audit process is outlined below. The process is similar whether for a "routine audit" or a "for cause audit".
 - 3.1. The HAARPO/designee obtains selected charts from the Investigational Pharmacist and initiates the audit using pharmacy audit tools and worksheet.
 - 3.2. The HAARPO/designee examines the pharmacy chart(s) and completes the audit tools in the following order:
 - i. Part 1 of "Pharmacy Audit Form C: Investigational Drug Service Audit Report" (this section contains information on the studies audited)
 - ii. "Study Subject Worksheet" (collects data needed to complete Form A)
 - iii. "Pharmacy Audit Form A: Investigational Drug Dispensing Tool" (contains information on the pharmacy files)
 - iv. "Pharmacy Audit Form B: Investigational Drug Log Tool" (specifically audits the drug log)
 - v. Parts 2-3 of the "Pharmacy Audit Form C: Investigational Drug Service Audit Report" (summarizes the findings)
 - 3.3. Each form has a companion guide which may be used by the auditor if necessary for guidance on completing the forms.
 - 3.4. If a problem is discovered, it is noted in the comments sections or in Part 3 of Form C.
 - 3.5. The auditor retains the original audit forms. Copies may be given to the Investigational Pharmacist. The auditor gives the pharmacist a copy of the Audit

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Report and schedules a follow-up review of resolutions for approximately two weeks from the date the report is given to the Investigational Pharmacist.

4. Formal reports will be developed as follows:
 - 4.1. Observations will be listed in the audit report (Part 3 of Form C) in order of decreasing significance.
 - 4.2. The audit report will also describe any resolution plan(s) and the compliance with or results of implementation of those plans.
 - 4.3. The final audit report will be presented to the R&D Committee, the ACOS/R&D, EPIC, the IRB, and regulatory agencies if necessary. The Chief, Pharmacy Service is also made aware of audit results with the addition of comments from the oversight committees. If applicable, the PI will be asked to respond to issues raised by the committees.
 - 4.4. Follow-up discussions, documentation, reports and letters will occur as necessary until the issue(s) are resolved to the greatest extent possible.
 - 4.5. The Full Audit report will summarize all of these developments and will be forwarded to the entities listed in 1.9 and 2.12 above.
 - 4.6. If necessary, regulatory agencies such as ORO, OHRP, the FDA, etc., will be notified. The PI and the Division Chair will be notified in writing if regulatory authorities have been notified.

REFERENCES

Pharmacy assessment tools from the Center on Assessment and Compliance Help (COACH)

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Appendix 1

R&D Service Pharmacy Audit Tools are available on the R&D Service website:
http://www.maryland.research.va.gov/research/human/human_subject_forms.asp

“Study Subject Worksheet”

“Pharmacy Audit Form A: Investigational Drug Dispensing Tool”

COMPANION TOOL for Pharmacy Audit Form A

“Pharmacy Audit Form B: Investigational Drug Log Tool”

COMPANION TOOL for Pharmacy Audit Form B

“Pharmacy Audit Form C: Investigational Drug Service Audit Report”