OFFICE OF RESEARCH OVERSIGHT

1. SUMMARY OF MAJOR CHANGES:

a. This directive combines and streamlines content contained in both the previous version of this directive and Veterans Health Administration (VHA) Directive 1058.01, Research Compliance Reporting Requirements, dated October 22, 2020. Previous versions of VHA Directive 1058.01 provided detailed processes for the reporting of Department of Veterans Affairs (VA) research-related events to research review committees relied upon by VA medical facilities and the review of such events by those committees. The scope of this directive, as it pertains to research-related reportable events, has been narrowed to primarily address required notifications of those research-related events to the Office of Research Oversight (ORO) so that it can effectively execute its oversight responsibilities.

b. This directive, which rescinds VHA Directive 1058.03, Assurance of Protection for Human Subjects in Research, dated September 17, 2020, incorporates the primary policy requirement of that Directive that each VA medical facility engaged in non-exempt human subjects research covered by 38 C.F.R. part 16 must hold a valid Federalwide Assurance (FWA) for human subjects research approved by the U.S Department of Health and Human Services (HHS) Office for Human Research Protections (OHRP). Further, this directive sets forth a requirement in VHA policy for an oversight mechanism to be implemented for assessing whether VA medical facilities hold an FWA when such an assurance is required.

2. RELATED ISSUES: VA Directive 6500, VA Cybersecurity Program, dated February 24, 2021; VA Handbook 6500, Risk Management Framework for VA Information Systems - VA Information Security Program, dated February 24, 2021; VHA Directive 1058.02, Research Misconduct, dated July 10, 2020; VHA Directive 1200.01(1), Research and Development Committee, dated January 24, 2019; VHA Directive 1200.02(1), Research Business Operations, dated March 10, 2017; VHA Directive 1200.05(3), Requirements for the Protection of Human Subjects in Research, dated January 7, 2019; VHA Directive 1200.07, VA Research with Animals, dated May 23, 2023; VHA Directive 1200.08(1), Safety of Personnel and Security of Laboratories Involved in VA Research, dated April 24, 2019; VHA Directive 1605.01, Privacy and Release of Information, dated July 24, 2023; and VHA Directive 1605.03(3), Privacy Compliance and Accountability Program, dated September 19, 2019.

3. POLICY OWNER: The Office of Research Oversight (10RO) is responsible for the contents of this directive. Questions may be referred to VHA10RResearchOversightAction@va.gov.

4. LOCAL DOCUMENT REQUIREMENTS: VA medical facility Research Compliance Officers are required to develop and maintain a written audit plan for conducting study audits and reporting the results of such audits (see paragraph 2.h.(3)).

5. RESCISSIONS: VHA Directive 1058, Office of Research Oversight, dated December 13, 2021; VHA Directive 1058.01, Research Compliance Reporting Requirements, dated October 22, 2020; and VHA Directive 1058.03, Assurance of Protection for Human Subjects in Research, dated September 17, 2020, are rescinded.

6. RECERTIFICATION: This VHA directive is scheduled for recertification on or before the last working day of November 2029. This VHA directive will continue to serve as national VHA policy until it is recertified or rescinded.

7. IMPLEMENTATION SCHEDULE: This directive is effective upon publication.

BY DIRECTION OF THE OFFICE OF THE UNDER SECRETARY FOR HEALTH:

/s/ Steven Lieberman, MD
Deputy Under Secretary for Health

NOTE: *All references herein to VA and VHA documents incorporate by reference subsequent VA and VHA documents on the same or similar subject matter.*

DISTRIBUTION: Emailed to the VHA Publications Distribution List on November 12, 2024.

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APPENDIX A

CONTENT AND SUBMISSIONS OF NOTIFICATIONS TO ORO A-1

OFFICE OF RESEARCH OVERSIGHT

1. POLICY

It is Veterans Health Administration (VHA) policy that the VHA Office of Research Oversight (ORO) serves as the primary VHA office in advising the Under Secretary for Health on matters of compliance related to human subject protections, laboratory animal welfare, research safety, research laboratory security, research information security, research misconduct, and other research improprieties. It is VHA policy that ORO functions independently of entities within VHA with responsibility for the conduct of medical research programs, and that the Executive Director, ORO reports directly to the Under Secretary for Health without delegation. It is also VHA policy that Department of Veterans Affairs (VA) medical facilities that conduct research must notify ORO of certain research-related events, as set forth in this directive, and that each VA medical facility engaged in non-exempt human subjects research covered by the requirements of the Federal Policy for the Protection of Human Subjects hold a valid written assurance committing the facility to compliance with that Federal policy. **AUTHORITY:** 38 U.S.C. § 7307.

2. RESPONSIBILITIES

a. **Under Secretary for Health.** The Under Secretary for Health is responsible for:

(1) Ensuring overall VHA compliance with this directive.

(2) Supporting ORO with implementation and oversight of this directive.

(3) Supporting the development of mitigation or corrective actions to address noncompliance with this directive.

(4) Ensuring that the Executive Director of ORO reports directly to the Under Secretary for Health without delegation.

b. **Assistant Under Secretary for Health for Operations.** The Assistant Under Secretary for Health for Operations is responsible for:

(1) Communicating the contents of this directive to each of the Veterans Integrated Service Networks (VISNs).

(2) Assisting VISN Directors to resolve implementation and compliance challenges in all VA medical facilities within that VISN.

(3) Overseeing VISNs to ensure the effectiveness of and compliance with this directive.

(4) Transmitting to VA medical facilities, either directly or through the VISN Directors, the VA medical facility Director's Certification of Research Oversight research compliance self-assessment and data collection instrument administered by ORO.

c. **Executive Director, Office of Research Oversight.** The Executive Director, ORO is responsible for:

(1) Ensuring that ORO conducts periodic reviews of VA medical facility research programs to assess for compliance with applicable laws, regulations, and policies pertaining to human subject protections, laboratory animal welfare, research safety, research laboratory security, and research information security. This includes ensuring that select ORO reviews include an assessment of whether:

(a) A VA medical facility engaged in non-exempt human subjects research holds a valid Federalwide Assurance (FWA) approved by the U.S. Department of Health and Human Services (HHS) Office for Human Research Protections (OHRP) or an equivalent assurance of compliance recognized and approved by ORO and the VHA Office of Research & Development (ORD). See paragraph 8.b.

(b) A VA medical facility's internally operated Institutional Review Board (IRB), if one exists, is appropriately registered in accordance with HHS-OHRP and U.S. Food and Drug Administration (FDA) requirements.

(c) Events reportable under this directive were reported to ORO as required.

(d) VA medical facility Research Compliance Officers (RCOs) have fulfilled their auditing responsibilities under this directive.

(2) Conducting or directing ORO workgroups to conduct for-cause reviews into serious concerns raised about VA research, including investigations into VA medical facility research oversight programs or VHA program offices, when it is determined by the Executive Director, ORO, or the Under Secretary for Health that such concerns fall within ORO's oversight purview and are best investigated independently of the entity that is engaged in, or otherwise responsible for, the research.

(3) Ensuring that appropriate ORO subject matter experts review VA research-related incidents reported to ORO (see paragraph 3 of this directive and paragraph 3 of Appendix A).

(4) Ensuring that appropriate ORO subject matter experts provide oversight of remediation efforts by a VA medical facility or VHA program office to resolve serious or continuing noncompliance reported to ORO in accordance with the requirements of this directive and noncompliance identified by ORO directly or through other means (see paragraph 2.f.(19)).

(5) Recommending to the Under Secretary for Health that research activities of a VA medical facility be restricted or suspended when the Executive Director, ORO reasonably believes that such action is necessary to safeguard the safety, rights, or welfare of human subjects who participate in VA research; the safety of VA personnel who conduct VA research; or the welfare of animals used in VA research.

(6) Pursuant to 38 U.S.C. § 7307(c)(3)(B), halting or limiting the activities of a VA research project that the Executive Director, ORO reasonably believes places human subjects' lives or health at imminent risk.

(7) Ensuring ORO develops, or otherwise makes available, study auditing education and tools for VA medical facility RCOs.

(8) Ensuring that ORO oversees VA medical facility inquiries and investigations of alleged research misconduct (i.e., fabrication, falsification, or plagiarism in research) in VHA, as set forth in VHA Directive 1058.02, Research Misconduct, dated July 10, 2020.

(9) Collaborating with other Federal, VA, and VHA offices regarding the interpretation of regulations, policies, and procedures related to human subject protections, laboratory animal welfare, research safety, research laboratory security, research information security, and research misconduct.

(10) Liaising with other Federal, VA, and VHA program offices on research compliance matters for which those offices have joint oversight jurisdiction for VA research.

(11) Establishing and maintaining a field advisory committee that serves as a consultative body to provide recommendations to ORO to enhance the efficiency and effectiveness of ORO research compliance oversight activities. At a minimum, the committee membership includes, but is not limited to, the Executive Director, ORO; a VA medical facility Director, an Associate Chief of Staff for Research and Development (ACOS/R&D); a chairperson of a VA medical facility research review committee; and a VA medical facility RCO.

(12) Ensuring that Congress and other Federal entities are notified of ORO's oversight activities, as appropriate and in accordance with applicable law. This includes submitting, by March 15 of each year, a report to the Committees on Veterans' Affairs of the Senate and House of Representatives describing the activities of ORO during the preceding calendar year. The report must include:

(a) A summary of reviews of individual medical research programs completed by ORO.

(b) Directives and other substantive communications issued by ORO to VISNs and VA medical facilities.

(c) Results of any investigations by ORO.

(d) Other pertinent information about ORO that would be of interest to the Committees with regard to ORO's oversight activities.

(13) Reporting periodically to the Under Secretary for Health, the Secretary of Veterans Affairs, and the Committees on Veterans' Affairs of the Senate and House of Representatives any suspected lapse, from whatever cause or causes, in protecting the

safety of human subjects and others, including VA employees, in VA medical facility research programs. ***NOTE:*** *Unless more frequent reporting is requested, ORO's annual report submission to the Committees on Veterans' Affairs of the Senate and House of Representatives in accordance with paragraph 2.c.(12) above constitutes fulfillment of the requirement to periodically report to the Committees.*

d. **VHA Program Office Director.** VHA program office Directors are responsible for:

(1) Cooperating fully, and ensuring that their staff cooperates fully, with ORO's site reviews, investigations, and oversight activities, including ensuring that ORO requests for information (whether oral or in writing) are promptly and completely answered.

(2) In the event that a VHA program office enters into an agreement such as a memorandum of understanding (MOU), reliance agreement, or service agreement for reliance on a non-VA research review committee for the review, approval, and ongoing oversight of VA research, ensuring that the agreement stipulates that all applicable documents (or applicable excerpts) related to the non-VA research review committee's review, approval, and ongoing oversight of VA research must be readily available to ORO upon request.

e. **Veterans Integrated Service Network Director.** The VISN Director is responsible for:

(1) Ensuring that all VA medical facilities within the VISN comply with this directive and informing the Executive Director, ORO and the Assistant Under Secretary for Health for Operations when barriers to compliance are identified.

(2) Overseeing corrective actions to address noncompliance at the VISN and VA medical facilities within the VISN.

f. **VA Medical Facility Director.** The VA medical facility Director whose VA medical facility has a research program is responsible for:

(1) Serving as the Institutional Official (IO) responsible for the VA medical facility's research program.

(2) Ensuring that the VA medical facility holds a valid FWA approved by HHS-OHRP if the facility is engaged in non-exempt human subjects research covered by the requirements of the Federal Policy for the Protection of Human Subjects ("Common Rule"), which for VA is incorporated at 38 C.F.R. part 16. ***NOTE:*** *In rare cases and with both ORO and ORD concurrence, an equivalent written assurance of compliance with the requirements of the Common Rule may be recognized in lieu of an FWA. The requirement to hold an FWA (or equivalent assurance of compliance) does not apply to VA medical facilities engaged solely in human subjects research that is exempt from the requirements of the Common Rule.*

(3) Ensuring that the VA medical facility's research review and oversight programs function effectively. This includes ensuring that there is adequate support at the facility

to enable compliance with the reporting requirements of this directive and the timely implementation of sustainable remedial actions to mitigate the risks of, correct, or otherwise prevent reoccurrence of the underlying issues or causes of the events covered by this directive.

(4) Notifying the Executive Director, ORO or applicable ORO workgroup in advance of the initiation of a research program or the substantial alteration of an existing research program that is related to the implementation, suspension, or termination of an Animal Care and Use Program (ACUP), HRPP, or Research Safety and Security Program (RSSP). ***NOTE:*** *ORO workgroup contact information is available at https://www.va.gov/ORO/ORO_Contact_Information.asp.*

(5) Appointing at least one full-time VA medical facility RCO to conduct research informed consent and regulatory audits unless ORO has approved a written request from the VA medical facility Director to appoint a part-time VA medical facility RCO due to the facility having a small number of research studies such that the research auditing workload would not justify employing of a full-time RCO. ***NOTE:*** *With prior approval from ORO, the same individual may serve as a part-time VA medical facility RCO at more than one VA medical facility. Other arrangements may be approved by ORO on a situation-specific basis such as a VISN electing to employ a full-time dedicated VISN-level RCO to fulfill the VA medical facility RCO responsibilities at one or more VA medical facilities.*

(6) Ensuring that the VA medical facility RCO (or a lead VA medical facility RCO if one is designated in instances where a VA medical facility employs more than one RCO) reports directly to and is supervised by either the VA medical facility Director or a senior individual who both reports directly to and is supervised by the VA medical facility Director and whose primary responsibilities at the VA medical facility pertain directly to compliance.

(7) Ensuring that the RCO has direct access to the VA medical facility Director for purposes of reporting research noncompliance and other research-related concerns.

(8) Ensuring that VA medical facility RCO activities are not determined or managed by the ACOS/R&D or any other individual or research review committee in a VA medical facility's Research Service, regardless of to whom the VA medical facility RCO (or lead RCO if one has been designated) directly reports.

(9) Ensuring that the VA medical facility RCO's primary responsibilities at the VA medical facility pertain directly to compliance unless ORO has approved a written request from the VA medical facility Director otherwise.

(10) Ensuring that the VA medical facility RCO has the necessary education and experience at the time of hire or appointment to fulfill the duties of the RCO position. ***NOTE:*** *Expertise must include an understanding of the research review and oversight infrastructure required by Federal laws and regulations, and the principles and concepts of the conduct of biomedical or clinical research.*

(11) Ensuring that the VA medical facility RCO has ready access to research program and study documentation so that the VA medical facility RCO can effectively fulfill the responsibilities of the position, including access to documentation necessary to fulfill RCO research auditing requirements such as research review committee meeting minutes, study approval letters, approved study protocols, and investigator study documentation. ***NOTE:*** *In situations where the VA medical facility relies upon a non-VA research review committee, the VA medical facility Director must ensure that the agreement (such as an MOU, reliance agreement, or service agreement) to rely on the committee requires that the VA medical facility's RCO be provided access to the non-VA research review committee's records to the extent necessary for the RCO to fulfill research auditing requirements.*

(12) Ensuring that VA medical facility RCO audits are complete and timely, and that the results of those audits are reported as required by this directive. See paragraph 2.h.(4).

(13) Notifying ORO within 5 business days of an RCO annual quality assurance review determination that events covered by this directive were not reported to ORO as required. See paragraph 2.h.(6) and Appendix A, paragraph 3.

(14) Reporting any VA medical facility RCO appointment, resignation, or substantive change in duties or effort to ORO within 5 business days after the action takes effect. See Appendix A, paragraph 3.

(15) Implementing processes, consistent with all applicable VHA policy, to ensure that:

(a) Events covered by this directive are promptly reported to the VA medical facility Director so that the VA medical facility Director, or designee, can submit required notifications to ORO within the timeframes specified in this directive. ***NOTE:*** *If the VA medical facility Director designates another individual to submit required notifications to ORO on their behalf, the VA medical facility Director must still be notified by VA medical facility personnel of the events covered by this directive and the actions taken or to be taken to mitigate the risks of, correct, or otherwise prevent reoccurrence of the underlying issues/causes of the events.*

(b) Events covered by this directive are reported to ORO within the timeframes specified in paragraphs 2 and 3. ***NOTE:*** *In some instances, it may be necessary for a VA medical facility Director, or designee, to submit an initial (preliminary) report to ORO to ensure compliance with the deadlines stipulated in this directive, followed by subsequent report(s) as needed to convey all relevant information. The reporting of events to ORO does not otherwise obviate the additional reporting of such events by VA medical facility personnel to pertinent Federal agencies (such as HHS-OHRP, the HHS Office of Research Integrity, the National Institutes of Health Office of Laboratory Animal Welfare (NIH-OLAW), FDA, the NIH Office of Science Policy (NIH-OSP), and the Occupational Safety and Health Administration (OSHA)), research sponsors, and accrediting bodies in accordance with the requirements of those entities.*

(c) The VA medical facility's RCO is copied on notifications to ORO required by this directive, unless the VA medical facility Director determines that it is inappropriate to do so. ***NOTE:*** *For example, it would not be appropriate to copy the VA medical facility RCO on a notification of a confidential matter (such as a matter pertaining to an investigation involving another VA employee) if the RCO does not have a need-to-know or on a notification of a sensitive matter that pertains directly to the VA medical facility RCO (such as the VA medical facility RCO failing to perform required responsibilities).*

(16) Ensuring that all research compliance reports from any state or Federal oversight entity (including ORO), as well as research accreditation reports and determinations, are provided to the VA medical facility ACOS/R&D or equivalent, the Research & Development Committee (R&DC), any other relevant research review committees, and the VA medical facility RCO within 5 business days after receipt.

(17) Cooperating fully, and ensuring that VA medical facility personnel cooperate fully, with ORO's site reviews, investigations, and oversight activities, including ensuring that ORO requests for information (whether oral or in writing) are promptly and completely addressed.

(18) Ensuring that all applicable documents related to the review, approval, and ongoing oversight of VA research are promptly furnished to ORO in conjunction with ORO's research oversight activities. ***NOTE:*** *In the event that a VA medical facility relies upon a non-VA research review committee, the agreement (such as an MOU, reliance agreement, or service agreement) executed by the VA medical facility and the non-VA entity operating the research review committee establishing the role of that research review committee in the oversight of the VA medical facility's research must stipulate that all applicable documents (or applicable excerpts) related to the committee's review, approval, and ongoing oversight of the VA medical facility's research must be promptly furnished to VA medical facility personnel and ORO upon request. Unless indicated otherwise by ORO, it is the responsibility of VA personnel subject to an ORO compliance review or investigation at the VA medical facility to obtain documents requested by ORO from the non-VA research review committee.*

(19) Ensuring timely implementation and documentation of remedial actions within the VA medical facility to mitigate the risks of, correct, or otherwise prevent reoccurrence of the underlying issues or causes of the events covered by this directive. See paragraph 2.c.(4) for requirements related to the role of ORO in oversight of remedial actions within the VA medical facility. ***NOTE:*** *For events that pose risk of harm to the safety, rights, or welfare of human research subjects or others as a result of participation in VA research, events that pose risk of harm to the safety of VA personnel conducting VA research, and events that pose risk to the welfare of animals used in VA research, appropriate actions to mitigate, correct, or otherwise prevent realization of such risks must be implemented as soon as practicable.* This includes:

(a) Ensuring that actions to remediate noncompliance identified by ORO are completed within 180 calendar days of notification by ORO, except where extenuating

circumstances exist (e.g., remediation requires substantial renovation or fiscal expenditure, hiring, or legal negotiations).

(b) Ensuring that actions to remediate, mitigate risks associated with, and otherwise prevent reoccurrence of events reportable to ORO pursuant to this directive are completed within 180 calendar days of reporting to ORO, except where extenuating circumstances exist (e.g., remediation requires substantial renovation or fiscal expenditure, hiring, or legal negotiations).

(c) When remedial actions cannot be completed within 180 calendar days, providing the appropriate ORO workgroup(s) with written justification and a reasonable timeline for completion for each action prior to the elapsing of the 180-calendar-day period for remediation. ***NOTE:*** *This responsibility cannot be delegated.*

(20) Ensuring accurate and timely completion of the VA medical facility Director's Certification of Research Oversight administered by ORO. Certification requirements, instructions, and due dates are posted on ORO's SharePoint website at https://dvagov.sharepoint.com/sites/VACOVHAORO/RCO/default.aspx. ***NOTE:*** *This is an internal VA website that is not available to the public.*

g. **VA Medical Facility Associate Chief of Staff for Research & Development.** The VA medical facility ACOS/R&D (or Coordinator for R&D for small research programs if one is appointed instead) is responsible for:

(1) Assisting the VA medical facility Director with the development and implementation of event reporting processes to ensure that events covered by this directive are promptly reported to the VA medical facility Director so that the Director, or designee, can submit required notifications to ORO within the timeframes specified in this directive.

(2) Ensuring that VA medical facility personnel whose actions or involvement are necessary to effect prompt reporting to the VA medical facility Director of events covered by this directive have awareness of the VA medical facility reporting processes.

h. **VA Medical Facility Research Compliance Officer.** The VA medical facility RCO is appointed by the VA medical facility Director and is responsible for:

(1) Promoting awareness and understanding of this directive among VA medical facility employees who administer the research program, VA medical facility employees who conduct or are otherwise engaged in VA research, internally operated research review committees, and, to the extent practicable, non-VA research review committees relied upon by the VA medical facility.

(2) Serving as a point of contact at the VA medical facility to whom VA personnel may submit research-related concerns, including initial reports of the occurrence of events addressed in this directive. ***NOTE:*** *The VA medical facility RCO is not necessarily the primary point of contact to whom such initial reports or other concerns should be submitted. Rather, the VA medical facility RCO must be an available resource*

to whom initial reports may be submitted by VA medical facility personnel or others if they so choose.

(3) Developing a written audit plan for performing informed consent and regulatory audits of approved study protocols and other post-approval monitoring activities as specified by ORO. ***NOTE:*** *Examples of audit plans can be found on ORO's SharePoint website at* https://dvagov.sharepoint.com/sites/VACOVHAORO/RCO/RCO/Forms/AllItems.aspx*. This is an internal VA website that is not available to the public.* The written audit plan must describe the VA medical facility RCO's auditing process, including:

(a) Procedures for planning and executing audits.

(b) Procedures for soliciting study investigators' responses to preliminary audit findings.

(c) Procedures for reporting audit findings of noncompliance to relevant research review committees or committee coordinators with primary oversight of the research promptly, but no later than 30 calendar days after completion of an audit with findings.

(4) Auditing VA medical facility research projects in accordance with the written audit plan specified in paragraph 2.h.(3), ensuring the accuracy of those audits, and ensuring the results of audits identifying noncompliance are promptly reported to relevant research review committees or committee coordinators with primary oversight of the research.

(5) Notifying the VA medical facility Director and ORO within 5 business days of becoming aware that the auditing responsibilities described in paragraph 2.h.(4) cannot be fulfilled.

(6) Conducting a quality assurance review at least annually to determine whether events covered by this directive were reported to ORO as required, including whether such events were reported within the specified timeframes and submitting a written copy of the results to the VA medical facility Director and ACOS/R&D.

(7) Performing additional research compliance-related duties as assigned by their supervisor including assisting in research compliance education to investigators, research staff, and research committee members; assisting with research program accreditation activities; assisting with the completion of the VA medical facility Director's Certification of Research Oversight; conducting ad hoc audits of individual studies or programs; and conducting quality assurance activities designed to ensure that research compliance responsibilities at the VA medical facility are being satisfied. ***NOTE:*** *Such duties must not conflict with or delay completion of the VA medical facility RCO's research auditing responsibilities. VA medical facility RCOs must refrain from substantively participating in the pre-submission review of a study protocol or otherwise being involved in the approval of a research study as such activities would create a conflict of interest when the RCO is subsequently called upon to audit the protocol for compliance. Correspondingly, VA medical facility RCOs must not serve as voting or*

non-voting members (including as ex-officio members) of research review committees and may attend research review committee meetings only by invitation or agreement of such committees.

i. **VA Personnel.** VA personnel who become aware of the occurrence of research-related events described in paragraph 3 of this directive are responsible for promptly reporting the events to the appropriate VA medical facility point(s)-of-contact designated to receive such reports at the VA medical facility that approved the research. ***NOTE:*** *If VA personnel are unsure as to whom to report an event, they should report the event to the RCO at the VA medical facility that approved the research. VA personnel who choose to avail themselves of an anonymous reporting mechanism to report an event addressed in this directive are considered to have fulfilled their reporting obligation.*

3. VA RESEARCH-RELATED EVENTS REPORTABLE TO ORO

a. The events delineated in this paragraph, should they occur in VA research, must be reported by the VA medical facility Director promptly and within the timeframes specified in this paragraph to the appropriate ORO workgroup (see Appendix A, paragraph 3). ***NOTE:*** *The VA medical facility Director must implement processes within their respective VA medical facilities to ensure that the events covered by this directive are promptly reported to the VA medical facility Director so that the VA medical facility Director can submit required notifications to ORO within the timeframes specified. The timeframes specified in this directive for reporting events to ORO establish the maximum allowable time for reporting; once a reportable event is known to have occurred, it should be reported to ORO as soon as possible. Reporting requirements pertaining to research misconduct, as defined in paragraph 8.h. of this directive, are addressed separately in VHA Directive 1058.02.*

b. **Systemic Deficiencies.** The VA medical facility Director must notify ORO promptly of, but not later than 60 calendar days after, the identification of a systemic deficiency within the VA medical facility that has a reasonable likelihood of substantially compromising the VA medical facility's research oversight programs (ACUP, HRPP, and RSSP) or research information security processes, including persistent failure by any research review committee relied upon by the VA medical facility to adhere to applicable requirements governing VA research.

c. **VA Human Subjects Research.** The following events involving exempt or non-exempt VA human subjects research must be reported to ORO:

(1) **Deaths of Human Subjects Participating in VA Human Subjects Research.** The VA medical facility Director must notify ORO within 1 business day after VA medical facility personnel first become aware of the death of a human subject enrolled in a study approved by the VA medical facility that is believed to be both unexpected and related or possibly related to participation in a VA human subjects research study. ***NOTE:*** *For a multisite study, this subparagraph applies to the death of a human subject enrolled in the study under the auspices of the VA medical facility (as opposed to the death of a human subject enrolled into the same multisite study by a non-VA entity and for which*

the study activities pertaining to the enrolled human subject are under the auspices of a non-VA entity).

(2) **Unanticipated Problems Involving Risks to Subjects or Others in VA Human Subjects Research.** The VA medical facility Director must notify ORO promptly, but no later than 60 calendar days after VA medical facility personnel first become aware, of the occurrence of an unanticipated problem involving risks to subjects or others (UPIRTSO). ***NOTE:*** *See Appendix A, paragraph 3 for details on notifications to ORO. See paragraph 8.o. for the definition of UPIRTSO*.

(3) **Serious or Continuing Noncompliance Involving VA Human Subjects Research.** The VA medical facility Director must notify ORO promptly, but no later than 60 calendar days after VA medical facility personnel first become aware, of the occurrence of serious or continuing noncompliance with applicable laws, regulations, policies, and agreements pertaining to VA human subjects research. This includes, but is not limited to, serious or continuing noncompliance with 38 C.F.R. § 16, VHA Directive 1200.05(3), Requirements for the Protection of Human Subjects in Research, dated January 7, 2019, VA medical facility policies, standard operating procedures (SOPs), and MOUs (or equivalent) related to human subjects research, Institutional Review Board (IRB)-approved protocols, and the requirements or determinations of the IRB. ***NOTE:*** *Exempt human subjects research protocols may be under the primary oversight purview of a research review committee other than an IRB. For purposes of paragraph 3.c, any reference to IRB should be regarded as a reference to the research review committee with primary oversight of the exempt human subjects research study.*

(4) **Other Events Involving VA Human Research Protection Programs Reportable to ORO.** The VA medical facility Director must notify ORO promptly, but no later than 5 business days after VA medical facility personnel first become aware, of any of the following:

(a) The suspension or early termination of a VA human research study by the IRB, R&DC, or IO due to the study not being conducted in accordance with applicable regulations, policies, agreements, or IRB requirements or due to concerns about the safety, rights, or welfare of human subjects or others*.* ***NOTE:*** *The notification of suspension or early termination of a VA study by the IRB, R&DC, or IO must include a statement of the reason for the IRB's or IO's action.*

(b) A change in the status (e.g., expiration, restriction, suspension, or termination) of the VA medical facility's human subjects research FWA.

(c) The termination or non-renewal of the HHS-OHRP registration of any IRB relied upon by the VA medical facility for review and oversight of VA research.

(d) A failure of the VA medical facility to achieve or maintain full accreditation of its HRPP if such accreditation is sought by the VA medical facility.

(e) The issuance of a research-related citation or determination of noncompliance by a state or Federal entity (including the VA Office of Inspector General) or an accrediting

organization, pertaining to the VA medical facility's HRPP and human subjects research portfolio.

d. **VA Animal Research.** The following events involving VA animal research must be reported to ORO:

(1) **Human Deaths Associated with VA Animal Research.** The VA medical facility Director must notify ORO within 1 business day after VA medical facility personnel first become aware of the occurrence of a human death that is believed to have resulted from or possibly resulted from working with, caring for, or having other contact with animals used in VA research. ***NOTE:*** *See Appendix A, paragraph 3 for details about notifications to ORO.*

(2) **VA Animal Research Events Involving Serious Accident, Injury, Illness, or Exposure of a Human.** The VA medical facility Director must notify ORO promptly, but no later than 60 calendar days after VA medical facility personnel first become aware, of the occurrence of a serious accident, injury, illness, or exposure of a human that resulted from or possibly resulted from working with, caring for, or having other contact with research animals.

(3) **Serious or Continuing Noncompliance Involving VA Animal Research.** The VA medical facility Director must notify ORO promptly, but no later than 60 calendar days after VA medical facility personnel first become aware, of the occurrence of serious or continuing noncompliance with applicable laws, regulations, policies, and agreements pertaining to VA animal research. This includes, but is not limited to, serious or continuing noncompliance with 7 U.S.C. § 2131 et seq.; 9 C.F.R. parts 1-3; U.S. Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals; VHA Directive 1200.07, VA Research with Animals, dated May 23, 2023; VA medical facility policies, SOPs, and MOUs (or equivalent) related to animal research, as required by VHA Directive 1200.07 and to the extent developed; Institutional Animal Care and Use Committee (IACUC)-approved protocols; and the requirements or determinations of the IACUC. This also includes unapproved departures from the most recent edition of the *Guide for the Care and Use of Laboratory Animals (see https://grants.nih.gov/grants/olaw/guide-for-the-care-and-use-of-laboratory-animals.pdf*).

(4) **VA Animal Research Events Reportable to NIH-OLAW.** For VA animal research events reportable to NIH-OLAW pursuant to section IV.F.3. of the PHS Policy on Humane Care and Use of Laboratory Animals and NIH Notice No. NOT-OD-05-034, Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals (see https://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-034.html) and not otherwise covered by paragraphs 3.d.(1) through 3.d.(3), the VA medical facility Director must notify ORO within 60 calendar days of VA medical facility personnel becoming aware of the occurrence of the event or concomitantly with any notification of the event sent to NIH-OLAW, whichever is sooner.

(5) **Other Events Involving VA Animal Care and Use Programs Reportable to ORO.** The VA medical facility Director must notify ORO promptly, but no later than 5

business days after VA medical facility personnel first become aware, of any of the following:

(a) The suspension or early termination by the IACUC, R&DC, or IO of a VA study involving animals due to the study not being conducted in accordance with applicable regulatory, policy, or IACUC requirements or due to animal or research personnel welfare concerns. ***NOTE:*** *The notification of suspension or early termination of a VA study by the IACUC, R&DC, or IO must include a statement of the reason for the IACUC's or IO's action.*

(b) Any change in the status (e.g., expiration, termination) of the PHS Animal Welfare Assurance that covers the VA medical facility's ACUP.

(c) A substantial revision of the PHS Animal Welfare Assurance that covers the VA medical facility's ACUP, regardless of whether the PHS Animal Welfare Assurance is held by the VA medical facility or an academic affiliate. Such revisions include, but are not necessarily limited to, a change in the institution holding the PHS Animal Welfare Assurance that covers the VA medical facility's ACUP or the establishment or closing of a Veterinary Medical Unit by a VA medical facility. In instances where the PHS Animal Welfare Assurance is held by an entity other than the VA medical facility, such revisions should only be reported to ORO to the extent that they pertain to the VA medical facility's ACUP.

(d) The establishment of a new internally operated IACUC by a VA medical facility that previously relied upon an external IACUC or the elimination of an internally operated IACUC and transition to reliance on an external IACUC.

(e) The placement of the VA medical facility (or the institution holding the accreditation for a VA medical facility's ACUP) on deferred, conditional, probationary, or revoked status by AAALAC International (formerly referred to as the Association for Assessment and Accreditation of Laboratory Animal Care International).

(f) The granting of initial IACUC approval of VA research involving sensitive animal species (i.e., canines, felines, non-human primates, and other species if designated as such by VHA ORD).

(g) The issuance of a research-related citation or determination of noncompliance by a state or Federal entity (including the VA Office of Inspector General) or an accrediting organization, pertaining to the VA medical facility's ACUP and animal research portfolio.

e. **VA Laboratory Research.** The following events involving VA laboratory research must be reported to ORO:

(1) **Human Deaths Associated with VA Laboratory Research.** The VA medical facility Director must notify ORO within 1 business day after VA medical facility personnel first become aware of a human death that is believed to have resulted from or possibly resulted from work (or other activity) in a VA research laboratory or dedicated VA research area (e.g., research specimen storage area), or involving VA research

conducted in a research laboratory or dedicated research area owned or operated by a non-VA entity. ***NOTE:*** *This does not cover deaths of human subjects participating in VA human subjects research. Such events are addressed in paragraph 3.c.(1).*

(2) **VA Laboratory Research Events Involving Serious Accident, Injury, Illness, or Exposure of a Human.** The VA medical facility Director must notify ORO promptly, but no later than 60 calendar days after VA medical facility personnel first become aware, of the occurrence of a serious accident, injury, illness, or exposure of a human that resulted from or possibly resulted from work or other activity in a VA research laboratory or dedicated VA research area (e.g., research specimen storage area), or involving VA research conducted in a research laboratory or dedicated research area owned or operated by a non-VA entity.

(3) **Serious or Continuing Noncompliance Involving VA Laboratory Research.** The VA medical facility Director must notify ORO promptly, but no later than 60 calendar days after VA medical facility personnel first become aware, of the occurrence of serious or continuing noncompliance with applicable laws, regulations, policies, and agreements pertaining to the conduct of VA laboratory research. This includes, but is not limited to, serious or continuing noncompliance with VHA Directive 1200.08(1), Safety of Personnel and Security of Laboratories Involved in VA Research, dated April 24, 2019; VA research laboratory security requirements; VA medical facility SOPs, and MOUs (or equivalent) related to laboratory research; Subcommittee on Research Safety (SRS)-approved protocols; and the requirements or determinations of the SRS.

(4) **VA Laboratory Research Safety and Security Events Reportable to Other Federal Entities.** For research safety and security events involving VA laboratory research that are reportable to the NIH-OSP, Centers for Disease Control and Prevention (CDC), Environmental Protection Agency, OSHA, or other Federal entities and not otherwise covered by paragraphs 3.e.(1) through 3.e.(3), the VA medical facility Director must notify ORO within 60 days of VA medical facility personnel becoming aware of the occurrence of the event or at the same time notification of the event is sent to the other Federal entity, whichever is sooner.

(5) **Other Events Involving VA Research Safety and Security Reportable to ORO.** The VA medical facility Director must notify ORO promptly, but no later than 5 business days after VA medical facility personnel first become aware, of any of the following:

(a) The suspension or early termination of a VA study by the SRS (or equivalent safety committee), Institutional Biosafety Committee (IBC), R&DC, or IO due to research laboratory safety or security concerns, including concerns about the safety of individuals conducting VA laboratory research, or environmental concerns attributed to VA laboratory research. ***NOTE:*** *The notification of suspension or early termination of a VA study by the SRS, IBC, R&DC, or IO must include a statement of the reason for SRS, IBC, R&DC, or IO action.*

(b) The expiration or termination of the NIH-OSP registration of any IBC relied upon by the VA medical facility for review and oversight of the VA medical facility's research.

(c) A security concern involving:

1. An unauthorized intrusion, physical security breach, break-in, or other significant security incident in an area where VA laboratory or animal research is conducted; or

2. Any physical loss or theft of VA research materials or equipment, the loss or theft of which poses risk of harm to people, animals, or the environment.

(d) The initiation of VA research involving Biosafety Level 3 (BSL-3) containment, select agents or toxins (see https://www.selectagents.gov/sat/list.htm), or dual use research of concern (see https://www.phe.gov/s3/dualuse/Pages/default.aspx).

(e) The issuance of a research-related citation or determination of noncompliance by a state or Federal entity (including the VA Office of Inspector General) or an accrediting organization, pertaining to the VA medical facility's RSSP and VA laboratory research portfolio.

f. **VA Research Information Security and Privacy.** The following events involving VA research must be reported to ORO:

(1) **Information Security and Privacy Incidents Involving VA research.** The VA medical facility Director must notify ORO promptly, but no later than 60 calendar days after VA medical facility personnel first become aware, of the occurrence of information security or privacy incidents (inappropriate access, loss, theft, or noncompliant storage, transmission, removal or destruction, of protected health information (PHI) or other VA research information deemed to be sensitive; theft, loss, or noncompliant destruction of equipment containing PHI or other VA research information deemed to be sensitive; uses and disclosures of PHI for research without legal authority (e.g., without a valid authorization or waiver of authorization) related to VA research that constitute serious or continuing noncompliance or a UPIRTSO. ***NOTE:*** *The reporting requirements set forth in this paragraph do not supersede applicable reporting requirements set forth in other VA and VHA policies (including the VA National Rules of Behavior and VA Handbook 6500, Risk Management Framework for VA Information Systems - VA Information Security Program, dated February 24, 2021) with regard to reporting such incidents to an individual's supervisor and the applicable Information System Security Officer (ISSO), Privacy Officer (PO) or Records Management official.*

(2) **Other Information Security and Privacy Incidents Involving VA Research Reportable to ORO.** The VA medical facility Director must notify ORO promptly, but no later than 5 business days after VA medical facility personnel first become aware, of any the following:

(a) The suspension or early termination of a VA study due to research information security or privacy concerns. ***NOTE:*** *The notification of suspension or early termination of a VA study must include a statement of the reason for the action.*

(b) The issuance of a research-related citation or determination of noncompliance by a state or Federal entity (including the VA Office of Inspector General) or an accrediting organization, pertaining to the facility's research-related information security and privacy processes and practices.

4. OVERSIGHT AND ACCOUNTABILITY

a. **Internal Controls.** Internal controls for this directive include:

(1) **ORO Site Reviews.** Select ORO site reviews involve an assessment component to provide reasonable assurance that: events reportable under this directive are reported to ORO; VA medical facilities with active research programs have appointed at least one full-time RCO or obtained a waiver to appoint a part-time RCO; RCOs have fulfilled their auditing responsibilities; and VA medical facilities engaged in non-exempt human subjects research hold active, approved FWAs (or equivalent assurances of compliance recognized and approved by ORO and VHA ORD).

(2) **ORO's Case Management Database**. ORO uses a case management database to track VA medical facility actions to remediate noncompliance identified by ORO and to mitigate, correct, or otherwise prevent reoccurrence of events covered by this directive. This includes tracking remedial action status and timeframes for implementation.

(3) **ORO's Field Advisory Committee**. This committee provides feedback about the efficiency and effectiveness of ORO's research compliance oversight activities and ORO's strategic approach to executing its oversight activities.

b. **Metrics.** To facilitate the effectiveness of this directive:

(1) 100% of ORO's Combined Program Reviews (or equivalent) involve an assessment of whether events reportable under this directive were reported to ORO.

(2) 100% of ORO's Combined Program Reviews (or equivalent) involve an assessment of whether RCOs have fulfilled their auditing responsibilities.

(3) At least 95% of actions to remediate noncompliance identified by ORO are completed by VA medical facility personnel within 180 calendar days of identification by ORO or have a documented justification on file with ORO for why such actions were not completed within 180 calendar days.

(4) At least 95% of actions to remediate, mitigate risks associated with, or otherwise prevent reoccurrence of events reportable to ORO are completed by VA medical facility personnel within 180 calendar days of reporting to ORO or have a documented justification on file with ORO for why such actions were not completed within 180 calendar days. See paragraph 2.f.(19).

(5) 100% of VA medical facilities with active research programs have at least one full-time RCO or obtained a waiver from ORO to allow for appointment of a part-time

RCO or coverage by an RCO from another VA medical facility. ***NOTE:*** *VA medical facilities that are actively recruiting to fill a vacant RCO position are considered as fulfilling this metric provided that it has not been longer than 1 year since the position was vacated or otherwise required to be filled.*

(6) 100% of VA medical facilities actively engaged in non-exempt human subjects research hold an approved FWA (or equivalent assurance of compliance recognized and approved by ORO and VHA ORD).

5. TRAINING

There are no formal training requirements associated with this directive.

6. RECORDS MANAGEMENT

All records regardless of format (for example, paper, electronic, electronic systems) created by this directive must be managed as required by the National Archives and Records Administration (NARA) approved records schedules found in VHA Records Control Schedule 10-1. Questions regarding any aspect of records management can be addressed to the appropriate Records Officer.

7. BACKGROUND

a. ORO was established in 2003 pursuant to Public Law (P.L.) 108–170 (see 38 U.S.C. § 7307) to advise the Under Secretary for Health on matters of research compliance; perform periodic reviews and inspections of VA medical research programs; and conduct investigations into VA medical research impropriety and misconduct.

b. Pursuant to 38 U.S.C. § 7307, ORO must function independently of entities within VHA with responsibility for the conduct of medical research programs, and the Executive Director of ORO must report directly to the Under Secretary for Health without delegation.

c. VA conducts basic, translational, and clinical research that involves human research participants, PHI and other VA sensitive information (VASI), laboratory animals, and hazardous agents. Given its breadth, VA research is subject to a broad array of requirements, including requirements pertaining to research noncompliance, events that may pose a genuine risk of harm to the safety, rights, or welfare of human research subjects or others as a result of participation in VA research, events that may pose a genuine risk of harm to the safety of VA personnel conducting VA research, and events that may compromise the care or welfare of animals used in VA research. Depending on the nature of such events and the outcome of institutional reviews of such events, VA medical facility Directors may be required to report the events to ORO. ***NOTE:*** *The reporting requirements of this directive do not alter or replace any additional requirements for the reporting of research noncompliance and other research-related events to other internal or external entities as mandated by law, regulation, policy, or agreement.*

8. DEFINITIONS

a. **Adverse Event in Human Subjects Research.** An adverse event in human subjects research is any untoward physical or psychological occurrence in a human subject participating in research, whether or not considered related to the subject's participation in research. ***NOTE:*** *See paragraph 8.l. for the definition of a Serious Adverse Event in Human Subjects Research.*

b. **Assurance of Compliance (Human Subjects) or Federalwide Assurance.** An Assurance of Compliance (Human Subjects) or Federalwide Assurance is a legally binding written document that commits an institution to complying with the Federal Policy for the Protection of Human Subjects ("Common Rule"), which for VA is incorporated at 38 C.F.R. part 16. ***NOTE:*** *The term "Federalwide Assurance" (also colloquially referred to as an "FWA") refers to a specific type of assurance that is approved by HHS-OHRP for Federalwide use as specified in 38 C.F.R. 16.103(a).*

c. **Continuing Noncompliance.** For purposes of this directive, continuing noncompliance means repeated instances of same or similar noncompliance with applicable laws, regulations, policies, agreements, or determinations of a research review committee or the prolonged persistence of noncompliance after its identification, awareness, or implementation of a corrective action intended to effectively resolve the noncompliance.

d. **Exempt Human Subjects Research.** Exempt human subjects research is research involving human subjects determined to be exempt, as applicable, under 38 C.F.R. 16.104 of the 2018 Common Rule or under 38 C.F.R. 16.101(b) of the pre-2018 Common Rule. ***NOTE:*** *Research deemed to be exempt under 38 C.F.R. 16 may not necessarily be exempt from the requirements of other regulations that may apply to the research including regulations promulgated by the FDA.*

e. **Noncompliance.** For purposes of this directive, noncompliance is any failure to adhere to applicable requirements for overseeing, reviewing, approving, or conducting VA research set forth in law, regulation, policy, or study agreements (such as reliance agreements, memoranda of understanding, data use agreements), including any failure to conduct research in accordance with a VA study protocol approved by a research review committee.

f. **Protected Health Information.** Protected health information (PHI), as defined by the Health Insurance Portability and Accountability Act (HIPAA), is individually identifiable health information transmitted or maintained in any form or medium by a covered entity, such as VHA. ***NOTE:*** *For more information, see VHA Directive 1605.01, Privacy and Release of Information, dated July 24, 2023.*

g. **Research.** Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this directive, whether or not they are conducted or supported under a program that is

considered research for other purposes. For example, some demonstration and service programs may include research activities. In accordance with VHA Directive 1200.05(3) clinical investigations, including clinical investigations as defined under FDA regulations in 21 C.F.R. §§ 50.3, 312.3(b) and 812.3(h), are considered research. ***NOTE:*** *Regarding activities involving animals, VHA Directive 1200.07 defines animal research as any activity in which animals are the subjects of procedures that are necessary for specific research or teaching projects.* For purposes of this directive, the following activities are not considered research:

(1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during an event or crisis that threatens public health (including natural or man-made disasters).

(3) Collection and analysis of information, biospecimens or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

(4) Authorized operational activities (as determined by each Federal agency) in support of intelligence, homeland security, defense, or other national security missions.

h. **Research Misconduct.** Research misconduct is fabrication, falsification, or plagiarism in proposing, performing, or reviewing research or in reporting research results. ***NOTE:*** *For more information, see Federal Policy on Research Misconduct 65 Federal Register (FR) 76262 (December 6, 2000) and VHA Directive 1058.02.*

i. **Research Review Committee.** A research review committee is any committee or subcommittee designated by a VA medical facility to review, approve, and provide oversight of VA research. For purposes of this directive, research review committees include IACUCs IBCs, IRBs, R&DCs, and SRS, or the equivalents of any such committees, that are relied upon by a VA medical facility, regardless of whether the committees are operated by a VA or a non-VA entity. ***NOTE:*** *For more information about the aforementioned committees, see VHA Directive 1200.01(1), Research and Development Committee, dated January 24, 2019; VHA Directive 1200.05(3); VHA Directive 1200.07 and VHA Directive 1200.08(1).* In addition, other subcommittees established by the R&DC to review, approve, or provide oversight of VA research are also considered research review committees for purposes of this directive.

j. **Select Agents and Toxins.** Select agents and toxins are regulated biological agents or toxins that could pose a severe threat to public health and safety or to animal or plant health as determined by HHS and the U.S. Department of Agriculture (USDA). ***NOTE:*** *For more information, see VHA Directive 1200.08(1) as well as 7 C.F.R. part 331, 9 C.F.R. part 121 and 42 C.F.R. part 73.*

k. **Serious Accident, Injury, Illness, or Exposure of a Human.** Accidents, injuries, illnesses, or exposures of a human are considered serious if they: (1) require medical attention or treatment, other than basic first aid provided at the site where the accident, injury, illness, or exposure occurred; (2) require time away from work or restricted work activities; (3) require medical surveillance of the affected individual(s) that may include sequential serology or other medical testing; or (4) lead (or could potentially lead) to serious long term health complications or death.

l. **Serious Adverse Event in Human Subjects Research.** A serious adverse event (SAE) in human subjects research is an untoward occurrence, whether or not considered related to a subject's participation in research, that results in death, a life-threatening experience, inpatient hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, congenital anomaly or birth defect, or that requires medical, surgical, behavioral, social, or other intervention to prevent such an outcome.

m. **Serious Noncompliance.** For purposes of this directive, serious noncompliance is any failure to adhere to requirements for conducting research that may reasonably be regarded as:

(1) Presenting a genuine risk of substantive harm to the safety, rights, or welfare of human research subjects or others, including their rights to privacy and confidentiality of identifiable private information;

(2) Presenting a genuine risk of substantive harm to the safety of research personnel who conduct research;

(3) Presenting a genuine risk of substantive harm to the health or welfare of animals used in research;

(4) Presenting a genuine risk of substantive reputational harm to VA; or

(5) Substantively compromising a VA medical facility's Animal Care and Use Program (ACUP), Human Research Protection Program (HRPP), Research Safety and Security Program (RSSP), or research information security processes.

n. **Systemic Deficiency.** For purposes of this directive, a systemic deficiency is a fundamental, underlying problem that compromises the effectiveness of a VA medical facility's research oversight system(s) regarding the safeguarding of the safety, rights, and welfare of human subjects who participate in VA research; the safety of VA personnel who conduct VA research; or the welfare of animals used in VA research.

o. **Unanticipated Problem Involving Risks to Subjects or Others in Human Subjects Research.** A UPIRTSO in human subjects research is an incident, experience, or outcome that is unexpected; related or possibly related to participation in the research; and indicative of the research placing subjects or others at greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized. ***NOTE:*** *This description is adapted from guidance published by HHS-OHRP. See https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html. For purposes of this directive, an unexpected SAE that is related or possibly related to participation in human subjects research constitutes a UPIRTSO.*

(1) **Unexpected.** For purposes of the definition of UPIRTSO, the term "unexpected" refers to an incident, experience, or outcome that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol-related documents and the characteristics of the study population.

(2) **Related to Participation in the Research.** For purposes of the definition of UPIRTSO, the phrase "related to participation in the research" means a logical sequence of cause and effect that shows study procedures were the reason for the incident, experience, or outcome. The phrase "possibly related to participation in the research" implies a lesser degree of certainty about causality and refers to an incident, experience, or outcome for which there is some evidence to reasonably suggest a causal relationship between study procedures and the incident, experience, or outcome.

p. **VA Personnel.** VA personnel means individuals holding compensated, without compensation (WOC), or Intergovernmental Personnel Act (IPA) appointments with VA.

q. **VA Research.** VA research is research conducted by VA investigators (serving on compensated, WOC, or IPA appointments) while on VA time or on VA property. The research may be funded by VA, other sponsors, or be unfunded.

9. REFERENCES

a. P.L. 108–170.

b. 7 U.S.C. § 2131 et seq.

c. 38 U.S.C. § 7307.

d. 7 C.F.R. part 331.

e. 9 C.F.R. parts 1 – 4, 121.

f. 21 C.F.R. parts 50, 312, 812.

g. 38 C.F.R. part 16.

h. 42 C.F.R. part 73.

i. Federal Policy on Research Misconduct 65 Federal Register (FR) 76262 (December 6, 2000).

j. VA Handbook 6500, Risk Management Framework for VA Information Systems - VA Information Security Program, dated February 24, 2021.

k. VHA Directive 1058.02, Research Misconduct, dated July 10, 2020.

l. VHA Directive 1200.01(1), Research and Development Committee, dated January 24, 2019.

m. VHA Directive 1200.05(3), Requirements for the Protection of Human Subjects in Research, dated January 7, 2019.

n. VHA Directive 1200.07, VA Research with Animals, dated May 23, 2023.

o. VHA Directive 1200.08(1), Safety of Personnel and Security of Laboratories Involved in VA Research, dated April 24, 2019.

p. VHA Directive 1605.01, Privacy and Release of Information, dated July 24, 2023.

q. VHA Office of Research Oversight: ORO Contact Information, https://www.va.gov/ORO/ORO_Contact_Information.asp.

r. VHA Office of Research Oversight: ORO SharePoint website, https://dvagov.sharepoint.com/sites/VACOVHAORO/RCO/default.aspx. ***NOTE:*** *This is an internal VA website that is not available to the public.*

s. VHA Office of Research Oversight SharePoint website: ORO Research Compliance and Technical Assistance, https://dvagov.sharepoint.com/sites/VACOVHAORO/RCO/RCO/Forms/AllItems.aspx. ***NOTE:*** *This is an internal VA website that is not available to the public.*

t. Guide for the Care and Use of Laboratory Animals (The Guide), 8th edition. Institute for Laboratory Animal Research, National Research Council of the National Academies, Washington, DC: The National Academies Press, 2011, http://grants.nih.gov/grants/olaw/Guide-for-the-Care-and-Use-of-Laboratory-Animals.pdf.

u. U. S. Department of Health and Human Services, Public Health Emergency: Dual Use Research of Concern, https://www.phe.gov/s3/dualuse/Pages/default.aspx.

v. U.S. Department of Health and Human Services. Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events: OHRP Guidance, 2007, https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html.

w. U.S. Department of Health and Human Services and U.S. Department of Agriculture: Select Agents and Toxins List, https://www.selectagents.gov/sat/list.htm.

x. U.S. Public Health Service, Policy on Humane Care and Use of Laboratory Animals, last revised 2015, https://olaw.nih.gov/policies-laws/phs-policy.htm.

y. Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals, February 24, 2005, https://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-034.html.

APPENDIX A

CONTENT AND SUBMISSIONS OF NOTIFICATIONS TO ORO

1. PURPOSE

This appendix sets forth the minimum information that should be included, if and as applicable, in Department of Veterans Affairs (VA) medical facility notifications sent to the Veterans Health Administration (VHA) Office of Research Oversight (ORO). ***NOTE:*** *In some instances, it may be necessary for a VA medical facility Director to submit an initial report, which does not contain all the information stipulated in paragraph 2 of this appendix, to fulfill the requirements for prompt reporting to ORO within the deadlines stipulated in paragraph 3 of the body of the directive. In such instances, subsequent reports must be submitted when the information becomes available or as otherwise directed by ORO. During its oversight, ORO may request additional information not addressed in this appendix (such as research review committee meeting minutes from when an event was reviewed by the committee, or documentation of completion of remedial actions).*

2. MINIMUM CONTENT TO BE INCLUDED IN NOTIFICATIONS TO ORO

a. **Systemic Deficiencies.** Notifications to ORO required by this directive pertaining to systemic deficiencies must include, as applicable and to the extent known at the time of notification:

(1) Name of the reporting VA facility.

(2) A detailed description of the systemic deficiency, including whether and how the deficiency:

(a) Poses a genuine risk of harm to the safety, rights, or welfare of human research subjects or others as a result of participation in VA research, including their rights to privacy and confidentiality.

(b) Poses a genuine risk of harm to the safety of VA personnel conducting VA research.

(c) Compromises the care or welfare of animals used in VA research.

(d) Compromises the effectiveness of a VA medical facility's research oversight program.

(3) Date that VA medical facility personnel first identified or otherwise became aware of the event.

(4) A description of how the deficiency was identified, including whether identified internally (by VA medical facility personnel or entities acting as agents of the facility such as a research review committee operated by another entity but relied upon by the

facility through a formal agreement) or externally (e.g., by individuals *not* associated with or acting as agents of the facility such as by a VHA program office, external monitoring/auditing/accreditation organization).

(5) Name of the research review committee(s) that reviewed the reported deficiency and any resulting determination(s) made by the committee.

(6) Actions the facility has taken or plans to take to address the systemic deficiency and anticipated dates for completing any pending or proposed actions.

(7) Indication of whether the systemic deficiency represents a repeat of the same type of systemic deficiency or noncompliance involving the facility's research program within the past 3 years.

(8) Names of other Federal agencies or entities notified, or to be notified, of the systemic deficiency and the date(s) of notification.

(9) Name and contact information (telephone number and email address) of the VA medical facility point of contact with whom ORO can follow-up for additional information.

(10) If the systemic deficiency pertains to a particular protocol/project or a limited set of related protocols/projects, providing the following additional information:

(a) Title and identification number of the research protocol(s)/project(s) involved, as well as the name of the principal investigator(s)/local site investigator(s) for the research protocol(s)/project(s).

(b) Sponsor(s) and grant number(s) associated with support for the research protocol(s)/project(s) involved.

(c) Indication of whether the research protocol(s)/project(s) involved are being conducted as part of a multi-site study and, if so, the name of the institution serving as the coordinating center.

(d) Risk level associated with the research protocol(s)/project(s) involved (e.g., whether minimal risk or more than minimal risk for human subjects research; assigned biosafety level for laboratory research; and animal species involved).

(e) Indication of whether the deficiency involves noncompliance by a same individual or study team responsible for other research noncompliance within the past 3 years.

b. **Human Subjects Research.** Notifications to ORO required by this directive pertaining to human subjects research must include as applicable and to the extent known at the time of notification:

(1) Name of the reporting VA facility.

(2) Title and identification number of the research protocol(s)/project(s) involved, as well as the name of the principal investigator(s)/local site investigator(s) for the research protocol(s)/project(s).

(3) Sponsor(s) and grant number(s) associated with support for the research protocol(s)/project(s) involved.

(4) Indication of whether the research protocol(s)/project(s) involved are being conducted as part of a multi-site study and, if so, the name of the institution serving as the coordinating center.

(5) Risk level associated with the research protocol(s)/project(s) involved (e.g., whether minimal risk or more than minimal risk for human subjects research).

(6) Indication of whether investigational drugs or devices are used in the research and, if so, the associated Investigation New Drug (IND)/Investigational Device Exemption (IDE) number.

(7) Clinicaltrials.gov number.

(8) Date that VA medical facility personnel first identified or otherwise became aware of the event.

(9) A detailed description of the event, including:

(a) The date(s) of the event.

(b) The type of reportable event (e.g., serious adverse event, unanticipated problem involving risk to subjects or others (UPIRTSO), serious or continuing noncompliance, suspension or termination).

(c) Number of research subjects affected.

(d) Underlying cause(s) and outcome(s) of the event.

(10) A description of how the event was identified, including whether identified internally (by VA medical facility personnel or entities acting as agents of the facility such as a research review committee operated by another entity but relied upon by the facility through a formal agreement) or externally (e.g., by individuals *not* associated with or acting as agents of the facility such as by a VHA program office, external monitoring/auditing/accreditation organization).

(11) Name of the Institutional Review Board (IRB) or other research review committee(s) that reviewed the event and any resulting determination(s) made by the committee(s).

(12) Actions the facility is taking or plans to take to address the event (e.g., protocol or informed consent document revisions, subject enrollment suspensions, protocol

terminations, enrolled subjects notifications, increased monitoring, education/training, return/transition to clinical care or standard of care management of disease or condition) and anticipated dates for completing any pending or proposed actions.

(13) Indication of whether the event represents a repeat of the same type of noncompliance involving the facility's research program within the past 3 years.

(14) Indication of whether the event involves noncompliance by the same individual or study team responsible for other research noncompliance within the past 3 years.

(15) Names of other Federal agencies or entities (e.g., U.S. Department of Health and Human Services Office for Human Research Protections (HHS-OHRP), U.S. Food and Drug Administration (FDA)) notified, or to be notified, of the event and the date(s) of notification.

(16) Name and contact information (telephone number and email address) of the VA medical facility point of contact with whom ORO can follow-up for additional information.

c. **Animal Research.** Notifications to ORO required by this directive pertaining to animal research must include as applicable and to the extent known at the time of notification:

(1) Name of the reporting VA facility.

(2) Title and identification number of the research protocol(s)/project(s) involved.

(3) Sponsor(s) and grant number(s) associated with support for the research protocol(s)/project(s) involved.

(4) Indication of risks/risk level associated with the research protocol(s)/project(s), including assigned biosafety level for animal/laboratory research and whether the research involves use of non-exempt recombinant DNA or select agents or toxins.

(5) Date that VA medical facility personnel first identified or otherwise became aware of the event.

(6) A detailed description of the event, including:

(a) The date(s) and location(s) of the event.

(b) Species and number of animals involved in the event.

(c) The type of reportable event (e.g., human accident, injury, or exposure, serious or continuing noncompliance, suspension or termination).

(d) Underlying cause(s) of the event and outcome(s) of the event.

(7) A description of how the event was identified, including whether identified internally (by VA medical facility personnel or entities acting as agents of the facility such as a research review committee operated by another entity but relied upon by the facility through a formal agreement) or externally (e.g., by individuals *not* associated with or acting as agents of the facility such as by a VHA program office, external monitoring/auditing/accreditation organization).

(8) Name of the Institutional Animal Care and Use Committee (IACUC) or other research review committee(s) that reviewed the event and any resulting determination(s) made by the committee(s).

(9) Actions the facility is taking or plans to take to address the event (e.g., protocol revisions, increased monitoring of animal research activities, education/training) and anticipated dates for completing any pending or proposed actions.

(10) Indication of whether the event represents a repeat of the same type of noncompliance involving the facility's research program within the past 3 years.

(11) Indication of whether the event involves noncompliance by a same individual or study team responsible for other research noncompliance within the past 3 years.

(12) Names of other Federal agencies or entities (e.g., National Institutes of Health Office of Laboratory Animal Welfare (NIH-OLAW); AAALAC, International; VHA Office of Research & Development (ORD), Office of the Chief Veterinary Medical Officer (CVMO)) notified, or to be notified, of the event and the date(s) of notification.

(13) Name and contact information (telephone number and email address) of the VA medical facility point of contact with whom ORO can follow-up for additional information.

d. **Research Laboratory Safety and Security.** Notifications to ORO required by this directive pertaining to research laboratory safety and security must include as applicable and to the extent known at the time of notification:

(1) Name of the reporting VA facility.

(2) Title and identification number of the research protocol(s)/project(s) involved, as well as the name of the principal investigator(s)/local site investigator(s) for the research protocol(s)/project(s).

(3) Sponsor(s) and grant number(s) associated with support for the research protocol(s)/project(s) involved.

(4) Indication of risks/risk level associated with the research protocol(s)/project(s), including assigned biosafety level for animal/laboratory research and whether the research involves use of non-exempt recombinant DNA or select agents or toxins.

(5) Date that VA medical facility personnel first identified or otherwise became aware of the event.

(6) A detailed description of the event, including:

(a) The date(s) and location of the event.

(b) The type of reportable event (e.g., human accident, injury, or exposure, serious or continuing noncompliance, security-related, suspension or termination).

(c) Indication of whether required safety equipment, containment, personal protective equipment, and safe handling practices were being followed at the time of the event.

(d) Underlying cause(s) of the event and outcome(s) of the event.

(7) A description of how the event was identified, including whether identified internally (by VA medical facility personnel or entities acting as agents of the facility such as a research review committee operated by another entity but relied upon by the facility through a formal agreement) or externally (e.g., by individuals *not* associated with or acting as agents of the facility such as by a VHA program office, external monitoring/auditing/accreditation organization).

(8) Name of the Subcommittee on Research Safety (SRS), Institutional Biosafety Committee (IBC), or other research review committee(s) that reviewed the event and any resulting determination(s) made by the committee(s).

(9) Actions the facility is taking or plans to take to address the event (e.g., protocol revisions, increased monitoring of laboratory research activities, education/training, medical surveillance, occupational health follow-up) and anticipated dates for completing any pending or proposed actions.

(10) Indication of whether the event represents a repeat of the same type of noncompliance involving the facility's research program within the past 3 years.

(11) Indication of whether the event involves noncompliance by a same individual or study team responsible for other research noncompliance within the past 3 years.

(12) Names of other Federal agencies or entities (e.g., National Institutes of Health Office of Science Policy (NIH-OSP), Centers for Disease Control and Prevention (CDC), Occupational Safety and Health Administration (OSHA), VA Police Services) notified, or to be notified, of the event and the date(s) of notification.

(13) Name and contact information (telephone number and email address) of the VA medical facility point of contact with whom ORO can follow-up for additional information.

e. **Research Information Security and Privacy.** Notifications to ORO required by this directive pertaining to research information security or research privacy must include as applicable and to the extent known at the time of notification:

(1) Name of the reporting VA facility.

(2) Title and identification number of the research protocol(s)/project(s) involved, as well as the name of the principal investigator(s)/local site investigator(s) for the research protocol(s)/project(s).

(3) Sponsor(s) and grant number(s) associated with support for the research protocol(s)/project(s) involved.

(4) Indication of whether the research protocol(s)/project(s) involved are being conducted as part of a multi-site study and, if so, the name of the institution serving as the coordinating center.

(5) Indication of risks/risk level associated with the research protocol(s)/project(s) involved (e.g., whether minimal risk or more than minimal risk for human subjects research; assigned biosafety level for laboratory research; animal species involved).

(6) Indication of whether investigational drugs or devices are used in the research and, if so, the associated Investigation New Drug (IND)/Investigational Device Exemption (IDE) number.

(7) Clinicaltrials.gov number.

(8) Date that VA medical facility personnel first identified or otherwise became aware of the event.

(9) A detailed description of the event, including:

(a) The date(s) of the event.

(b) The type of reportable event (e.g., UPIRTSO, serious or continuing noncompliance, suspension or termination).

(c) Number of research subjects and research records affected.

(d) Description of any VA Sensitive Information (VASI) involved, including specific elements of Protected Health Information (PHI) involved.

(e) Indication of whether unauthorized use, disclosure or transmission of VASI/PHI occurred.

(f) Indication of whether the event being reported is related to any existing or previously submitted reports.

(g) Underlying cause(s) and outcome(s) of the event.

(10) A description of how the event was identified, including whether identified internally (by VA medical facility personnel or entities acting as agents of the facility such as a research review committee operated by another entity but relied upon by the facility through a formal agreement) or externally (e.g., by individuals *not* associated

with or acting as agents of the facility such as by a VHA program office, external monitoring/auditing/accreditation organization).

(11) Name of the research review committee(s) that reviewed the event and any resulting determination(s) made by the committee(s).

(12) Indication of whether a review of the event has been conducted, and a resulting determination made, by the Information System Security Officer (ISSO), Privacy Officer (PO), and Data Breach Response Service (DBRS).

(13) Actions the facility is taking or plans to take to address the event (e.g., protocol or informed consent document revisions, subject enrollment suspensions, protocol terminations, enrolled subjects notifications, issuance of notifications to subjects impacted including issuance of credit monitoring letters, education/training) and anticipated dates for completing any pending or proposed actions.

(14) Indication of whether the event represents a repeat of the same type of noncompliance involving the facility's research program within the past 3 years.

(15) Indication of whether the event involves noncompliance by a same individual or study team responsible for other research noncompliance within the past 3 years.

(16) Names of other Federal agencies or entities (e.g., HHS-OHRP, HHS Office for Civil Rights (OCR)) notified, or to be notified, of the event and the date(s) of notification.

(17) Name and contact information (telephone number and email address) of the VA medical facility point of contact with whom ORO can follow-up for additional information.

3. SUBMISSION OF NOTIFICATIONS TO ORO

a. Notifications of events reportable to ORO must be directed to the relevant ORO workgroups described below. In some instances, where an event may be overseen by more than one ORO workgroup, VA medical facility personnel need only send the initial notification to one of the ORO workgroups with applicable oversight responsibilities. ***NOTE:*** *Contact information for ORO workgroups is available on ORO's website at https://www.va.gov/ORO/ORO_Contact_Information.asp. The reporting of events to ORO does not otherwise obviate the additional reporting of such events by VA medical facility personnel to pertinent Federal agencies (such as HHS-OHRP, FDA, NIH-OLAW, NIH-OSP, CDC, and OSHA), research sponsors, and accrediting bodies in accordance with the requirements of those entities.*

(1) Reportable events pertaining to noncompliance with VHA Directive 1200.01(1), Research and Development Committee, dated January 24, 2019, including Research & Development Committee (R&DC) operations and research solely under the oversight of the R&DC should be reported to ORO's Comprehensive Research Oversight Workgroup (CROW).

(2) Reportable events pertaining to noncompliance with Research Compliance Officer (RCO) responsibilities should be reported to ORO's CROW.

(3) Reportable events pertaining to human subjects research and IRB operations should be reported to ORO's Human Research Protection (HRP) Workgroup.

(4) Reportable events pertaining to animal research and IACUC operations should be reported to ORO's Research Safety and Animal Welfare (RSAW) Workgroup.

(5) Reportable events pertaining to research laboratory safety and security and SRS or IBC operations should be reported to ORO's RSAW Workgroup.

(6) Reportable events pertaining to research information security and privacy should be reported to ORO's Research Information Security (RIS) Workgroup.