|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ADMINISTRATIVE INFORMATION[[1]](#endnote-1)** | | | | | | | | | |
| **Principal Investigator:** | | | **Protocol Title:** | | | | | | |
| **Protocol Number:** | | | **Sponsor / Source of Funding:** | | | | | | **FDA Regulated[[2]](#endnote-2)** |
| **Study Site(s):** (check all that apply)**:** VA Facility Academic AffiliateOther | | | | | | | **Protocol subject to:  Pre-2018 CR requirements[[3]](#endnote-3)**  **2018 CR requirements** | | |
| **IRB of record :**  local VA  VA CIRB  Affiliate  NIH NCI  other  **Risk level :** Minimal Risk Greater than Minimal Risk | **Initial approvals reviewed previous audit[[4]](#endnote-4)** | | | | **Y** | **N** | |  | |
| **IRB Approval Prior to Research?  NA-Exempt** | | | | **Y** | **N** | | **Date Protocol was first approved by IRB:** | |
| **R&DC Approval Prior to Research?** | | | | **Y** | **N** | | **Date Protocol was first approved by R&DC:** | |
| **ACOS/R Letter Prior to Research?** | | | | **Y** | **N** | | **Date of ACOS/R letter:** | |
| **Final PO Review Prior to Final R&DC Approval?[[5]](#endnote-5)** | | | | **Y** | **N** | | **Date of Final PO Review:** | |
| **ISSO Review Prior to Final R&DC Approval?[[6]](#endnote-6)** | | | | **Y** | **N** | | **Date of ISSO Review:** | |
|  | | | |  |  | | **Date of Exemption determination:** | |
| |  |  |  | | --- | --- | --- | | **Study Component: (check all that apply)** | **International Study[[7]](#endnote-7)** | **Facility Director approval memo on file?  Y  N** | |  | **Study involves children[[8]](#endnote-8)** | **Facility Director approval memo on file?  Y  N** | |  | **Study involves prisoners[[9]](#endnote-9)** | **ORD/CRADO approval on file?  Y  N** | | | | | | | | | | |
|  | | | | | | | | | |
| **Date of Current Audit:** | | **Auditor(s):** | | **Review level:** FullExpedited[[10]](#endnote-10) #       Exempt | | | | | |
| |  |  |  | | --- | --- | --- | | **Status at time of Current Audit:** | **Actively enrolling new subjects** | **New enrollment temporarily suspended/on hold** | | (check all that apply) | **Active only for long-term observation** | **Closed to enrollment** | |  | **Active only for long-term data analysis**  **Data Repository[[11]](#endnote-11)** | **Closed**[[12]](#endnote-12) **- date:**  **Terminated[[13]](#endnote-13) – date:** | | | | | | | | | | |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **IS THIS PROTOCOL AN IRB-EXEMPT PROTOCOL SUBJECT TO THE 2018 COMMON RULE?[[14]](#endnote-14)  Yes  No** | | | | |
|  | **Y** | **N** | **NA** | ***COMMENTS*** |
| Was the exempt category determination documented? |  |  |  | Exempt Category: |
| Does the exempt category determination appear to match the regulatory description of the category?[[15]](#endnote-15) |  |  |  | If no, provide additional details: |
|  | **Y** | **N** | **NA** | ***COMMENTS*** |
| Did protocol require a limited IRB review?[[16]](#endnote-16) |  |  |  |  |
| Did protocol receive a limited IRB review? |  |  |  | If no, provide additional details: |
| If the exempt study involves direct interaction with human subjects, did the study documents include provisions for giving the subjects the information outlined in VHA Directive 1200.05(2) § 10.c.?[[17]](#endnote-17) |  |  |  |  |
| **CONTINUING REVIEWS[[18]](#endnote-18)** | | | | |
|  | **Y** | **N** | **NA** | ***COMMENTS*** |
| Is IRB Continuing Review (CR) required by VHA Directive 1200.05(2)? |  |  | **☐** |  |
| If CR was NOT required by 1200.05(2), did the IRB require CR? |  |  |  |  |
| If the IRB did require CR, was the rationale for requiring CR documented? |  |  |  |  |
| If CR was required by either 1200.05(2) or by the IRB did CR occur as scheduled? |  |  |  |  |
| If CR did not occur as required, did any research occur during the lapse? |  |  |  |  |
| **IS THIS PROTOCOL SUBJECT TO THE SINGLE IRB REVIEW REQUIREMENT?[[19]](#endnote-19)  Yes  No** | | | | |
|  | **Y** | **N** | **NA** | ***COMMENTS*** |
| Was the study reviewed by a single IRB? |  |  |  |  |
| If the study was reviewed by a single IRB that was external to the VA medical facility, was a valid reliance agreement in place for the VA medical facility to rely on that external IRB? |  |  |  |  |
| If that study was not reviewed by a single IRB, was a valid exception granted by ORD or another Federal entity supporting the research? |  |  |  |  |

**NOTE:** If a human protocol is opened and closed without enrolling human subjects or accessing any records or data at this site, completing the audit tool to this point satisfies the requirement for the HRPP audit.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **DOES THIS PROTOCOL INVOLVE THE USE OF INVESTIGATIONAL DRUGS?[[20]](#endnote-20)  Yes  No** | | | | | | | | | | |
|  | | | | **Y** | **N** | | **NA** | ***COMMENTS*** | |
| Does the investigational drug log or accountability record contain the required elements?[[21]](#endnote-21) | | | |  |  | |  |  | |
| Are investigational drugs stored separately from regular pharmacy stock?[[22]](#endnote-22) | | | |  |  | |  |  | |
|  | | | | | | | | | | |
| **IRB SUBMISSIONS, APPROVALS, AND OTHER ACTIONS[[23]](#endnote-23)** | | | | | | | | | | |
| **Protocol Amendments, Continuing Approval etc.** | **IRB Dates[[24]](#endnote-24)** | | **Research & Development Committee Approval**  **Date or N/A[[25]](#endnote-25)** | | | **Submission & Approval letters on file?[[26]](#endnote-26)**  **Y/N/ N/A** | | | *Comments* | |
| **Approval** | **Expiration** |
|  |  |  |  | | |  | | |  | |
|  |  |  |  | | |  | | |  | |
|  |  |  |  | | |  | | |  | |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **INFORMED CONSENT RELATED IRB SUBMISSIONS, APPROVALS, & OTHER ACTIONS[[27]](#endnote-27)** | | | | | | |
| *Informed Consent Version Date* | *Informed Consent Version Number* | **Date of IRB Approval[[28]](#endnote-28)** | *Reason for Revision* | **Re-consent Required?[[29]](#endnote-29)**  **Y/N** | **IRB Approval date on ICD[[30]](#endnote-30)**  **Y/N/n/a** | *Comments* |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **LOCAL APPARENT UNANTICIPATED PROBLEMS INVOLVING RISKS TO SUBJECTS OR OTHERS (UPIRTSOS)**  **SIGNIFICANT SAFETY REPORTS / DATA MONITORING COMMITTEE (DMC) REPORTS[[31]](#endnote-31)** | | | | | | | | | | |
| **Date event Occurred[[32]](#endnote-32)** | **Date Learned of Event[[33]](#endnote-33)** | **Subject ID** | **Event** | **Date reported to IRB** | **Reported to RRC within required time period**  **Y/N/NA[[34]](#endnote-34)** | Reviewed & categorizedwithin required time period[[35]](#endnote-35) Y/N/N**A** | **CATEGORIZED BY IRB\*** | | | **Reported to ORO[[36]](#endnote-36)**  **Y/N/NA** |
| **U**  **Y/N** | **R**  **Y/N** | **Risk[[37]](#endnote-37)**  **Y/N** |
|  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |

**\* U – Unanticipated R – Related or Possibly Related to study participation Risk- Increased Risk**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **STUDY STAFF TRAINING[[38]](#endnote-38)** | | | | | | |
| **Site Personnel** | **All human research training current**  **Y/N**  (if yes, skip next column) | **If training not current, Training ever completed**  **y/n** | *Current WOC?*  *Y/N/NA* | *Role in Study*  *PI/SC/SI* | *Comments* |
|  |  |  |  | Principal Investigator |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **SUBJECT RECORD REVIEW**  **Assess Timing of Consent, Compliance with Eligibility Criteria, ETC.**  **Total number of subjects who passed screening and were included for analysis in study in this period =\_\_\_\_\_\_\_\_\_\_**  **If 10 or fewer subjects in this period, audit all of them**  **If 11-100 subjects in this period, audit a random sample of10 of them**  **If 101-300 subjects in this period, audit a random sample of 10% of them**  **If more than 300 in this period, audit a random sample of 30 of them** | | | | |
| **Subject Study ID** | **Documentation that consent obtained prior to initiation of study procedures[[39]](#endnote-39)**  **Y/N/NA** | **For Greater than Minimal Risk Research--Subject included in research not meeting inclusion or meeting exclusion criteria[[40]](#endnote-40)**  **Y/N/NA** | **If Progress Note was required in VHA health record, was it present?[[41]](#endnote-41)**  **Y/N/NA** | *Other issues found, specify on line below* |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| ***AUDIT PREPARATION TOOL*** | | | | | |
| *Document – Investigator Regulatory Files* | *Present and Reviewed*  *Y/N/NA* | *Comments* | *Document – Investigator Regulatory Files* | *Present and Reviewed*  *Y/N/NA* | *Comments* |
| *Protocol & Amendments* |  |  | *R&D Correspondence* |  |  |
| *Approved Case Report Forms* |  |  | *Notes-to-File* |  |  |
| *IRB Approved Consent Forms*  *-Information Provided to Subjects*  *-HIPAA Forms*  *-Advertisements*  *-Record of Approved Consent Form Versions* |  |  | *Site-Sponsor Correspondence, if app.*  *-Conference call minutes*  *-E-mails*  *-Newsletters*  *-Conference calls*  *-Letters, memos, faxes* |  |  |
| *Subject Log (current/accurate)* |  |  | *Study Site Personnel*  *Signatures, Qualifications, Training, Scope of Practice, CVs, Delegation* |  |  |
| *IRB Correspondence* |  |  | *Signed Attestation or Investigator’s Agreement (Sponsor, Institution, FDA)* |  |  |
| *IRB Submissions, Notifications, Approvals* |  |  | *Official Documents*  *Letters, Memos, etc.* |  |  |
| *Unanticipated Problems/Safety Reports* |  |  | *Signed PI Conflict of Interest/Disclosure Statement* |  |  |
| *Investigator Brochure/VA Form 10-9012* |  |  | *Investigational Products, if applicable*  *Accountability, Handling, Pharmacy, Elsewhere* |  |  |
| *IRB reliance agreement for use of single IRB/documentation single IRB exception granted by ORD* |  |  |  |  |  |
| *Are there local IRB requirements for record keeping?  Yes  No  NA Comments:* | | | | | |

1. GENERAL INSTRUCTIONS FOR PERFORMING AN AUDIT OF PROTOCOLS INVOLVING HUMAN SUBJECTS WITH THE HRPP AUDIT TOOL

   All active research protocols followed by the IRB must be audited at least once every 3 years. Details for all ORO audit requirements, including HRPP audits, are updated annually and posted on the ORO internet website and the ORO Research Compliance and Technical Assistance SharePoint site. The ORO guidance memo relevant to this reporting period is entitled “2023 – 2024 ORO Guidance Regarding RCO Research Audit and Training Requirements.”

   For certain studies some of the data on the HRPP tool may be not applicable, and the auditor may simply note this as “n/a”. For example, the IRB commonly waives informed consent for human subjects research that only involves retrospective chart review, in which case there are no informed consent documents to review. Therefore, on the subject record review page, the column entitled “Documentation that consent obtained prior to initiation of study procedures” would be “n/a” for these cases.

   RCOs are free to audit additional information if described in their standard operating procedures (SOPs) and helpful for monitoring the quality, safety and compliance of their facility’s research program. All GREY areas of the audit tool are optional, and not collected by ORO. Some RCOs have found these elements useful for auditing and they are included here for consideration.

   The HRPP audit tool should be used to audit all protocols that are overseen by the IRB and all exempt research under the 2018 Common Rule. Remember that certain protocols involving human subjects may have safety concerns as well, and if the protocol is also overseen by the Subcommittee on Research Safety (SRS), the Research Safety Audit Tool should be used when such a protocol is audited. Examples of protocols involving human subjects that may have safety concerns requiring review by the SRS include any research use outside of normal clinical settings of hazardous chemicals, radioactive materials, controlled substances, and/or blood products, among others.

   The shaded areas on the HRPP audit tool are optional fields. The intent of most is described in the instructions below. In addition, there are optional pages to help RCOs (or other auditors) during the process. The optional page entitled “Audit Preparation Tool” is intended as a list of possible documents that may be useful as sources for information necessary to complete the HRPP audit tool. Some RCOs have found this list useful in preparing for an audit. Some RCOs have given this list, customized for their facility, to Principal Investigators and research staff and asked them to help assemble the documentation in advance in order to make the audit process more efficient.

   The Administrative Information section is intended to summarize information that identifies and describes each protocol. Information related to initial approval that never changes should be completed once for each protocol that receives an HRPP audit. Sections that contain information that changes should be updated with each consecutive audit. Every RCO is free to add further information fields that may be useful for their facility, and to reformat the information as long as all required information is collected. If an electronic version of the HRPP audit tool is used, much of the Administrative Information may be able to be pre-filled from the research program office’s administrative databases at some facilities.

   Every RCO must have an SOP or audit plan that describes how they accomplish their audits. The SOP should address the source documents reviewed to locate necessary information, the roles and responsibilities of the RCO, the PI, and the research staff in planning, scheduling and conducting audits, how the RCO monitors progress towards audit goals and solicits study investigators’ responses to preliminary audit findings, and how the results of ALL audits are reported to the IRB and the R&DC, including timelines. Specific types of required audits should be described in the SOP or an attachment to allow for planning of the number of audits that need to be done in the audit period to meet requirements. In addition, it is a good practice to include in the RCO’s local SOPs where the audit results are maintained. Audit results may be maintained on paper, electronically, or both. Some facilities store audit results in specific files in the RCO’s office, others in the protocol file. Each facility has discretion to customize tools and solutions that work best in their situation; however these solutions should be described in SOPs and then followed.

   Under “IRB of record” indicate the type of the IRB that reviewed the study for the facility; for “Risk Level” indicate minimal risk or greater than minimal risk. [↑](#endnote-ref-1)
2. FDA-regulated research includes all clinical investigations regulated by the Food and Drug Administration (FDA) under sections 505(i) and 520(g) of the Federal Food, Drug, and Cosmetic Act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the FDA, including foods, including dietary supplements, that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. (see 21 CFR 312 and 21 CFR 812.) [↑](#endnote-ref-2)
3. If the study is subject to the pre-2018 common rule, fill out the entire tool except for "IS THIS PROTOCOL AN IRB-EXEMPT PROTOCOL SUBJECT TO THE 2018 COMMON RULE?" and "IS THIS PROTOCOL SUBJECT TO THE SINGLE IRB REVIEW REQUIREMENT?" [↑](#endnote-ref-3)
4. If the study was previously audited and the initial approvals and dates were reviewed in a previous audit, mark “Y” for this question and move to the “Study Component” section. [↑](#endnote-ref-4)
5. Final PO review can occur after contingent approval by R&DC; but final PO review has to occur before research starts and final approval by the R&DC. Note that final PO review does have to occur after IRB approval. Documentation of privacy review [VHA FORM 10-250] must remain with the research protocol. (VHA Directive 1605.03(2) § 5.n.(18); VHA Directive 1200.01(1) §5.k; VHA Directive 1200.01(1) §5.h(6)] [↑](#endnote-ref-5)
6. Final ISSO review can occur after contingent approval by R&DC; but final ISSO review has to occur before research starts and final approval by the R&DC. Note that final ISSO review does have to occur after IRB approval. If an ISSO Review is not required (such as when the Enterprise Research Data Security Plan [ERDSP] form indicates that it is not required) then enter “N/A” in this box. (VHA Directive 1200.01(1) §5.i; VHA Directive 1200.01(1) §5.h(6)). [↑](#endnote-ref-6)
7. “International Study” VHA Directive 1200.05(2) - January 7, 2019 requires approval from the Facility Director for a VA investigator to conduct international research except for CSP research which requires approval from the CRADO. ORO will ask for the number of such studies that are audited to be reported annually as part of the Facility Director’s Certification. Guidance on approval of international research can be found at <http://www.research.va.gov/resources/policies/guidance/intl-research.pdf>. [↑](#endnote-ref-7)
8. “Study involves children?” VHA Directive 1200.05(2) - January 7, 2019 requires approval from the Facility Director for a VA investigator to conduct research involving children. ORO will ask for the number of such studies that are audited to be reported annually as part of the Facility Director’s Certification. Guidance on approval of research involving children can be found at <http://www.research.va.gov/resources/policies/guidance/research-involving-children.pdf>. [↑](#endnote-ref-8)
9. “Study involves prisoners?” A research protocol that includes prisoners requires written permission from the CRADO. ORO will ask for the number of such studies that are audited to be reported annually as part of the Facility Director’s Certification. (VHA Directive 1200.05(2) §20.) [↑](#endnote-ref-9)
10. If the most recent review (initial or continuing) of the study was conducted by expedited review, enter the expedited review category number and confirm the risk level is not greater than minimal risk. If a study is greater than minimal risk but was reviewed by expedited review, document this here and, *if confirmed*, report this as apparent serious noncompliance. This question refers to expedited review/approval of the main study (not the addition of a local site through an amendment). (VHA Directive 1200.05(2) §11. and Appendix B.) [↑](#endnote-ref-10)
11. When auditing a research repository, if data collection resulted from study interventions in a different research study, then the subject record review (on page 6 of the audit tool) is not required. If research interventions were conducted and data collected as part of the research repository protocol then a review of subject records is required. It will be necessary to review informed consent documents if subjects provided informed consent as part of the research repository protocol and not via another study.

    [↑](#endnote-ref-11)
12. If an approved research study using human subjects has closed without enrolling any subjects or accessing any records or data (i.e. no activity occurred) at the local facility, then an abbreviated audit including only the information on the Administrative Section (first page and first half of second page) of the HRPP audit tool is sufficient. If any human subjects were enrolled or their data collected at the local facility, whether or not informed consent was waived, this exclusion should not be used and the remaining audit must be completed, unless there has been a previous regulatory audit. [↑](#endnote-ref-12)
13. Termination refers to a permanent halt in all research activities due to concerns about the safety, rights, or welfare of human subjects, research personnel, or others, regardless of whether the action to terminate was taken by an investigator, facility official, research review committee, or external entity. Termination does not refer to interruptions for other reasons, including the expiration of project approval periods. [↑](#endnote-ref-13)
14. If the protocol is exempt under the pre-2018 rule, there is no need to conduct an HRPP audit of the study. If the protocol is exempt under the 2018 rule, complete the administrative portion of this tool, as well as the STUDY STAFF QUALIFICATIONS AND TRAINING portion of the tool. [↑](#endnote-ref-14)
15. If the exempt category determination does not appear to match the regulatory description of the category, confer with the person(s) who made the exempt determination; if an incorrect determination is confirmed, report this as apparent serious noncompliance. If there is disagreement about the determination, please confer with ORO. The categories of exempt research under the 2018 Rule are:

    Category 1. Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

    Category 2. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met: (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects; (ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or (iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and **an IRB conducts a limited IRB review** to make the determination required by section 12.a.(7) of this directive.

    Category 3. Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

    (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects; (ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or (iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and **an IRB conducts a limited IRB review** to make the determination required by section 12.a.(7) of VHA Directive 1200.05(2) (4) For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else. (5) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

    Category 4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met: (1) The identifiable private information or identifiable biospecimens are publicly available; (2) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects; (3) The research involves only information collection and analysis involving the investigator’s use of identifiable health information when that use is regulated under 45 CFR Parts 160 and 164, Subparts A and E, for the purposes of health care operations or research as those terms are defined at 45 CFR 164.501 or for public health activities and purposes as described under 45 CFR 164.512(b); or

    (4) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for non-research activities; if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501. NOTE: If all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a; and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

    Category 5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. (1) Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended. (2) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal website or in such other manner as the Federal department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

    NOTE: The determination of exempt status for research and demonstration projects meeting the criteria for exempt category 5 in section e. in this Appendix must be made by the Under Secretary for Health on behalf of the Secretary of VA, after consultation with Office of Research and Development (ORD), Office of Research Oversight (ORO), Office of General Counsel (OGC), and other experts, as appropriate.

    Category 6. Taste and food quality evaluation and consumer acceptance studies: (1) If wholesome foods without additives are consumed, or (2) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

    Category 7. Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if **an IRB conducts a limited IRB review** and makes the determinations required by section 12.a.(8) of this directive.

    Category 8. Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met: (1) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with section 17.f of VHA Directive 1200.05(2); (2) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with section 17 of VHA Directive 1200.05(2); (3) **An IRB conducts a limited IRB review** and makes the determination required by section 12.a.(7) of VHA Directive 1200.05(2) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph h.(1) of this section; and (4) The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results. [↑](#endnote-ref-15)
16. Exempt categories requiring a limited IRB review include Categories 2(iii), 3(i)(C), 7 and 8. [↑](#endnote-ref-16)
17. VHA Directive 1200.05(2) § 10.c. requires that for exempt research activities involving the Investigator interacting with human subjects or obtaining information by educational tests, survey or interview procedures, or behavioral interventions, the following information must be given to the prospective human subject as applicable in writing or orally: (1) The activity is research; (2) Participation is voluntary; (3) Permission to participate can be withdrawn; (4) Permission for use of data can be withdrawn for exempt research activities involving the collection and use of identifiable data; and (5) Contact information for the VA Investigator. [↑](#endnote-ref-17)
18. For research subject to the pre-2018 Common Rule, continuing IRB review is required for all non-exempt human subjects research. For research subject to the 2018 Common Rule, continuing IRB review is not required for (a) Research eligible for expedited review; or (b) Research reviewed by the IRB in accordance with the limited IRB review; or

    (c) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study: 1. Data analysis, including analysis of identifiable private information or identifiable biospecimens, or 2. Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care (see VHA Directive 1200.05(2) §9.e.(2)). For research subject to the 2018 Requirements, if the IRB requires continuing review for any of the above circumstances, it must document its rationale for requiring continuing review in its communication to the investigator and institution. The R&D Committee is not required to conduct continuing review (see VHA Directive 1200.05(2) §9.e.(2)). Continuing review audits require a look-back to the beginning of the study or the date of the last audit. When a study has transitioned to the 2018 Common Rule during the look-back period and the study no longer requires continuing review, indicate “N” for “Is IRB Continuing Review (CR) required by VHA Directive 1200.05(2)?” Note that annual check-ins required locally do not count as continuing review; failure to conduct a locally-required check-in would be noncompliance with local SOPs, but not national Policy.

    [↑](#endnote-ref-18)
19. RESEARCH SUBJECT TO THE SINGLE IRB REVIEW REQUIREMENT: All VA non-exempt human subjects research with more than one institution engaged and the other institution(s) is a Federal institution (including another VA Facility) or the other non-Federal institution(s) is a recipient of federal government funding or support for that research activity requires review by a single IRB . When the facility engages the services of another entity’s IRB as its IRB of Record, the IO is responsible for, among other things: Establishing and signing a Memorandum of Understanding (MOU) or Authorizing Agreement with other VA facilities or external organization(s) providing IRB services. Exceptions to the single IRB review requirement: When more than single IRB review is required by law (including tribal law); or whenever any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context. (38 CFR 16.114) To determine if the study is subject to the sIRB review requirements, RCOs may want to check with research coordinator/sponsor or the VAIRRS cover sheet. If the study was reviewed by a single IRB that was external to the VA medical facility, was a valid reliance agreement in place for the VA medical facility to rely on that external IRB? If not, enter “N” for the second question. If the study was not reviewed by a single IRB, was a valid exception granted by the VHA Office of Research & Development or another Federal entity supporting or conducting the research, as appropriate? If not, check “N” for the third question. [↑](#endnote-ref-19)
20. For studies in which the drug is sent from a centralized pharmacy and mailed to subjects, RCOs are not to audit the pharmacy for such protocols; enter N/A for the questions related to the drug log and pharmacy procedures. (VHA Handbook 1108.04 §15.) [↑](#endnote-ref-20)
21. Does the investigational drug log or accountability record contain the following:

    a. Name of the drug, dosage form, and strength;

    b. Manufacturer or other supply source;

    c. Date of receipt of the drug;

    d. Quantity received;

    e. Expiration, retest, or repass date;

    f. Control, lot number, or other identification (ID) number;

    g. Name of LSI;

    h. Protocol name or number;

    i. Name of subject or other subject identifier for individuals receiving the medication;

    j. Quantity dispensed;

    k. Balance of drug currently available (when amenable to protocol design);

    l. Recorder’s initials;

    m. A final entry is made when drug therapy for the entire study (at the site) has ended. (VHA Handbook 1108.04 §10.b(3)) [↑](#endnote-ref-21)
22. Are investigational drugs and supplies securely stored in the pharmacy; separate from all non-investigational drugs and supplies and clearly identified as to which study they are assigned? *Note: Storage does not require a separate locked area within pharmacy, unless the medication has specific storage requirements. (*VHA Handbook 1108.04 §10.b(1)) [↑](#endnote-ref-22)
23. The first step in HRPP audits is to review the IRB file, including the protocol and all IRB actions since initial approval or the last audit. A protocol history should result, including all actions of the IRB related to the audited protocol, usually in chronological order. This would include approval, changes, amendments, continuing review/approval, changes in staff, and any other action. The exceptions would be actions related to matters on the next few pages of the audit tool. IRB actions related to the informed consent document and actions related to local unanticipated problems involving risks to subjects or others are recorded separately on the pages of the tool that follow. Many RCO auditors choose to reorganize these 3 pages into one single, chronological protocol history including all types of actions. As long as the RCO auditor obtains all information required by this HRPP tool they may organize the information the manner they choose to be most useful. The auditor should note any possible compliance issues related to IRB actions on this page of the audit tool, using the comment section. If the study no longer requires continuing review, note that on the “comments” section. [↑](#endnote-ref-23)
24. The date should be verified for every IRB action. This will allow the auditor to determine, as relevant, the timeliness of the action and the timeliness of any further actions that may be required by regulation, such as continuing review of approved protocols within 365 days, when required. Date of expiration of the action, if any, should also be recorded by the auditor. If the IRB action was anything other than approval, make a note in the "Comments" section. [↑](#endnote-ref-24)
25. Date of Research and Development Committee (R&DC) approval of the IRB action should be entered, if R&DC approval is required. Some IRB actions, for example minor amendments to protocol staffing, do not require R&DC approval, and “N/A” may be recorded if no R&DC approval is required. Lack of timely approval, when required, should be noted in the comments and appropriately reported by the auditor. The R&DC is only required to provide initial approval. There is no requirement for the R&DC to provide approval for amendments or continuing review. (VHA Directive 1200.01(1) §9.) [↑](#endnote-ref-25)
26. In most cases the protocol file should include documentation of the submission of the request for an action, and a letter communicating the action to the PI by either the IRB, ACOS, or as designated by policy. Record whether appropriate documentation of required action notification is found during the audit, or “N/A” if no documentation is required for the action by policy. (VHA Directive 1200.01(1) §11.) [↑](#endnote-ref-26)
27. This page of the HRPP audit tool is to be used to record sequentially the versions of the informed consent document that have been approved by the IRB for this protocol, the date of approval, and whether re-consent was required. The RCO may wish to check to ensure that the HIPAA authorization and informed consent document are not inconsistent; this is optional. [↑](#endnote-ref-27)
28. The date of IRB approval of each version of the informed consent document (ICD) is necessary for the auditor to assure that every subject received the current version of the ICD on the date of his/her signature. The date of the writing or revision of the document is used by some facilities as an identifier to refer to the ICD version; other facilities use a version number or other method. These document identifiers may be recorded in the first, optional columns of this page of the tool, or the RCO may redesign this tool adding additional information that makes it more effective for their facility and local standard operating procedures. [↑](#endnote-ref-28)
29. If the auditor finds that re-consent was required but did not occur, these findings should be noted in comments and reported appropriately. It is useful for the RCO to double-check that all subjects from whom re-consent was obtained were included in the ICD audit for that period. In lieu of reconsent, the IRB can require a PI to provide the new information to subjects (verbally or through an information sheet); this may be accounted for in the comments. [↑](#endnote-ref-29)
30. The auditor should also check that the appropriate IRB date stamp or equivalent was used when required by local policy. Other information used locally to identify the ICD version may be optionally tracked, and as always the RCO auditor may add other fields as needed. A clear chronology of approved ICDs is necessary for the auditor to ascertain that all enrolled subjects received the version of the ICD that was appropriate on the date of their enrollment in the research. If the IRB does not use approval dates or stamps on the ICD indicate N/A. [↑](#endnote-ref-30)
31. This page of the audit tool is intended to record all local apparent unanticipated problems involving risks to subjects or others (UPIRTSOs) and significant safety reports or Data Monitoring Committee (DMC) reports. The RCO should review each event or report to ascertain whether the required review and determinations occurred in the manner and time required by VA policy. VHA Directive 1058.01 requires local UPIRTSOs be reported to the IRB and reviewed by the IRB in an expedited manner. (VHA Directive 1058.01 § 7.b.) [↑](#endnote-ref-31)
32. “Date event occurred” - Record here the date the event actually occurred, according to the documentation available, regardless of when it was first recognized and/or reported. [↑](#endnote-ref-32)
33. “Date learned of event” - Record here the date the event was first recognized to have occurred by any member of the research staff, or the RCO. Under VHA policy, such recognition begins a timeline for reporting, evaluation and possible action. [↑](#endnote-ref-33)
34. The time between the date the event was learned of and the date the report was made to the relevant review committee (RRC) should be checked for compliance with both local SOP and VHA Directive 1058.01 (within 5 business days), whichever is the shorter time. Record whether the report was made in a manner compliant with time requirements here. [↑](#endnote-ref-34)
35. VHA Directive 1058.01 requires that once the IRB has received a report of a local UPIRTSO the IRB Chair or a qualified IRB member-reviewer must DETERMINE and DOCUMENT whether any actions are warranted to eliminate apparent IMMEDIATE HAZARDS to subjects within 5 business days, and, if so, initiate those actions. The IRB MUST REVIEW the incident and the determination of the IRB Chair or qualified IRB member-reviewer at its next CONVENED MEETING (not to exceed 30 calendar days after the date of written notification) and must DETERMINE and DOCUMENT that:

    (a) whether the incident, experience, or outcome was unexpected and related to or possibly related to participation in the research and indicative of the research placing subjects or others at substantively greater risk of harm than was previously known or recognized (i.e., whether the incident, experience or outcome constituted an actual UPIRTSO); and

    (b) what, if any, protocol or informed consent modifications are warranted. If modifications are warranted, the convened IRB must determine and document whether or not investigators must notify or solicit renewed or revised consent from previously enrolled subjects; and if so, when such notification or consent must take place and how it must be documented. Local SOPs may require quicker review. The RCO auditor should check that review occurred as required by policy. [↑](#endnote-ref-35)
36. If the IRB determines that the incident, experience, or outcome constituted an actual UPIRTSO, then reporting to ORO should occur as described in VHA Directive 1058.01.  Answer “Yes” if reporting occurred in compliance with VHA and local policy, “No” if reporting did not occur in compliance with VHA and local policy, or “N/A” if the determination did not require reporting. [↑](#endnote-ref-36)
37. This column relates to to whether the IRB determined that the incident was indicative of the research placing subjects or others at substantively greater risk of harm than was previously known or recognized. [VHA Directive 1058.01 § 3.q. & 7.b.] [↑](#endnote-ref-37)
38. RCOs should check that research-related training is current for all staff participating in the protocol on the date of the audit. Refer to <https://www.research.va.gov/programs/orppe/education/ord_training/default.cfm> for current training requirements. For research staff identified only by job title in the protocol, the auditor may need to request a list of names of staff from the PI. RCOs should audit training that is specific to the research program, and need not confirm additional training required of all VA or VHA employees. Research-specific training should be audited to assure it is current at the time of the audit or date of closure if the study previously closed. Unlike some other auditing elements, there is no expectation that training is checked for any lapse during the last 3 years or since the last audit. The auditor should simply assure that training is current at the time of the audit or study closure. If human subjects training is not current as of the time of the audit, check and see if such training was ever completed for this staff member's involvement in this research. If there is no evidence of training ever being completed, this rare circumstance should be noted in the appropriate column. The Research Service is not required to maintain a real-time (up-to-the minute) record of training compliance. If the RCO relies on a list of training compliance maintained by the Research Service, any items that *appear* to indicate a deficiency (lapse in training) must be checked against primary records (e.g., TMS) to verify whether a deficiency in fact exists at the time of the RCO audit.

    [↑](#endnote-ref-38)
39. The date the subject signed the ICD should be compared with the documented date that study procedures began for the subject, to ascertain that informed consent preceded beginning research. For research procedures that began on the same date that the subject signed consent, the auditor should follow the local policy regarding what documentation is necessary to determine that consent occurred before study procedures began. This comparison should be made for all studies requiring a signed informed consent document- including studies of minimal risk, such as questionnaire research, and also studies involving interventions of more than minimal risk; but the RCO only needs to audit a percentage of consents as noted in the heading. When documentation does not allow this determination, the auditor should ask for the study staff to describe the process they use to ensure that consent is always obtained prior to research procedures. If concerns remain, the auditor should discuss the concerns with the PI and IRB Chair. (VHA Directive 1200.05(2) §18.) [↑](#endnote-ref-39)
40. Auditing of documentation of inclusion/exclusion criteria is only required if the study involves an intervention that is greater than minimal risk; in auditing incl/excl criteria for such studies the RCO only needs to audit a percentage of consents (as above). In determining if a subject was included in research not meeting inclusion or meeting exclusion criteria we do not expect the RCO to review the inclusion or exclusion criteria against that patient’s medical record to determine if the subject is enrolled properly. The RCO should review all pertinent documentation available about each subject including (but not limited to) inclusion/exclusion criteria checklists, sponsor monitor/audit reports, protocol deviation submissions, CPRS study enrollment note, etc. If there is evidence that the subject did **not** meet the inclusion or did meet exclusion criteria and the subject was inappropriately enrolled in the study, this box should be marked “Yes.” This is noncompliance. If no documentation is available regarding inclusion/exclusion criteria for the subject, the auditor should seek guidance from the PI or study coordinator on how the criteria were assessed.

    [↑](#endnote-ref-40)
41. Audit for the presence of a progress note in VHA health record, if required. It is not required to audit the content of the health record note, only the presence. Answer “n/a” if no progress note in the VHA health record is required by VHA Directive 1200.05(2) §5.g.(16): Creating or updating a VHA health record and creating a progress note for all research subjects (Veterans or non-Veterans) who receive research procedures or interventions as inpatients or outpatients at VA medical facilities that are either used in or may impact the medical care of the research subject at a VA medical facility or at facilities contracted by VA to provide services to Veterans (e.g., Community-Based Outpatient Clinics or community living centers). Informed consent and HIPAA authorization documents are not required to be in the health record. [↑](#endnote-ref-41)