Standard Operating Procedure
Walter Reed Army Institute of Research

SOP:	**Safety Reporting for Clinical Trials**	**SOP No.:**	**UWS-HP-619**
		Version:	**.06**
Effective Date:	21 June 2024	**Page:**	1 of 18

Signatures and Dates:

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QA Review:

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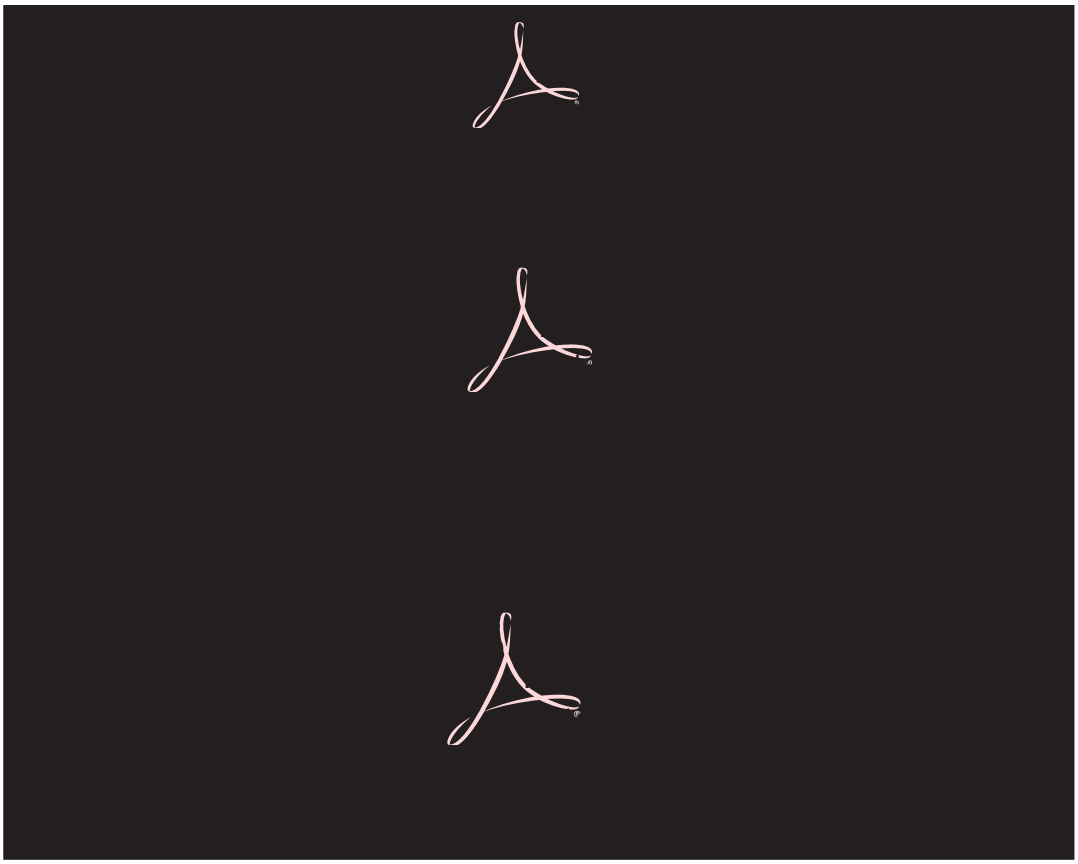

Review/Approval for unchanged documents

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1. Purpose and Applicability

This standard operating procedure (SOP) outlines the process for documentation and review of safety reports, and exceptions to safety reporting/documentation within the context of a clinical trial where a drug, biologic, device, or combination product is being used or evaluated as the primary focus of the study.

A safety report includes any of the following: serious adverse event (SAEs) (related & unexpected) / serious unexpected suspected adverse reaction (SUSAR) reports (an investigator's initial, follow-up, final report, Department of Defense [DoD] Research Monitor independent report, as applicable), an unanticipated adverse device effect (UADE), summary from a Data and Safety Monitoring Board (DSMB)/Independent Data Monitoring Committee (IDMC)/Safety Monitoring Committee (SMC) or Sponsor's safety reports submitted to the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), or other countries' regulatory agency overseeing the investigational product being used in the study, or a report of a clinical hold/study halt notification. The reporting of unanticipated problems and deviations is covered under a separate SOP, UWS-HP-621, Deviation and Unanticipated Problem Reporting.

This SOP specifically outlines reporting requirements for safety reports, which include unanticipated serious adverse events or unanticipated serious adverse device effects reporting in the context of a clinical trial where a drug, biologic, device, or combination product is being used or evaluated as the primary focus of the study. There are times when a SAE/SUSAR or an UADE may also be considered an unanticipated problem involving risks to subjects or others (UPIRTSO). If a SAE/SUSAR or UADE meets the definition of an UPIRTSO, then this safety report will also need to be triaged, reviewed and reported as a potential UPIRTSO as per SOP UWS-HP-621, Deviation and Unanticipated Problem Reporting.

This SOP applies to the Human Subjects Protection Branch (HSPB) staff, the WRAIR Institutional Review Board (IRB), investigators, DoD Research Monitors (as applicable), and WRAIR Commander (Institutional Official; IO). This SOP applies the U.S. FDA definitions and requirements, as they are the most stringent, and is applicable to all clinical trials involving drugs, biologics, devices or combination products.

2. Background and Investigator Guidance

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

a. Safety Monitoring Plan

Prior to submitting protocols to the WRAIR IRB, Principal Investigators (PIs) and the Sponsor should ensure that DSMBs/IDMCs/SMCs (if applicable) are established and that a safety monitoring plan and DSMB/IDMC/SMC charter is included with their initial submission for initial triage by the WRAIR HSPB. The safety monitoring plan for Phase I clinical trial studies may be included within the protocol. The collaborative plans between the PI and Sponsor should be robust and commensurate with the degree of risk expected to be incurred by study participants and the vulnerability of the study population. The safety monitoring plans must outline the expectations for safety reporting.

Before research is approved, the WRAIR IRB receives the safety monitoring plan and gives appropriate consideration to the spectrum of potential, expected and unexpected safety-related elements that might be anticipated to occur in study subjects. These safety reporting elements may include or be inclusive of:

1) Adverse Events (AEs)
2) Serious Adverse Events (SAEs)
3) Adverse Reactions (ARs)
4) Serious Unexpected Suspected Adverse Reactions (SUSARs)
5) Serious Adverse Device Effects (SADEs), and
6) Unanticipated Adverse Device Effects (UADEs)

The WRAIR IRB is responsible for the review and approval of the safety monitoring plan and ensuring the reporting requirements are outlined in the research protocol and are appropriate to the research.

b. Safety Reports

Safety report requirements are based on multiple National, International and Organizational definitions and guidance for clinical trials involving drugs, biologics, devices, and combination products. If there are conflicting

requirements by one or more organizational policy or guidance, the general default is to apply the U.S. FDA regulations or guidance.

A full-cycle safety report includes a PI's initial, follow-up(s), and final report. Reports may include a description of events, surrounding circumstances and any corrective action plans or measures taken to address the events.

In addition to PI descriptions of events, reports may include summaries or identifications of events and information from:

1) DoD Research Monitor independent reports, as applicable
2) Participants
3) An unanticipated adverse device effect and summary from a DSMB/IDMC/SMC
4) Sponsor's safety reports submitted to the US FDA, EMA, or other countries' regulatory agency overseeing the product being used in the study, or
5) A report of a clinical hold/study halt notification.

c. The PI is advised to:

1) 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.
2) Promptly submit any SAEs/SUSARs, unexpected AEs/ARs, and UADEs, subject withdrawals, pregnancy notifications, clinical hold/study halt notifications, as applicable, to the WRAIR IRB via the WRAIR HSPB, including associated DoD Research Monitor reports, as applicable, and safety summaries from the DSMB/IDMC/SMC during the course of the trial and at the time of continuing review.

   Timing Expectations for Prompt Safety Report Submissions:

   a. During the course of the trial and at the time of continuing review, reports must promptly be submitted to the WRAIR IRB via the WRAIR HSPB, for AEs, SAEs, ARs, SUSARs, ADEs, UADEs, subject withdrawals, pregnancy notifications, and clinical hold/study halt notifications, along with associated DoD Research Monitor reports, as applicable, and safety summaries from the DSMB/IDMC/SMC.

b. All subject pregnancies and subject withdrawals should be reported to the IRB within 48 hours of the PI being notified, 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.
c. All study deaths should be reported to the WRAIR IRB within 48 hours of the PI being notified, regardless of relatedness. The IRB Chair (or Designee) will determine which reports of subject deaths should be forwarded to the full board.
d. When PIs become aware of clinical holds or study halts, PIs shall report by telephone, facsimile or email, within 24 hours, information as it becomes available, pertaining to the circumstances of the hold or halt.
e. Serious, Unexpected and Suspected Adverse Events:

    1. When PIs become aware of events, prompt reporting (within 48 hours) is required by telephone, facsimile or email for events that meet the following criteria:

        a) SERIOUS (delineated in the safety monitoring plan), and
        b) UNEXPECTED (not delineated in the safety monitoring plan) and
        c) SUSPECTED (based on the PIs clinical judgement).

    2. Follow-up in writing is required within 10 working days from knowledge of the event. Failure to report events/reactions that meet any of the above-described criteria is considered non-compliance (refer to WRAIR SOP UWS-HP-606, Non-Compliance Procedures).

3) In addition to the WRAIR IRB reporting requirements outlined above, submission of reports will be made to the Sponsor in accordance with the Sponsor's requirements, and to the U.S. FDA as required by the U.S. FDA reporting requirements in 21 CFR 312 and 812.
4) PIs are expected to respond to documentation and information requests from the WRAIR IRB and WRAIR HSPB in a timely manner.
5) PIs are responsible for maintaining the correspondence with the reviewing IRBs, Sponsors, and regulatory authorities, as appropriate.
6) Failure to report SAEs/SUSARs meeting any of the above-described criteria is considered non-compliance (refer to WRAIR SOP UWS-HP-606, Non-Compliance Procedures).

7) Devices: When PIs becomes aware of UADEs, prompt reporting (within 48 hours) is required by telephone, facsimile or email. PIs must follow-up in writing within 10 working days from knowledge of the event.
8) Failure to report UADEs is considered non-compliance (refer to WRAIR SOP UWS-HP-606, Non-Compliance Procedures).
9) Submit any SAEs/SUSARs and UADEs, as applicable, to the Sponsor in accordance with the Sponsor's requirements and to the U.S. FDA as required by the U.S. FDA reporting requirements. These requirements are in addition to reporting to the WRAIR IRB.
10) Investigators shall report by telephone, facsimile or email (within 24 hours) clinical holds or study halts when s/he becomes aware of the event and provide additional information as it becomes available.
11) 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.
12) Respond to requests for documentation and information from the WRAIR IRB and WRAIR HSPB.
13) Maintain correspondence with the reviewing IRBs, Sponsor, and regulatory authorities, as appropriate.

Note: The reporting of unanticipated problems and deviations is covered under a separate SOP, UWS-HP-621, Deviation and Unanticipated Problem Reporting.

3. Responsibilities

a. The HSPB Point of Contact (POC) is the HSPB staff member assigned to review the protocol and manage the IRB documentation for that study, to include all safety reports submitted for review. The HSPB POC is responsible for filling out the Safety Reporting Action Sheet (Appendix A) and submitting the safety report with the completed Safety Reporting Action Sheet to the WRAIR IRB Chair (or Designee) for review. If the safety report is referred to the fully convened WRAIR IRB, the HSPB POC is responsible for scheduling the report for the meeting and preparation of all communications with the study team.

b. The WRAIR IRB Chair (or Designee) reviews the safety reports and exceptions to the safety monitoring plan and takes appropriate action.

c. The WRAIR IRB Administrator reviews the safety reports and exceptions to the safety monitoring plan as outlined below for protocols where the WRAIR is relying on another institution for their IRB review, and acknowledges receipt of information and notes the action that the other IRB has taken.

d. The WRAIR IRB ensures an adequate safety plan for all protocols approved by the IRB, and reviews safety reports referred from the WRAIR IRB Chair (or Designee) for a fully convened IRB Review. The IRB assesses appropriate action for any issues cited in the report to ensure the safety of study participants.

e. PIs are responsible for submitting the safety reports to the WRAIR IRB as per the reporting requirements outlined in the protocol and safety monitoring plan.

f. DoD Research Monitors (and their designated alternates) may be appointed to assist the IRB with issues of individual subject/participant management and safety, as requested. This role is no longer required and has been removed from the DODI 3216.02. At the direction of the IRB, they may:

1. Oversee clinical trial procedures (e.g., observe recruitment, enrollment procedures, and the consent process for individuals, groups or units); oversee study interventions and interactions; review safety monitoring plans and UPIRTSO reports; and oversee data matching, data collection, and analysis.
2. Promptly report discrepancies or problems to the IRB.
3. 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 safety and well-being of research subjects until the IRB can assess the DoD Research Monitor's report.
4. Review all unanticipated problems involving risks to subjects or others (UPIRTSOs, as outlined in SOP UWS-HP-621, Deviation and Unanticipated Problem Reporting), SAEs/SUSARs, unanticipated adverse device effects, and all subject deaths, and provide an unbiased written report of the event promptly (within 48 hours) to the WRAIR IRB by email (usarmy.detrick.medcom-wrair.mbx.hspb@mail.mil), or by facsimile at (301) 319-9961.
5. 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. If the event is determined not be related, the DoD Research

Monitor's written report will be provided to the PI to file with the event report in the protocol regulatory binder.

If a DoD Research Monitor is requested by the IRB, their roles and responsibilities will be outlined within the protocol.

g. The WRAIR Commander (IO) approves exceptions to the safety monitoring plan and submits any SAEs/SUSARs and UADEs, that meet the definition of an UPIRTSO via an EXSUM, to the U.S. Army Medical Research and Development Command, Office of Human and Animal Research Oversight, Office of Human Research Oversight (USAMRDC OHARO OHRO) for reporting through the Senior Designated Official to the Director, Office for Human Research Protection (DOHRP) through the COHRP within 5 business days of the report's completion in accordance with DoDI 3216.02 § 3.1.h.

4. Materials and Equipment

Not applicable

5. Procedures

a. Prior to Protocol Approval:

1) Prior to protocol approval, 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 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 because the IRB may not have the expertise to serve as a safety monitoring board. However, the IRB does have a duty to ensure that the Sponsor's safety officer and/or the DSMB/IDMC/SMC assigned to safety oversight of a particular clinical trial are impartial and qualified to perform its safety assessment.
3) Safety Charter and Monitoring Committee:

a) A safety monitoring charter should include a list of members serving on the safety committee and their qualifications, and must be provided to the WRAIR IRB as part of the protocol submission for review.
b) All DSMBs, IDMCs, or SMCs should have at least one impartial member.
c) Conflict of interest statements for all safety committee members should be maintained in the Sponsor's regulatory file (Investigator's regulatory file for Investigator-initiated research), and be available to the IRB upon request.

b. WRAIR HSPB POC Receipt and Initial Review of Safety Reports

1) Safety reports are initially received by the HSPB POC for that study. The HSPB POC provides the safety report, including additional documentation (i.e., Sponsor's opinion and the DoD Research Monitor's report, as applicable) and the corresponding Safety Reporting Action Sheet (see Appendix A) to the WRAIR IRB Chair (or Designee) for review and submits to the fully convened WRAIR IRB, as appropriate, for review.
2) The reviewed Safety Report Action Sheet is placed in the respective study file; the Safety Report 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 PI and/or appropriate study team members. Emails are also sent to obtain additional information and documentation for review of a safety report.

c. WRAIR IRB

1) A health care provider member of the IRB or the IRB Chair (in consultation with a health care provider member of the IRB) is responsible for:
   a) Reviewing all safety reports.
   b) During their review, determining if any SAE/SUSAR or UADE meet the criteria for an UPIRTSO.
   c) Review all clinical hold/study halt notifications made by the Sponsor and request additional information from the study team as appropriate.

2) The WRAIR IRB Chair (or Designee) takes appropriate action(s) at his/her discretion through:
   a) Requests for additional information;
   b) Refers to the full WRAIR IRB for review;
   c) Refers to the full WRAIR IRB for information only;
   d) Acceptance with no further action required;

e) Acceptance with minor corrections to the safety reports;
f) Acceptance with required modification to protocol-related documents;
g) Referring for review as an UPIRTSO; or
h) No actions/file only. (See Appendix A)

SAEs/SUSAR reports, UADE reports, are paired up by the HSPB POC with the DoD Research Monitor reports, as applicable, and any subsequent follow-up and final reports, to provide additional context for final disposition.

3) IRB Review of Reports
   a) 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. These are generally provided in real time for IRB Chair (or Designee) review and then with the continuing review submissions for the fully convened WRAIR IRB unless there are some major safety issues identified in the reports, at which point they would be referred to the fully convened WRAIR IRB in real time.
   b) All clinical hold/study halt notifications are initially reviewed by the WRAIR IRB Chair (or Designee), and then provided to all IRB members for review or information only, depending on the nature of the hold/halt.
   c) The WRAIR IRB will use the Review Form in Appendix D of SOP UWS-HP-621 to review the safety report and determine if any additional information needs to be provided and if any corrective actions need to be taken, such as revising the protocol and/or consent form and other supporting documentation.
   The WRAIR IRB will also indicate what reporting is required for the event:
      1. Refer to the USAMRDC OHARO OHRO for review and approval;
      2. Notify the IO, who reports to the U.S. Department of Health and Human Services, Office of Human Research Protections (DHHS OHRP) or the OHARO, as appropriate;
      3. Submit to TSG Sponsor's Representative;
      4. Submit to U.S. Department of Health and Human Services (HHS) Office of Human Research Protections (OHRP); and/or

5. No further reporting required.

4) Safety Reports Requiring Fully Convened WRAIR IRB Review
The following outlines the criteria for a fully convened IRB review of safety reports:
   a) Related and Unanticipated SAEs/SUSARs for an investigational product, determined by the WRAIR IRB Chair (or Designee) to require full board review. All other related WRAIR Site SAEs/SUSARs will be provided to the fully convened WRAIR IRB for information purposes only;
   b) All UADEs for an investigational device;
   c) All deaths as requested by the IRB Chair (or Designee); and
   d) Any SAE/SUSAR or UADE determined to also meet the criteria for an UPIRTSO (will also be triaged under SOP UWS-HP-621, Deviation and Unanticipated Problem Reporting).

5) Exceptions to the Safety Monitoring Plan
   a) Any alterations or exceptions to safety monitoring plans or reporting expectations should be requested by PIs prior to IRB-approval 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.
   b) Review 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 POC for that study. The HSPB POC provides the request to the WRAIR IRB Chair (or Designee) for review and approval. This review is performed by a health care provider IRB Chair Designee.
      2. The WRAIR IRB Chair (or Designee) may request additional information from the DSMB/IDMC/SMC, and others, where appropriate, before providing an 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 within 5 calendar days (NOT business days).
      4. All exceptions to the safety monitoring plan are accepted and approved by a written memorandum from the WRAIR IRB Chair (or

Designee) and provided to the WRAIR Commander (IO) for approval authorization.

d. WRAIR IRB Administrator Review of Safety Reports (WRAIR IRB is Not the IRB of Record)

1) Safety reports for studies, where the WRAIR IRB is Not the IRB of Record and they rely on another institution for IRB review, are reviewed by the WRAIR IRB Administrator (or Designee). The HSPB POC provides the safety report, including additional documentation (i.e., Sponsor's opinion and the reviewing IRB's action regarding the safety report) and the corresponding Safety Report Action Sheet (see Appendix A) to the WRAIR IRB Administrator (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 is sent to the appropriate study team members. Emails are also sent to request additional information pertinent to the review of the safety reports.
2) All subject pregnancies, subject withdrawals, clinical hold/study halt notifications, where the WRAIR IRB is Not the IRB of Record and they rely on another institution for IRB review, are submitted to the WRAIR IRB Administrator (or Designee), along with any action or notification from the reviewing IRB. The reviewed Safety Report Action Sheet is placed in the respective study file. An email acknowledgment is sent to the appropriate study team members.
3) All study deaths, where the WRAIR IRB is not the IRB of record and thereby rely on another institution for IRB review, are submitted to the WRAIR IRB Administrator (or Designee), along with any action from the reviewing IRB. The reviewed Safety Report Action Sheet is placed in the respective study file. An email acknowledgement is sent the appropriate study team members.
   a) Refer all SAEs/SUSARs and/or UADEs that also meet the definition of an UPIRTSO for review as per SOP UWS-HP-621, Deviation and Unanticipated Problem Reporting.
   b) The WRAIR IRB Administrator (or Designee) takes appropriate action(s) at his/her discretion:
      1. Request for more information;
      2. Acknowledge; no further action needed;
      3. Triage for review as an UPIRTSO;
      4. No action/file only.

c) The WRAIR IRB Administrator (or Designee) requests reporting, as applicable:
   1. Refer to the USAMRDC OHARO OHRO) for review and approval; and/or
   2. Notifies the IO.

e. Communications to the Principal Investigator/Study Team

1) Safety reports are accepted by the IRB Chair (or Designee). The HSPB communicates this via an e-mail and may include a request for additional information or further action, as requested by the WRAIR IRB Chair (or Designee).
2) Safety reports, where the WRAIR IRB is not the IRB of record and they rely on another institutions' IRB for review, are acknowledged by the WRAIR IRB Administrator (or Designee) and the HSPB communicates this via an email and may include a request for additional information.
3) Safety reports may be submitted to the fully convened WRAIR IRB for review or for information only. As a result, the following action(s) may occur:
   a) If the full board review determines that the safety report warrants a modification of the protocol, consent form and/or other supporting documentation, an email ("Communication to PI" section from the respective IRB meeting minutes) is sent to the study team by HSPB. A more official communications path may also occur in which an official memorandum signed by the WRAIR IRB Chair (or Designee) is sent to the PI/Study Team.
   b) If the safety report is submitted to the fully convened WRAIR IRB for information only, no further action is required unless the IRB has comments or recommendations to provide to the study team; then a "Communication to PI" is sent by the HSPB to the PI/Study Team (refer to WRAIR SOP UWS-HP-628, Review of Human Subjects Research by the Fully Convened WRAIR Institutional Review Board).

f. Additional Reporting Requirements by the WRAIR IRB to the USAMRDC OHARO OHRO

The following are reported by the WRAIR HSPB to the USAMRDC OHARO OHRO, in accordance with the USAMRDC Policy 17, Event Reporting Requirements for Human Subjects Research Conducted by the USAMRDC:

1) Any SAEs/SUSARs UADEs, or deaths that meet the criteria for an UPIRTSO; and
2) All clinical hold/study halt notifications.

g. Reporting to Federal Regulatory Agencies

1) Department of Health and Human Services (HHS) 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 HHS, the WRAIR HSPB/IRB reports any internal SAEs/SUSARS or UADEs, (i.e. safety reports that occur at our sites) that meet the criteria as an UPIRTSO to the OHRP and to the supporting HHS agency head (or Designee). This report is submitted after WRAIR IRB review is completed and a determination as an UPIRTSO is made (as per SOP UWS-HP-621). A copy of this report is provided to the Sponsor and PI/Study Team.

2) Reporting to the U.S. FDA

For clinical trials that are funded by the Army Office of The Surgeon General (OTSG), The Surgeon General's Sponsor's Representative to the US FDA reports events in accordance with AR 40-7, 21 CFR 312.50, 21 CFR 812.150. For trials that are Sponsored by external entities (i.e., industry Sponsors), events are reported by the respective Sponsor.

3) Reporting to the Director, DOHRP

Reports will be reported to the Director, DOHRP, through the COHRP within 5 business days of the report's completion in accordance with DoDI 3216.02 § 3.1.h.

6. Explanation of Abbreviations, Acronyms, and Definition of Terms

Abbreviations and acronyms have been defined in the text at the time of first use.

7. References

Reference Number or Author	Document Title

10 USC 980	Title 10 of the United States Code, Section 980 (10 USC 980), Limitation on Use of Humans as Experimental Subjects
21 Code of Federal Regulations (CFR) 56	Institutional Review Boards
21 CFR 312	Investigational New Drug Application
21 CFR 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
32 CFR 219	Department of Defense, Protection of Human Subjects
45 CFR 46	Health and Human Services, Protection of Human Subjects
48 CFR 252.235-7004	Defense Federal Acquisition Regulation (48 CFR 252.235-7004) (“DFARS clause”)
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
USAMRDC OHARO Memo	Waiver of DOD-Unique Human Subjects Protection Requirements When USAMRDC Subordinate Commands Provide Assistance to Non-DoD Institutions, 17 November 2022
DASG-ZH Department of the Army Office of the Surgeon General (OTSG); Memo	Delegation to the Institutional Review Board (IRB) Chair of Waiver Authority of the Research Monitor (RM) Requirement for Greater Than Minimal Risk (GTMR) Army–Conducted and –Supported Human Subjects Research Where the Remaining Activities May be Reviewed by Expedited Procedure, 09 JUN 2017

DoDI 3216.02	Department of Defense Instruction 3216.02, Protection of Human Subjects and Adherence to Ethical Standards in DOD-Supported Research (DODI 3216.02)
FDA Guidance	Guidance for Industry and Investigators: Safety Reporting Requirements for INDs and BA/BE Studies 12 December 2012
FDA Guidance	Safety Assessment for IND Safety Reporting Guidance for Industry, December 2015
FDA Guidance	Adverse Event Reporting to IRBs — Improving Human Subject Protection Guidance for Clinical Investigators, Sponsors, and IRBs, January 2009
Headquarters USAMRDC Memo	Delegation of The Surgeon General's Sponsor Representative to the US Food and Drug Administration (FDA) to the US Army Research and Development Command (USAMRDC) Principal Assistant for Acquisition (PAA) 27 March 2013
HHS OHRP	OHRP Guidance on the Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events (2007)
ICH – E6(R2)	Food and Drug Administration, Good Clinical Practice: Integrated Addendum to ICH E6(R1)
USAMRDC Command Policy 17	Event Reporting Requirements for Human Subjects Research Conducted by the USAMRDC
NIH	Expedited Review of Human Subjects Research
WRAIR SOP UWS-HP-606	Non-Compliance Procedures
WRAIR SOP UWS-HP-618	Continuing Review and Continuation Determination
WRAIR SOP UWS-HP-621	Deviation and Unanticipated Problem Reporting

WRAIR SOP UWS-HP-628	Review of Human Subjects Research by the Fully Convened WRAIR Institutional Review Board

8. Forms and Appendices

Form or Number	Title
Appendix A	WRAIR IRB Safety Report Action Sheet
Appendix D from UWS-HP-621	Deviation and Unanticipated Problem Reporting

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	Revisions (in draft only)
.02	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	1. Add new requirements and definitions with current FDA safety reporting guidance. 2. Editorial revisions to update Branch names, references, etc.	02 MAY 2018
.04	Update the SOP to clarify the role of the WRAIR IRB Administrator when reviewing safety reports for studies where the WRAIR IRB is not the IRB of record and they are relying on another institution's IRB. Other revisions to incorporate updated guidance, policies, regulations, and minor editorial clarifications.	XXXX

.05	Update the SOP to address recommendations from AHRPO; other administrative updates.	21 February 2023
.06	Reformatted using new WRAIR SOP template and other minor administrative and editorial changes.	21 June 2024