



WALTER REED ARMY INSTITUTE OF RESEARCH
 Human Subjects Protection Branch
 Standard Operating Procedure



SOP Title Safety Reporting for Clinical Trials	SOP No. UWZ-C-619
	Revision .03
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Signatures and Dates:

Authors: *(Handwritten mark)*

Signature on File at DHSP

5/8/13

 Date

25 Apr 13

 Date

Signature on File at DHSP

Approving
 Authority:

MAY 13

 Date

or

Review/Approval for unchanged documents

	Author/Date	QA Review/Date	Approving Authority/Date
1			
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1. Purpose/Applicability

This standard operating procedure (SOP) outlines the process for documentation and review of safety reports and exceptions to the safety monitoring plan received by the Walter Reed Army Institute of Research (WRAIR) Institutional Review Board (IRB) from investigators, DoD research monitors, Sponsors, or data and safety monitoring boards/independent data monitoring committees /safety monitoring committees (DSMB/IDMC/SMC).

The WRAIR IRB ensures that the safety monitoring plan and reporting requirements are outlined in the research protocol and are appropriate to the research. The IRB-approved protocol language supersedes this SOP.

A safety report includes any of the following serious adverse event (SAEs) (related & unexpected) / serious unexpected suspected adverse reaction (SUSAR) reports: an investigator initial, follow-up, final report, DoD Research Monitor independent report, an unanticipated adverse device effect and summary from a DSMB/IDMC/SMC or Sponsor's safety reports submitted to the U.S. Food and Drug Administration (FDA).

This SOP applies to the Human Subjects Protection Branch (HSPB) staff, the WRAIR IRB, investigators, DoD research monitors, and WRAIR Commander (Institutional Official; IO).

2. Responsibilities

- a. **HSPB Human Subjects Protection Scientist (HSPS)** is the HSPB staff member assigned to review the protocol and manage the IRB documentation for that study.
- b. **WRAIR IRB Chair or Designee** reviews safety reports and exceptions to the safety monitoring plan as outlined below, and takes appropriate action.
- c. **WRAIR IRB** ensures an adequate safety plan of all protocols approved by the IRB, and reviews safety reports as referred from the WRAIR IRB Chair or designee, and takes appropriate action for any issues cited in the report to ensure the safety of study participants.
- d. **Investigators** report as per required.
- e. **DoD Research Monitors** (and their designated alternates) are a DoD Unique Requirement and are appointed to assist the IRB with issues of individual subject/patient management and safety. Herein referred to as "research monitor".



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- f. **WRAIR Commander (IO)** approves exceptions to the safety monitoring plan.

3. Investigator Guidance

The Principal Investigator (PI) is advised to:

- a. Ensure that a DSMB/IDMC/SMC (if applicable) is established when submitting protocols to the WRAIR IRB and ensure that a safety monitoring plan and DSMB/IDMC/SMC charter is included with the initial submission to the WRAIR IRB for review and approval.
- b. Ensure that a research monitor and/or alternate research monitor is/are assigned in accordance with the requirements of the Department of Defense (DoD) Instruction 3216.02 for studies anticipated to be greater than minimal risk and supported by the DoD (funding, resources, personnel, etc.).
- c. Promptly submit any SAEs/SUSARs, unexpected AEs/ARs, unanticipated problems, and unanticipated adverse device effects, as applicable, to the WRAIR IRB via the WRAIR HSPB, including associated research monitor reports, and safety summaries from the DSMB/IDMC/SMC during the course of the trial and at the time of continuing review.
- d. Investigators should promptly (within 48 hours) report by telephone or email SAEs/SUSARs meeting the following criteria when s/he becomes aware of the event and then must follow-up in writing within 10 working days from knowledge of the event:
 - i. SERIOUS, and
 - ii. UNEXPECTED, and
 - iii. Suspected adverse reaction.

Failure to report SAEs/SUSARs meeting any of the above-described criteria is considered non-compliance (refer to WRAIR SOP, Non-Compliance Procedures, UWZ-C-606).



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Reporting:

- e. (Drugs, Biologics, Devices) Investigators should report promptly by telephone or email (within 48 hours) unanticipated problems, when s/he becomes aware of the event and then must follow-up in writing within 10 working days from knowledge of the event.

(Devices) Investigators shall report by telephone or email (within 48 hours) unanticipated adverse device effects, when s/he becomes aware of the event and then must follow-up in writing within 10 working days from knowledge of the event.

Failure to report the above is considered non-compliance (refer to WRAIR SOP, Non-Compliance Procedures, UWZ-C-606.01).

- f. Submit any SAEs/SUSARs, unexpected AEs/ARs, unanticipated problems, unanticipated adverse device effects, as applicable, to the Sponsor in accordance with the Sponsor's requirements and to the FDA as required by the FDA reporting requirements. These requirements are in addition to reporting to the WRAIR IRB.
- g. Investigators should request prior IRB-approval of exceptions to the safety monitoring plan (e.g., stopping/halting rules) whenever possible unless immediate action is needed to protect the rights, welfare, and safety of study subjects. If immediate action is taken, this must be reported to the IRB/HSPB within 24 hours.
- h. Respond to requests for documentation and information from the WRAIR IRB and WRAIR HSPB.
- i. Maintain correspondence with the reviewing IRBs, Sponsor, and regulatory authorities, as appropriate.

4. Materials and Equipment

Not applicable

5. Procedures

a. Prior to Protocol Approval

- 1) Before research is approved, the WRAIR IRB gives appropriate consideration to the spectrum of suspected adverse reactions that might be anticipated to occur in study subjects. A safety monitoring plan should be developed by the Sponsor and



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investigator and submitted as part of the protocol. This plan should be robust and commensurate with the degree of risk expected to be incurred by study subjects and the vulnerability of the study population. The WRAIR IRB is responsible for the review and approval of the safety monitoring plan.

- 2) Formal safety review is outside the scope of the WRAIR IRB, and the Board may not have the expertise to serve as a safety monitoring board. The IRB does have a duty to ensure that the Sponsor's safety officer, the designated DoD research monitor (and alternate research monitor as appropriate), and/or the DSMB/IDMC/SMC assigned to safety oversight of a particular clinical trial are impartial and qualified to perform its safety assessment. A list of members of safety committees and their qualifications is to be provided to the WRAIR IRB as part of the protocol review.
 - a. All DSMBs, IDMCs, or SMCs should have at least one impartial member. It is recommended that the DoD Research Monitor and/or alternate serve as a member of the DSMB/IDMC/SMC.
 - b. Conflict of interest statements for all safety committee members should be maintained in the Sponsor's regulatory file (Investigators regulatory file for Investigator-initiated research), and be available to the IRB upon request.

- 3) In accordance with the DoD Instruction (DoDI) 3216.02, all DoD-conducted research studies determined to be greater than minimal risk [as defined by 32 CFR 219.102(i)] require the appointment of an independent research monitor by the IRB. (Note: At the discretion of the IRB, a research monitor may also be assigned for minimal risk studies. This individual may be identified by the investigator, IRB or IO.).
 - a. Research monitors shall:
 1. Discuss research progress with the PI, interview subjects, consult on individual cases, or evaluate suspected adverse reaction reports on behalf of the IRB.
 2. Perform, at the direction of the IRB, oversight functions (e.g., observe recruitment, enrollment procedures, and the consent process for individuals, groups or units; oversee study interventions and interactions; review monitoring plans and UPIRTSO reports; and oversee data matching, data collection, and analysis)
 3. Promptly report discrepancies or problems to the IRB.
 4. Have the authority to stop a research study in progress, remove individual subjects from a study, and take whatever steps are necessary to protect the



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safety and well-being of research subjects until the IRB can assess the research monitor's report.

5. Review all unanticipated problems involving risks to subjects or others (UPIRTSOs), SAEs/SUSARs, unanticipated adverse device effects, and all subject deaths, and provide an unbiased written report of the event promptly to the WRAIR IRB by email (usarmy.detrick.medcom-wrair.mbx.hspb@mail.mil), or by facsimile (301) 319-9961. If the event is determined to be related, the DoD Research Monitor or their approved alternate will then submit written reports within 10 working days to the WRAIR IRB.

b. The IRB shall:

1. Appoint a research monitor whose expertise is consonant with the nature of risk(s) identified within the research protocol, and who is independent of the team conducting the research.
2. Approve a written summary of the monitors' duties, authorities, and responsibilities. This may be accomplished thru the IRB approval of the protocol when the research monitor's duties are defined within the protocol.
3. Communicate with the research monitor to confirm their duties, authorities, and responsibilities. This may be accomplished thru communication to the research monitor in the official IRB Recommendation of Approval memorandum.
4. Consider on a case-by-case basis a waiver to the requirement to have a research monitor when the inclusion of a research monitor is not necessary to provide additional protections for human subjects

b. Review of Safety Reports by the WRAIR IRB

- 1) Safety reports are initially received by the HSPB Human Subjects Protection Scientist (HSPS) POC for that study. The HSPS provides the safety report, including additional documentation (i.e., Sponsor's opinion and the research monitor's report) and the corresponding Safety Report Action Sheet (see Appendix A) to the WRAIR IRB Chair (or designee) for review. The reviewed Safety Report Action Sheet is placed in the respective study file; the action sheet is intended for internal use only and is not provided to the PI and/or study team. An email acknowledgement/acceptance is sent to the appropriate study team members.
- 2) A health care provider IRB member must review all safety reports.



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- 3) All subject pregnancies and subject withdrawals should be reported to the IRB, regardless of relatedness, unless otherwise stated in the protocol. The IRB Chair (or designee) will determine which reports should be forwarded to the full board.
- 4) All study deaths should be reported to the WRAIR IRB, regardless of relatedness. The IRB Chair (or designee) will determine which reports of subject deaths should be forwarded to the full board.
- 5) The WRAIR IRB Chair (or designee) takes appropriate action(s) at his/her discretion:
 - a) Request for more information;
 - b) Refer to full WRAIR IRB for review;
 - c) Refer to the full WRAIR IRB for information only;
 - d) Acknowledge or Accept; no further action required;
 - e) Acknowledge or Accept; with minor corrections to the safety reports;
 - f) Acknowledge or Accept; requires modification to protocol-related documents;
 - g) Refer to the U.S. Army Medical Research and Materiel Command, Office of Research Protections, Human Research Protections Office (USAMRMC ORP HRPO) for review and approval;
 - h) Notifies the IO, who reports to the U.S. Department of Health and Human Services, Office of Human Research Protections (DHHS OHRP), as appropriate;
 - i) No action/file only

(Note: If the WRAIR IRB is not the IRB of record and is maintaining an IRB shadow file only; this may be acknowledged by HSPB, not the IRB Chair).

6) SAEs/SUSAR reports, unanticipated adverse device effect reports, are paired up by the HSPS with the research monitor reports and any subsequent follow-up and final reports to provide additional context for final disposition.

7) The following safety reports require review by a fully convened WRAIR IRB:

- a) Related and Unanticipated SAEs/SUSARs for an investigational product, determined by the WRAIR IRB Chair to require full board review. All other



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related WRAIR Site SAEs/SUSARs will be provided to the fully convened WRAIR IRB for information purposes only;

b) All unanticipated adverse device effects;

c) All unanticipated problems that otherwise increase risk to subjects or others; and,

d) All deaths as requested by the IRB Chair.

8) All summary safety reports from the Sponsor or Sponsor-designated DSMB/IDMC/SMC are initially reviewed by the WRAIR Chair (or designee), and then provided to all IRB members for review or information only.

c. Review of Exceptions to the Safety Monitoring Plan by the WRAIR IRB

- 1) Requests for exceptions to the safety monitoring plan (e.g., waivers for stopping/halting rules) are initially received by the HSPB HSPS for that study. The HSPB HSPS provides the request to the WRAIR IRB Chair (or designee) for review and approval. This review is performed by a health care provider IRB member.
- 2) The WRAIR IRB Chair (or designee) may request additional information from the research monitor, DSMB/IDMC/SMC, and others, where appropriate, before providing a recommendation of approval to the WRAIR Commander (IO).
- 3) The WRAIR IRB Chair (or designee) may provide a verbal exception (eligibility) immediately if necessary to protect the rights, welfare, and safety of the study subject. If an exception is granted, follow-up documentation must be provided in writing.

d. Response to the Principal Investigator/Study Team

- 1) Safety reports are acknowledged/accepted by the IRB Chair (or designee) and the HSPB communicates this via an e-mail and may include a request for additional information or further action, as acted upon by the WRAIR IRB Chair (or designee).
- 2) Safety reports may be submitted to the WRAIR IRB for full board review or information only. As a result, the following action(s) may occur:



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If the full board review determines that the safety report warrants a modification of the protocol &/or supporting documentation, an email (“Communication to PI” section from the respective IRB meeting minutes) is sent to the study team. A more official path may occur in which an official memorandum signed by the WRAIR IRB Chair (or designee) is sent to the PI/Study Team.

If information only, a “Communication to PI” with no actions required, will be sent.

(Refer to WRAIR SOP, WRAIR IRB Meeting Minutes, UWZ-C-625).

- 3) All exceptions to the safety monitoring plan are acknowledged and recommended for approval by written memorandum from the WRAIR IRB Chair (or designee) and provided to the WRAIR Commander (IO) for implementation approval.

e. Continuing Review of Protocol

- 1) The WRAIR IRB reviews the safety data as part of the continuing review report to determine if any new information has emerged during the current review period that could alter the study’s risk:benefit assessment. Safety information reviewed includes, but is not limited to, interval summary of all SAEs/SUSARs, a cumulative summary of drug related AEs/SARs, current Investigator’s Brochure (with version number and date) and any new publications that may include new safety data. Additionally, all safety reports to include the DSMB/IDMC/SMC reports, provided to the IRB since the most recent continuing review are listed as an appendix to the report (Refer to WRAIR SOP, Continuing Review and Continuation Determination, UWZ-C-618). For multicenter studies, the PI and study team should provide an overall summary of safety information for all sites within the continuing review report. It is noted that all sites in a multi-center trial may not report their AE data at the same time and thus a roll-up of AE data from the study sponsor may reflect different reporting times and variable site inclusion, based on the sponsor’s receipt of data and the timing of sponsor reports.
- 2) The IRB confirms that any provisions for monitoring study data for safety of subjects have been implemented and are working as intended.

f. Additional Reporting Requirements by the WRAIR IRB to the USAMRMC ORP HRPO



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The following are reported by the WRAIR HSPB to the USAMRMC ORP HRPO, in accordance with the WRAIR SOP, Reporting Requirements to USAMRMC for Headquarters-Level Review, UWZ-C-636:

1. All related SAEs/SUSARs;
2. All unanticipated adverse device effects;
3. Unanticipated problems that increase risk to subjects or others; and
4. All deaths related to study participation.

g. Reporting to Department of Health and Human Services (DHHS) Office of Human Research Protections (OHRP)

To be in compliance with the requirements of the Federal-wide Assurance (FWA) for studies that are funded by the DHHS, the WRAIR HSPB/IRB reports any internal adverse events that are unanticipated to the OHRP and to the supporting HHS agency head (or designee). This report is submitted after WRAIR IRB review is completed. A copy of this report is provided to the Sponsor and PI.

h. Reporting to the U.S. FDA

For clinical trials that are Sponsored by the WRAIR (and its detachments) and the Army Office of The Surgeon General (OTSG), The Surgeon General's Sponsor's Representative to the FDA reports events in accordance with AR 40-7 and 21 CFR 312.5. For trials that are sponsored by external entities (i.e., industry sponsors), events are reported by the respective Sponsor.



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6) Explanation of Abbreviations and Terms

- Adverse Event** Any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related.
- Adverse Reaction** An adverse reaction means any adverse event caused by a drug. Adverse reactions are a subset of all suspected adverse reactions where there is reason to conclude that the drug caused the event.
- Clinical Trials** Any investigation in human subjects intended to discover or to verify the clinical pharmacological, pharmacokinetic, and/or other pharmacodynamic effects of an investigational agent, and/or to identify any adverse reactions to an investigational agent to assess the agent's safety and efficacy.
- Data & Safety Monitoring Board (DSMB)** An independent, chartered committee established by the sponsor to assess, at defined intervals, the ongoing scientific and ethical integrity of a study by reviewing and evaluating (unblinded) data and reports. The DSMB makes non-binding reports to the sponsor regarding study modification, suspension or termination. Synonymous terms include Data Monitoring Committee (DMC) and Independent Data Monitoring Committee (IDMC).
- DoD Research Monitor** An independent research monitor fulfills a unique DoD requirement in human subjects protection. The IRB appointed research monitors must have expertise consonant with the nature of risk(s) identified within the research protocol, and be independent of the team conducting the research. This individual must be capable of overseeing the progress of research protocols, especially issues of individual volunteer/ patient management and safety. Industry-sponsor medical monitors (i.e., the Sponsor's medical expert) generally do not meet the intent of the DoD Instruction.



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Healthcare Provider

Licensed provider of care (such as, physician, nurse, physician’s assistant, clinical psychologist, dentist, podiatrist, ophthalmologist, etc.)

Life-threatening Adverse Event or Life-threatening Suspected Adverse Reaction

An adverse event or suspected adverse reaction is considered “life-threatening if, in the view of either the investigator or sponsor, its occurrence places the patient or subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.

Safety Monitoring Committee

A committee established by the sponsor to review and evaluate the (unblinded) data from a study to assess safety risks to subjects. Typically less formal than a DSMB/IDMC, the committee must contain at least one member who is independent from the investigator and sponsor team.

Serious Adverse Event (OHRP)

OHRP defines *serious adverse event* as any adverse event that: 1) results in death; 2) is life-threatening (places the subject at immediate risk of death from the event as it occurred); 3) results in inpatient hospitalization or prolongation of existing hospitalization; 4) results in a persistent or significant disability/incapacity; 5) results in a congenital anomaly/birth defect; or 6) based upon appropriate medical judgment, may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).



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Serious Adverse Event (SAE) or Serious Suspected Adverse Reaction (SSAR) (FDA)

An adverse event or suspected adverse reaction is considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes: Death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Serious and Unexpected Suspected Adverse Reaction (SUSAR)

Any suspected adverse reaction that is both serious and unexpected. Reporting of an adverse event as a suspected adverse reaction must occur only if there is evidence to suggest a causal relationship between the drug and the adverse event, such as:

- (i) A singled occurrence of an event that is uncommon and known to be strongly associated with drug exposure (e.g., angioedema, hepatic injury, Stevens-Johnson Syndrome);
- (ii) One or more occurrences of an event that is not commonly associated with drug exposure, but is otherwise uncommon in the population exposed to the drug (e.g., tendon rupture);
- (iii) An aggregate analysis of specific events observed in a clinical trial (such as known consequences of the underlying disease or condition under investigation or other events that commonly occur in the study population independent of drug therapy) that indicates those events occur more frequently in



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the drug treatment group that in a concurrent or historical control group.

Sponsor

An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical trial.

Suspected Adverse Reaction (SAR)

Any adverse event for which there is a reasonable possibility that the drug caused the adverse event. For the purposes of FDA safety reporting, “reasonable possibility” means there is evidence to suggest a causal relationship between the drug and the adverse event. Suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction, which means any adverse event caused by a drug.

Unanticipated Problem Involving

Risks to Subjects or Others (UPIRTSO)

Any incident, experience, or outcome that meets all of the following criteria:

- a. Unexpected (in terms of nature, severity, or frequency) given the approved research procedures and the subject population studied;
- b. Related or possibly related to a subject’s participation in research; and
- c. Suggests that the research places subjects or others at greater risk of harm (physical, psychological, economic, or social harm) than was previously known or recognized.

Unanticipated Adverse Device Effect

Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a



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device that relates to the rights, safety, or welfare of subjects.

**Unexpected Adverse Event (UAE)
 Or Unexpected Suspected Adverse
 Reaction (USAR)**

An adverse event or suspected adverse reaction is considered "unexpected" if it is not listed in the investigator brochure or is not listed at the specificity or severity that has been observed; or, if an investigator brochure is not required or available, is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. "Unexpected," as used in this definition, also refers to adverse events or suspected adverse reactions that are mentioned in the investigator brochure as occurring with a class of drugs or as anticipated from the pharmacological properties of the drug, but are not specifically mentioned as occurring with the particular drug under investigation.



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7) References

Reference Number or Authors	Document Title
32 CFR 219	Protection of Human Subjects
21 CFR 56	Institutional Review Boards
21 CFR 312	Investigational New Drug Application
21 CFR 312 and 320	Final Rule: Investigational New Drug Safety Reporting Requirements for Human Drug and Biological Products and Safety Reporting Requirements for Bioavailability and Bioequivalence Studies in Humans, 29 September 2010
21 CFR 812	Investigational Device Exemptions
45 CFR 46	Protection of Human Subjects
DoDI 3216.02	Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research
AR 40-7	Use of Food and Drug Administration-Regulated Investigational Products in Humans Including Schedule 1 Controlled Substances
AR 70-25	Use Of Volunteers As Subjects of Research
ICH – E6	International Conference of Harmonization. (1997). Good Clinical Practice: Consolidated Guidance (ICH-E6). Section 3.
DHHS OHRP	OHRP Guidance on the Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events (2007)
USAMRMC Command Policy 2011-67	Reporting Suspensions or Terminations of IRB Approval and Unanticipated Problems Involving Risks to Subjects or Others (UPRITSOs) in Human Subjects Research Conducted or Supported by USAMRMC
HEADQUARTERS	Delegation of The Surgeon General's Sponsor Representative to



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NIH	Further Guidance On A Data And Safety Monitoring For Phase I And Phase II Trials (2000)
FDA	Guidance for Clinical Investigators, Sponsors and IRBs: Adverse Event Reporting – Improving Human Subject Protection (January 2009)
FDA	Guidance for Industry and Investigators: Safety Reporting Requirements for Investigational New Drugs and Bioavailability (BA)/ Bioequivalence (BE) Studies (December 2012)
WRAIR SOP UWZ-C-618	<i>Continuing Review and Continuation Determination</i>
WRAIR SOP UWZ-C-625	<i>Institutional Review Board Meeting Minutes</i>
WRAIR SOP UWZ-C-636	<i>Reporting Requirements to USAMRMC ORP HRPO for Headquarters-level Review and to AHRPO</i>



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8) Forms and Appendices

Form or Number	Title
Appendix A	WRAIR IRB Safety Report Action Sheet

9) Document Revision History

Version Number	Brief Description of Changes	Effective Date
.00	Original SOP	07 May 2007
.01	Biennial review, including organization name updates and references to current policies and procedures, and updating the SOP title for clarity.	Revisions (in draft only)
.02	<ol style="list-style-type: none"> 1. Align responsibilities and activities with current DOD regulations 2. Provide guidance for the principal investigators 3. Clarify procedures for safety reviews, monitoring plans, and reports. 	18 August 2010
.03	<ol style="list-style-type: none"> 1. Add new requirements and definitions with current FDA safety reporting guidance. 2. Editorial revisions to update Branch names, references, etc. 	JUN 05, 2013



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APPENDIX A

WRAIR IRB Safety Report Action Sheet

WRAIR Protocol #: _____ HSPB POC: _____

PI: _____ Sponsor: _____

Date of Event: _____ Subject Number: _____

Brief Description of Event: _____

Site: _____

Date Received by HSPB: _____

Date Submitted to Chair for Review: _____

SUSAR/SAE/UAE/UADE/UAP #: _____

Documentation Provided (check all that apply):

- Bundled SAE/SUSAR Package
- Initial SAE/SUSAR/Unexpected Event Report
- Unanticipated problem
- Follow-up SAE/SUSAR/Unexpected Event Report (# _____)
- Research Monitor's Report (date _____)
- Safety Summary from Safety Committee or DSMB/IDMC
- Safety Letter from Sponsor/MedWatch Report
- Pregnancy Notification
- Subject Withdrawal



WALTER REED ARMY INSTITUTE OF RESEARCH
 Human Subjects Protection Branch
 Standard Operating Procedure



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Other

HSPB Comments: _____

Action Taken (check all that apply):

Request for More Information: _____

- Refer to Full WRAIR IRB for Review
- Refer to WRAIR IRB for Information Only
- Acknowledged or Accepted; no further action required
- Acknowledged or Accepted; with minor corrections to the reports
- Acknowledged or Accepted; requires modification to protocol-related documents
- Referred to USAMRMC ORP HRPO
- Submit to OHRP
- Submit to TSG Sponsor's Representative to the FDA
- No action; file only



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Comments:

Signature: _____ Date: _____