



Walter Reed Army Institute of Research
 Division of Human Subjects Protection
 Standard Operating Procedure

SOP Title	DIRECTED (FOR CAUSE) MONITORING OF HUMAN SUBJECTS RESEARCH	SOP No. Version	UWZ-C-634 .01
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Signatures and Dates:

Author:

QA Director: For signatures, please see original in the Division of Human Subjects Protection

WRAIR IRB
 Administrative
 Director:

Review/Approval for unchanged documents

Date	Author	QA Review	Approving Authority



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- 1. Purpose/Applicability:** This Standard Operating Procedure (SOP) sets forth a mechanism for monitoring compliance with human subject protection requirements as required for Institutions that hold a United States (U.S.) Department of Health and Human Services (DHHS), Office for Human Research Protections (OHRP) Federalwide Assurance (FWA) and Department of Defense (DoD) Assurance. In addition, the findings provide opportunity to identify and develop focused training programs for Walter Reed Army Institute of Research (WRAIR) investigators, their research staff, Division of Human Subjects Protection (DHSP) staff and the WRAIR Institutional Review Board (IRB) members.

Directed reviews (monitoring) of human subjects protection compliance are conducted at the request of the WRAIR IRB, the Institutional Official (IO), or the DHSP Director due to unusual circumstances, potential significant risks to subjects, routine failure on the part of an investigator to comply with federal and/or institutional requirements, or allegations/concerns about the conduct of the study.

- 2. Responsibilities:** This SOP applies to the DHSP Director and Staff, WRAIR IRB members, the WRAIR IRB Chair/Designee and the IO.
 - a. The DHSP Staff (hereafter, referred to as the 'monitors') assist the IRB in conducting the monitoring visit and completing the subsequent report, and keep the DHSP Director informed of the monitoring activities.
 - b. WRAIR IRB members participate in the monitoring visit, complete a report and, identify/address non-compliance per SOP UWZ-C-606. If appropriate, provide this report for review and determination by the IRB.
 - c. The WRAIR IRB Chair/Designee reviews the monitoring report and, when appropriate, the response from the Principal Investigator (PI).
 - d. The IO and the Office of Quality Activities (OQA) are informed if non-compliance is discovered during directed monitoring, per the Non-Compliance SOP (UWZ-C-606).
 - e. The IO has the responsibility to review the recommendations of the WRAIR IRB and determine appropriate actions within the scope of his/her authority.



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3. Investigator Guidance:

The PI/WRAIR POC is expected to:

- a. Respond to all requests for information from the monitors and IRB, and
- b. Comply with any determinations made by the IRB and the IO regarding the research or appeal the decision in accordance with Appeal of IRB Decision SOP (UWZ-C-612).

4. Background:

Directed reviews are typically conducted by at least one WRAIR IRB member and one DHSP monitor. In addition, other appropriate individuals (i.e. quality assurance, regulatory affairs, etc.) may assist in directed reviews. All of the members of a given monitoring team are subject to the procedures outlined herein.

The monitors may review the WRAIR IRB's records to determine accuracy and consistency with the investigator's research records and to verify that the investigator made no material changes to the protocol without WRAIR IRB approval and WRAIR Commander's authorization to implement. Once the report has been drafted and finalized by DHSP, it is then sent to the IRB Chair, Office of Quality Activities and the IO. The findings of the directed review are then shared with the PI, research staff, and reported to the WRAIR IRB. If in reviewing the results of a directed review, the WRAIR IRB determines that the exposed deficiencies warrant suspension or termination of the research, the WRAIR IRB develops a plan for follow-up, which may entail, but is not limited to, a subsequent review or monitoring of the informed consent process.

When the WRAIR IRB receives reports of findings from directed reviews, the IRB determines whether to report the findings to the study Sponsor, other participating IRBs, the Food and Drug Administration (FDA), the OHRP, other regulatory agencies, or WRAIR management.

When the WRAIR IRB serves as the IRB of record and at a fully convened meeting makes a finding of serious non-compliance or continuing non-compliance, the findings must be promptly reported to the U.S. Army Medical Research and Materiel Command (USAMRMC) Human Research Protections Office (HRPO), in accordance with Command Policy 2010-03 and U. S. Army



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Human Research Protections Office (AHRPO), in accordance with ALARACT 031/2008, paragraph 4c(1).

5. Procedures:

- a. Upon notification that the WRAIR IRB, the IO or the DHSP Director has requested a directed review, the DHSP Human Subjects Protection Scientist (HSPS) confirms which specific protocol will undergo monitoring and enters the request into the WRAIR DHSP database to reflect initiation of the review request.
- b. Once it is determined which protocol(s) will undergo inspection, the IRB Chair or the DHSP Director notifies the PI by phone or in person of the upcoming directed review and explains the impetus of the directed review. This is followed by a written notice, which is copy-furnished to the PI's Department Chief, Division Director, and/or Detachment Commander. The time frame of advance notice of an on-site review will be determined on a case-by-case basis depending on what precipitates the directed review (i.e. subject safety, non-compliance with policy). When a review is to be conducted at a distant site location (i.e., U.S. Army Medical Research Unit-Kenya, U.S. Army Medical Research Unit-Europe, Armed Forces Institute of the Medical Sciences) travel preparation and time must be considered when establishing the review dates. Staffing the visit through the site coordinator(s) is essential.
- c. The monitors conduct entrance and exit interviews with the PI, and his/her Department Chief/Division Director/Detachment Commander, as appropriate. At the PI's discretion, select research staff may also attend.
- d. Prior to the visit, the monitors may study the IRB meeting minutes from the initial protocol review and any subsequent actions (i.e., amendments, continuing reviews), the WRAIR IRB records and database to become familiar with the protocol(s) and to identify any specific items to address during the review process.
- e. The entrance interview precedes the review of the PI's research records/ongoing study activities. The monitors may use this time to explain the goals of the review and the impetus behind the directed review. It also allows the PI/research staff an opportunity to explain what the protocol entails, respond to the issues which instigated the directed review, and answer any questions arising from the monitor's review of the WRAIR IRB protocol records.



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- f. The records, activities and items to be reviewed at the PI's site may consist of, but are not limited to, the following:
1. Protocol Binder/Regulatory Documentation - noting whether the records retained meet all applicable regulations, such as Federal, International Conference on Harmonisation/Good Clinical Practices, Institution and IRB guidelines;
 2. IRB Documentation - comparing the PI records with the IRB records. Review of IRB documentation affords the opportunity to determine whether the PI made material changes prior to WRAIR IRB approval and IO Implementation Authorization;
 3. Consent Forms - when applicable, examining consent forms used to enroll the subjects to ensure that the subjects signed the appropriate consent form for their respective study and that the forms were properly signed and dated;
 4. Case Report Forms (CRF) - when applicable, determining if the subjects met the inclusion criteria and none of the exclusion criteria for their respective study, the PI/research staff recorded and documented study activities properly and whether records serve as both a CRF and a source document;
 5. Source Documents/Medical Records- when applicable, reviewing medical records for clinical trials to verify the information in the CRFs, including storage and security, and documentation that a copy of the consent form has been provided to the volunteer(s);
 6. Electronic and hard copy study data to verify consistency with CRF, source documents and approved protocol;
 7. Sponsor monitoring reports and/or follow-up letters, if applicable;
 8. Study Logs –subject enrollment logs, PI delegation of authority logs, study team signature/initial logs, study-specific training, human subjects protection training, etc. and when applicable, drug accountability logs, specimen storage logs, will be reviewed;
 9. Observation of the consenting process and other study procedures;
 10. Direct contact with individual subjects; and



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11. Reports – serious adverse event reports, deviation reports, unanticipated problems involving risks to subjects, continuing review reports, etc.

NOTE: Activities 9 and 10 may occur at a separate time from the initial monitoring depending on the study schedule of events and subject availability.

For assistance/clarification during the review, the monitors may contact the PI directly or, if applicable, inquire with the PI's research staff.

- g. The WRAIR IRB may request monitoring of the consent process as part of the directed review, using procedures which include, but are not limited to:
 - 1) Questioning research subjects enrolled in the study about the informed consent process and their experience as a research subject;
 - 2) Witnessing administration of informed consent to subject candidates. Frequency of monitoring the consent process is determined on a case-by-case basis by the IRB; examples of determining factors include level of risk, enrollment activity, funding agency, and targeted subject population.
- h. The monitors conduct the exit interview after the completion of their review of the PI's records/study activities and may ask for clarification regarding the protocol or research procedures at that time. The monitors provide the investigator with a verbal summary of the findings and explain the remaining procedures for conclusion of the directed review. A hard copy of the Query and Clarification Form (Appendix D) will also be provided to the PI at the exit interview. The PI will be afforded the opportunity to clarify findings or correct inaccuracies at this time. The PI is encouraged to provide immediate correction to any misinterpretations presented by the monitors.
- i. After the exit interview, the monitors prepare a Monitoring report (Appendix B) outlining the findings of the review pertinent to the PI records, on-site observations and interviews with the investigator, research personnel and subjects, if applicable. All monitors will be given an opportunity to review and edit the report prior to finalization. As a means of maintaining confidentiality, the monitors will not record subject's protected health information in the directed review findings disseminated to the WRAIR IRB.
- j. The DHSP Director reviews the final report prior to it being sent to the PI. The deadline for completing the report will be on a case-by-case basis as to the urgency of the issue and the timeframe of the next WRAIR IRB meeting.



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Typically, the monitors have several weeks to complete their report. Please note: Issues which may put the study subjects at risk will be immediately reported to the IRB Chair. If there is a safety issue or serious or continuing non-compliance the WRAIR IRB Chair can halt the study. (See Non-compliance Procedures SOP UWZ-C-606)

- k. Once the review report is complete, the report is provided to the IO, WRAIR IRB Chair and members, DHSP Director, and Director, OQA.
- l. The DHSP or OQA then provides the report to the PI with a requested response date determined on a case-by-case basis. When a PI's response to the monitoring report is required, the response is reviewed by the DHSP Director, IRB Chair, or designee and OQA. In addition, consultants or WRAIR IRB members may be asked to review the report. These persons are referred to as sub-committee/subject matter experts. Unless previously determined, at this time a determination is made by the sub-committee/subject matter experts as to whether the report and response require review by a fully convened board. If appropriate, the DHSP schedules a review of the PI response with the full IRB at the next available convened meeting.

Only the fully convened IRB can make a determination of serious non-compliance or continuing non-compliance (Command Policy 2010-03).

- m. In the DHSP database, the HSPS enters that the protocol(s) was "Monitored by DHSP" and/or "WRAIR IRB" (Appendix C).
- n. For any findings requiring review by the full IRB, the IRB members vote for one of the following actions:
 - 1) Approved- No further action is required. The DHSP sends a notice to the PI describing the outcome of the WRAIR IRB review.
 - 2) Revision/additional information requested - The IRB may give the Chair the authority to approve the revisions/additional information or require review of the revisions/additional information at a convened meeting. If the IRB request necessitates further review, the DHSP acts accordingly and processes any additional findings/information for review based on the IRB determination at the convened meeting (either given to the Chair or assigned to a convened IRB meeting for review). If the IRB request necessitates a response from the PI, the IRB Chair or Director, DHSP informs the PI of the IRB's request.



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When the PI responds to the WRAIR IRB's request in writing, the DHSP processes the response based on the IRB determination at the convened meeting (either given to the Chair or assigned to a convened IRB meeting for review). If the Chair is the IRB's designated reviewer, he/she may decide to forward the response to the entire IRB for additional review, request additional information, or approve.

- 3) Suspension or termination of the research. (See Non-compliance Procedures SOP UWZ-C-606). The IRB Chair or DHSP Director communicates the outcome of the WRAIR IRB review to the PI. The outcome is provided to the PI in writing. Appeals are managed as per Appeal of IRB Decisions SOP (UWZ-C-612).

When the IRB receives reports of non-compliance findings from reviews, the IRB determines whether to report the findings to the study Sponsor, FDA, other regulatory agencies, OHRP, the IO, other participating IRBs, WRAIR management, USAMRMC ORP, and/or AHRPO, as appropriate. (See section 4)

- o. Copies of all correspondence and reports will be kept in the DHSP files for the protocol(s).
- p. Copies of query sheets & worksheets (Appendices A, C, & D) may be destroyed after final resolution of the Monitoring activity since these are worksheets and the information on these sheets may not coincide with the final monitoring report.



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6. Explanation of Abbreviations and Terms:

AHRPO	Army Human Research Protections Office
CRF	Case Report Forms
Directed Monitoring	A determination by the Institutional Official, WRAIR IRB or DHSP Director that an issue regarding human subject protections and/or compliance with human subject research regulations and policies needs timely planning and direct exploration.
DHHS	Department of Health and Human Services
DHSP	Division of Human Subjects Protection; the administrative support of the WRAIR IRB.
Human Subjects Research	Research involving humans as research subjects, or involving biological specimens, data, specimens from repositories or anatomical substances of human origin. This includes the administration of questionnaires or surveys, as well as research done in an educational setting.
IRB Chair	includes Designee (if recusal)
IRB of Record	The IRB that assumes primary responsibility of the human subjects protection review and oversight of a protocol, and that is designated in the institution's DoD Assurance of Compliance for the Protection of Human Research Subjects or through a signed DoD Institutional Agreement for IRB review.
IO	Institutional Official
Monitors	DHSP staff, IRB members and others, as requested, that are responsible for conducting monitoring visits
Non-Compliance	Failure of a person, group or organization to act in accordance with a law, regulation, or policy governing human subjects research, the requirements and/or determinations of the overseeing IRB, or the research protocol.
OHRP	Office of Human Research Protections



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PI Principal Investigator or WRAIR POC

POC Point of Contact

USAMRMC ORP HRPO U.S. Army Medical Research and Materiel Command, Office of Research Protections, Human Research Protections Office

WRAIR IRB WRAIR Institutional Review Board; the ethical review committee for research involving human subjects as per the cited regulations and policies at WRAIR, its CONUS detachments or Overseas Laboratories, or when WRAIR funding, facilities or personnel are involved in any way (investigator, medical monitor, consultant, collaborator, etc.). This includes protocols for which recruitment of subjects is through WRAIR. Formerly the WRAIR Human Use Review Committee (WRAIR HURC).



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7. References:

Reference Number or Authors	Document Title
WRAIR IRB Charter, Version 6	Walter Reed Army Institute of Research (WRAIR) Institutional Review Board (IRB) Charter, Version 6, dated 30 July 2008
WRAIR HRPP, Version 1.2	Walter Reed Army Institute of Research (WRAIR) Human Research Protections Program (HRPP), Version 1.2, dated 30 July 2008
Command Policy 2004-11	Standard Operating Procedures (SOP) for Food and Drug Administration (FDA) Regulated Activities within the Command, 1 September 2004.
Command Policy 2010-57	Policy for the Adherence to Good Clinical Practices During Food and Drug Administration-Regulated Clinical Research Activities
Command Policy 2010-03	Investigating, Managing, and Reporting Non-compliance with Human Subjects Research Regulatory Requirements for US Army Medical Research and Materiel Command (USAMRMC) Intramural Research
ALARACT 031/2008	Message, DTG, 14155YZ February 2008, subject: ALARACT 031/2008, Army Human Subject Protection Requirements
AR 40-7	Use of Investigational Drugs and Devices in Humans and the Use of Schedule 1 Controlled Drug Substances
AR 40-38	Clinical Investigation Program
AR-40-68	Clinical Quality Management, 26 February 2004.
AR-70-25	Use of Volunteers as Subjects of Research, 25 January 1990
DOD Directive 3612.02	Protection of Human Subjects and Adherence to Ethical Standards in DoD Supported Research
ICH-GCP-E6	<i>Guideline for Good Clinical Practice.</i>



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OHRP Guidelines	<i>Guidelines for Formulating Written WRAIR IRB Policies and Procedures, 11 July 2002. http://ohrp.osophs.dhhs.gov/WRAIR_IRB/WRAIR_IRB_guidebook.htm</i>
Titles 21, 32 and 45	<i>Code of Federal Regulations</i>
Title 10. 980	<i>Limitations on Use of Humans as Experimental Subjects</i>
Amdur, R. J. and Bankert, E. A.	<i>Institutional Review Board Management and Function. Boston: Jones and Bartlett Publishers, 2005.</i>
SOP UWZ-C-606	Non-Compliance Procedures Standard Operating Procedure
SOP UWZ-C-612	Appeal of IRB Decisions Standard Operating Procedure

7. Forms and Appendices:

Form or Appendix Number	Title
UWZ-C-634-A Appendix A	IRB Directed Monitoring Worksheet
UWZ-C-634-B Appendix B	Directed Monitoring Report Format
UWZ-C-634-C Appendix C	Worksheet for Monitoring Event entry in IRB Database
UWZ-C-634-D Appendix D	Query and Clarification Form



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8. Document Revision History:

Version Number	Brief Description of Changes	Effective Date
.00	New	15 October 2008
.01	Biennial Review; updated for consistency with current policies/procedures	APR 0 6 2011

Appendix A	IRB Directed Monitoring Worksheet	SOP No. Version	UWZ-C-634 .01
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WRAIR protocol #:

Date(s) Monitoring Conducted:

Monitor(s) (names):

Title of Project(s):

Principal Investigator (name):

IRB(s) of Record (name):

Other Collaborating IRB(s):

Directed Monitor Summary

At the Exit Interview an oral summary of the review and a hard copy of the Query and Clarification Forms were provided to the PI

Monitoring Report submitted to:

- Director, Division of Human Subjects Protections**
- Director, Office of Quality Activities**
- Chair, WRAIR IRB**
- WRAIR Commander**
- Principal Investigator**
- Others (specify): (Ex. Department Chief/Division Director/Detachment Commander)**

Monitors' Recommended Response:

- None**
- Exposed valid deficiencies require written response from the PI to the DHSP**
- Exposed valid deficiencies require written response from the PI to the IRB**
- Exposed valid deficiencies may require IRB reporting to the FDA, OHRP, the study sponsor, convened IRB, or others**

Status of Monitoring:

- Closed Date: _____**
- Remains open pending follow up**
Specify:

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Monitoring Team Comments:

Signature of Monitor

Date

**Note: Add signature lines for all participating monitor(s) and Institutional Review Board members, as applicable.*

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Part A – WRAIR IRB Regulatory File (Background Information)

1. Prior to the monitoring visit the reviewers may study the following to become familiar with the protocol and to identify any specific points to address during the review:

- | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>a. WRAIR IRB records (noting versions) to include:</p> <ul style="list-style-type: none"> - Current approved protocol - Current approved informed consent document(to include assents and back translations and v - Prior approved informed consents noting reason for revision - Investigator Brochure (if applicable) - Adverse Event or Unanticipated Problems reports - Amendments - Deviation reports - Continuing review application(s)/approval(s) - Host country approvals (to include continuing review approvals) - Collaborating IRB approvals (to include continuing review approvals) - Correspondence between the IRB and Investigator |
| b. WRAIR IRB database specific to the protocol(s) |
| c. WRAIR IRB Meeting Minutes specific to the protocol(s) |
| d. Any Previous Monitoring Reports |

Monitor Comments or Concerns:

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Part B – Investigator Regulatory File

2. Does the investigator have a comprehensive and secured file containing the following records:

	Yes	No	NA
a. IRB approved protocol (version _____)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Investigator's Brochure (version _____)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. IRB approved amendments	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Current IRB stamped/approved copy of the informed consent (version _____)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Translated consent forms and verification certificates			
f. Recruitment flyers/Study Advertising (version _____)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. Study Logs			
1. Study Team Signature/Initial	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Screening			
3. PI Delegation of authority			
4. Product (drug/biologic/device) accountability			
5. Deviation			
6. Training (SSPs, etc)			
7. AE/UAPs			
8. Specimen Storage/Shipping Log			
9. Subject Enrollment			
10. Other _____			
h. All Safety reports for investigational new product	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
i. Adverse Event reports	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
j. Other relevant safety information	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
k. Records of continuing reviews	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
l. IRB review and approval letters, and Command implementation approval, as applicable (i.e. protocol, informed consent, amendments, continuing review, adverse events, unanticipated problems, deviations)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
m. All correspondence between the IRB and Investigator	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
n. Sponsor Monitoring Reports/Follow-Up Letters	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
o. Financial Disclosure Forms	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
p. FDA form 1572	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
q. Secure and appropriate storage of Regulatory files	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
r. DSMB/SMC/IDMC reports/summaries	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
s. Training files (CVs, CITI, licenses, BLS, etc.)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
t. Normal clinical/research laboratory ranges (Lab certs: CLIA/CLIP/CAP)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
u. Other regulatory review approvals (IBC, RSC, RAC, OBA, PPB, etc.)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Comments or Concerns:

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Part C – Subject Documentation Review

3. Did the investigator implement the protocol as approved by the IRB according to the following criteria? (See “NOTE” below)

	Yes	No	NA
a. The current IRB-approved version of the consent form was used.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. The consent form(s) were signed and dated by the subject (initial and subsequent informed consent).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. IRB-approved inclusion and exclusion criteria for subject accrual were met.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. The date of the first intervention(s) is consistent with the date that the consent form was signed and after the WRAIR Commander’s Authority to Implement.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. All research related procedures performed were described in the IRB-approved protocol.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Subjects received only the approved dose range(s) of the study drugs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. All serious adverse events or unanticipated problems were promptly reported to the IRB	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h. All protocol modifications were implemented only after IRB approval and WRAIR Command implementation approval, except when in the immediate medical interest of the subject.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
i. The number of evaluable subjects accrued was within the IRB approved limit (briefed, screened vs. enrolled, replacements appropriate).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
j. The procedures for ensuring privacy and monitoring the confidentiality of data and specimens were implemented as approved by the IRB.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
k. Secure and appropriate storage of subject research documents, specimens/data	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
l. Documentation that Subject received a copy of the consent form	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
m. There are distribution log for payments.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

NOTE: Generally, the number of subject records (may include original data, case report forms (for FDA regulated studies), medical records, and electronic/hard copy study database) will be 10% of the total number of records. At a minimum, review 4-6 individual subject records. Four to six records may be sufficient if no major problems are identified. If major problems are identified it would be sensible to review additional records and even possibly all subject records. The number of individual subject records to be monitored may vary.

If applicable, use Query and Clarification Form (Appendix D) for noting specific problems.

Total Number of Subject Charts: _____ Total Number of Subject Charts Reviewed: _____

Comments or Concerns:

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Part D- Observations

4. Observation of the consent process:

- Direct observation of the consenting of subjects
- Individual interview with study subject
- Interview with Principal Investigator or Research personnel

	YES	NO
a. Was the environment in which the consent process took place conducive to rational and thoughtful decision making on the part of the subject? Observation:	<input type="checkbox"/>	<input type="checkbox"/>
b. Was the length of time devoted to the consent process sufficient? Observation:	<input type="checkbox"/>	<input type="checkbox"/>
c. Was the subject given an adequate explanation of the research using appropriate simplified language? Observation:	<input type="checkbox"/>	<input type="checkbox"/>
d. Was the subject given adequate opportunity to ask questions? Observation:	<input type="checkbox"/>	<input type="checkbox"/>
e. Did the subject demonstrate an acceptable understanding of the research before signing the consent form? Observation:	<input type="checkbox"/>	<input type="checkbox"/>
f. Is the individual performing the informed consent appropriate for the process? Observation:	<input type="checkbox"/>	<input type="checkbox"/>
g. Is the consent form available in the local language? Comment:	<input type="checkbox"/>	<input type="checkbox"/>

If the optimal direct observation of the consent process is not possible a direct subject interview (with appropriate consent) would be the next option. Otherwise request that the investigator and/or research personnel describe how the above processes were conducted. How does this compare to the approved protocol and the basic tenants of human subject protections?

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Observation of study procedures:

Observation of staff's training/ability to carry out the study safely:

	YES	NO
a. Did the subject meet all the inclusion and exclusion criteria? Observation:	<input type="checkbox"/>	<input type="checkbox"/>
b. Were the correct activities done for or by the subject at each visit? Observation:	<input type="checkbox"/>	<input type="checkbox"/>
c. Did the subject come in for each visit during the appropriate time period? Observation:	<input type="checkbox"/>	<input type="checkbox"/>
d. Was the subject given the appropriate drug and the appropriate amount at each visit? Observation:	<input type="checkbox"/>	<input type="checkbox"/>

5. Are there appropriate resources such as equipment, maintenance of equipment?

Describe the availability and appropriateness of the space utilized to conduct study activities.

Comments or Concerns:

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Part E- Interviews with the Investigator and Research Personnel

6. Did the investigator and/ or research personnel identify any of the following:

	YES	NO
a. Did the investigator encounter any problems in recruitment, subject retention, or other area? If so, what was the nature of the problem and how was it addressed?	<input type="checkbox"/>	<input type="checkbox"/>
b. Did any subject suffer a serious, unanticipated adverse event? If so, what was the nature of the event and how was the subject treated?	<input type="checkbox"/>	<input type="checkbox"/>
c. Do the investigator and/or research staff report any difficulties with the IRB review process, staff, etc.? If so, what are the problems and proposed solutions?	<input type="checkbox"/>	<input type="checkbox"/>

The interview is a time when problems identified during the records review can be discussed and any necessary clarifications obtained. It is also an ideal time to educate the investigator and his/her staff.

Comments or Concerns:

Part F- Preparation of the Report and Follow Up

6. After the monitoring visit is completed and all findings are analyzed and determined to be valid, construct a written report. Include recommendations for how deficiencies can be best corrected with appropriate citations of the federal regulations and institutional policies. (See attached report format)
7. If significant/major deviations from the approved protocol or non-compliance is found, a brief summary should be sent to the Director, DHSP and the IRB Chair. A determination will be made by the fully convened IRB regarding serious or continuing non-compliance. If evidence of serious and/or continuing noncompliance is found (please refer to the Non-Compliance Procedures SOP UWZ-C-606) this must be reported promptly to Institutional official and the OHRP, if applicable. If the research involves use of an FDA-regulated product noncompliance must also be report to the FDA.
8. If IRB review of this monitoring activity is required, submit the written report and, if required, the PI response report.

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[DATE]

(U) Directed Monitoring and Review of the Human Subjects Protection [Protocol # Title] On [date] the Walter Reed Army Institute of Research (WRAIR) Division of Human Subjects Protection (DHSP) and/or [IRB] conducted a [directed monitoring visit]

The primary purpose of the monitoring was to [add appropriate info here, i.e. to review study records for compliance with human subjects protection requirements, and to identify opportunities to provide additional support to [name] in the conduct of human subjects research].

NAME
Position
Contact Information

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MCMR-UWZ-C

[date]

MEMORANDUM FOR Commander, Walter Reed Army Institute of Research, 503 Robert Grant Avenue, Silver Spring, MD 20910

SUBJECT: Directed Monitoring Visit and Review of [name] Human Subjects Protection Program, [date of event]

1. References. [modify as appropriate]

- a. Belmont Report: Ethical Principles and Guidelines For Research Involving Human Subjects. Federal Register Document 79-12065
- b. 10 USC 980 Limitations on Use of Humans as Experimental Subjects
- c. International Conference on Harmonization (ICH): Guideline for Good Clinical Practices
- d. 32 CFR 219, Department of Defense (DoD) Protection of Human Subjects
- e. 45 CFR 46, Department of Human Health Services (HHS), Protection of Human Subjects, inclusive of Subparts A, B, C and D.
- f. 21 CFR Parts 50 and 56, Food and Drug Administration
- g. DoD Directive 3216.02, Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research
- h. Army Regulation (AR) 70-25, Use of Volunteers as Subjects of Research
- i. USAMRMC Command Policy 2008-10, USAMRMC Quality Policy
- j. WRAIR Human Research Protections Program, Version 1.2, dated 30 July 2008

2. Team Membership. The monitoring was conducted by the following representatives from the WRAIR Division of Human Subjects Protections (DHSP):

- a.
- b.
- c.

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WRAIR Institutional Review Board (if applicable):

- a.
- b.

U.S. Army Medical Research and Materiel Command (if applicable)

- a.
- b.

Others (if applicable)

- a.
- b.

3. Purpose/Plan. The purpose of the [type] visit was to:

- a.
- b. [add as appropriate to the specific monitoring]
- c.
- d.

4. Findings

- a. [add specific monitoring findings]

5. Areas in which continuing human subjects protection and regulatory compliance training are needed:

- a. [add any specific to this monitoring event]

6. Items that require further action/clarification:

- a. From DHSP or IRB to [site]

- b. From [site] to DHSP or IRB

7. Recommendations:

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Additional Attachments:

Appendix A: Review of records, databases and additional discussions

Appendix B: Documents provided to [site] during this visit:

Appendix C: Pertinent Documents prior to this report:

Appendix C	Worksheet for DHSP Database Entry of Monitoring Activity	SOP No. UWZ-C-634	Version .01
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Information to be recorded in the DHSP Database:

- **Date of Review Request**
- **Monitoring Type and Reason for the Monitoring**
- **Names of Monitor(s)**
- **Documentation of Communication to PI regarding notification of pending monitoring visit (to include means of communication, who communicated the information, location of the visit and any other pertinent discussion about the pending monitoring visit)**
- **Date(s) monitoring visit conducted, entering "Monitored by DHSP" and/or "WRAIR IRB"**
- **Brief Results of the monitoring visit and requirements for all parties involved (i.e. report to be reviewed by the convened IRB)**
- **Outcome (i.e. corrective action report by PI; PI required specific training to help him/her achieve desired level of compliance; noncompliance reporting to FDA, OHRP; additional monitoring by the IRB)**
- **Location of hard copy of the documents relating to the monitoring**
- **Any other pertinent information**

