

**Investigator Manual[[1]](#endnote-1)**

**Appendices**

**HRP-103a**

Revised December 1, 2023

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1. Additional Requirements for DHHS-Regulated Research[[2]](#footnote-1)
2. When a subject decides to withdraw from a clinical trial, the investigator conducting the clinical trial should ask the subject to clarify whether the subject wishes to withdraw from all components of the trial or only from the primary interventional component of the trial. If the latter, research activities involving other components of the clinical trial, such as follow-up data collection activities, for which the subject previously gave consent may continue. The investigator should explain to the subject who wishes to withdraw the importance of obtaining follow-up safety data about the subject.
3. Investigators are allowed to retain and analyze already collected data relating to any subject who chooses to withdraw from a research study or whose participation is terminated by an investigator without regard to the subject’s consent, provided such analysis falls within the scope of the analysis described in the IRB-approved protocol. This is the case even if that data includes identifiable private information about the subject.
4. For research not subject to regulation and review by FDA, investigators, in consultation with the funding agency, can choose to honor a research subject’s request that the investigator destroy the subject’s data or that the investigator exclude the subject’s data from any analysis.
5. When seeking the informed consent of subjects, investigators should explain whether already collected data about the subjects will be retained and analyzed even if the subjects choose to withdraw from the research.
6. When research is covered by a certificate of confidentiality, researchers:
	1. May not disclose or provide, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, the name of such individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for purposes of the research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or
	2. May not disclose or provide to any other person not connected with the research the name of such an individual or any information, document, or biospecimen that contains identifiable, sensitive information about such an individual and that was created or compiled for purposes of the research.
	3. May disclose information only when:
		1. Required by Federal, State, or local laws (e.g., as required by the Federal Food, Drug, and Cosmetic Act, or state laws requiring the reporting of communicable diseases to State and local health departments), excluding instances of disclosure in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding.
		2. Necessary for the medical treatment of the individual to whom the information, document, or biospecimen pertains and made with the consent of such individual;
		3. Made with the consent of the individual to whom the information, document, or biospecimen pertains; or
		4. Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human participants in research.
	4. Researchers must inform participants of the protections and limitations of certificates of confidentiality (see language in HRP-502 - TEMPLATE CONSENT DOCUMENT).
		1. For studies that were previously issued a Certificate and notified participants of the protections provided by that Certificate, NIH does not expect participants to be notified that the protections afforded by the Certificate have changed, although IRBs may determine whether it is appropriate to inform participants.
		2. If part of the study cohort was recruited prior to issuance of the Certificate, but are no longer activitely participating in the study, NIH does not expect participants consented prior to the change in authority, or prior to the issuance of a Certificate, to be notified that the protections afforded by the Certificate have changed, or that participants who were previously consented to be re-contacted to be informed of the Certificate, although the IRB may determine whether it is appropriate to inform participants.
	5. Researchers conducting research covered by a certificate of confidentiality, even if the research is not federally funded, must ensure that if identifiable, sensitive information is provided to other researchers or organizations, the other researcher or organization must comply with applicable requirements when research is covered by a certificate of confidentiality.
7. Additional Requirements for FDA-Regulated Research
8. When a subject withdraws from a study:[[3]](#footnote-2)
	1. The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed.
	2. An investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the subject’s information.
	3. If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous bullet, the investigator must obtain the subject’s informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). IRB approval of informed consent documents is required.
	4. If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study the subject’s medical record or other confidential records requiring the subject’s consent.
	5. An investigator may review study data related to the subject collected prior to the subject’s withdrawal from the study, and may consult public records, such as those establishing survival status.
9. For FDA-regulated research involving investigational drugs:
	1. Investigators must abide by FDA restrictions on promotion of investigational drugs:[[4]](#footnote-3)
		1. An investigator, or any person acting on behalf of an investigator, must not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug.
		2. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.
		3. An investigator must not commercially distribute or test market an investigational new drug.
	2. Follow FDA requirements for general responsibilities of investigators[[5]](#footnote-4)
		1. An investigator is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation.
		2. An investigator must, in accordance with the provisions of 21 CFR §50, obtain the informed consent of each human subject to whom the drug is administered, except as provided in 21 CFR §50.23 or §50.24 of this chapter.
		3. Additional specific responsibilities of clinical investigators are set forth in this part and in 21 CFR §50 and 21 CFR §56.
	3. Follow FDA requirements for control of the investigational drug[[6]](#footnote-5)
		1. An investigator must administer the drug only to subjects under the investigator's personal supervision or under the supervision of a sub-investigator responsible to the investigator.
		2. The investigator must not supply the investigational drug to any person not authorized under this part to receive it.
	4. Follow FDA requirements for investigator recordkeeping and record retention[[7]](#footnote-6)
		1. Disposition of drug:
			1. An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects.
			2. If the investigation is terminated, suspended, discontinued, or completed, the investigator must return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR §312.59.
		2. Case histories.
			1. An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation.
			2. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. The case history for each individual must document that informed consent was obtained prior to participation in the study.
		3. Record retention: An investigator must retain required records for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.
	5. Follow FDA requirements for investigator reports[[8]](#footnote-7)
		1. Progress reports: The investigator must furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.
		2. Safety reports: An investigator must promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator must report the adverse effect immediately.
		3. Final report: An investigator must provide the sponsor with an adequate report shortly after completion of the investigator's participation in the investigation.
		4. Financial disclosure reports:
			1. The clinical investigator must provide the sponsor with sufficient accurate financial information to allow an applicant to submit complete and accurate certification or disclosure statements as required under 21 CFR §54.
			2. The clinical investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study.
	6. Follow FDA requirements for assurance of IRB review[[9]](#footnote-8)
		1. An investigator must assure that an IRB that complies with the requirements set forth in 21 CFR §56 will be responsible for the initial and continuing review and approval of the proposed clinical study.
		2. The investigator must also assure that he or she will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risk to human subjects or others, and that he or she will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.
	7. Follow FDA requirements for inspection of investigator's records and reports[[10]](#footnote-9)
		1. An investigator must upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 312.62.
		2. The investigator is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.
	8. Follow FDA requirements for handling of controlled substances[[11]](#footnote-10)
		1. If the investigational drug is subject to the Controlled Substances Act, the investigator must take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.
10. For FDA-regulated research involving investigational devices:
	1. General responsibilities of investigators.[[12]](#footnote-11)
		1. An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the investigator's care, and for the control of devices under investigation. An investigator also is responsible for ensuring that informed consent is obtained in accordance with 21 CFR §50.
	2. Specific responsibilities of investigators[[13]](#footnote-12)
		1. Awaiting approval: An investigator may determine whether potential subjects would be interested in participating in an investigation, but must not request the written informed consent of any subject to participate, and must not allow any subject to participate before obtaining IRB and FDA approval.
		2. Compliance: An investigator must conduct an investigation in accordance with the signed agreement with the sponsor, the investigational plan, and other applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.
		3. Supervising device use: An investigator must permit an investigational device to be used only with subjects under the investigator's supervision. An investigator must not supply an investigational device to any person not authorized to receive it.
		4. Financial disclosure:
			1. A clinical investigator must disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements required under 21 CFR §54.
			2. The investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.
		5. Disposing of device: Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator must return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.
	3. Maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:[[14]](#footnote-13)
		1. All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.
		2. Records of receipt, use or disposition of a device that relate to:
			1. The type and quantity of the device, the dates of its receipt, and the batch number or code mark.
			2. The names of all persons who received, used, or disposed of each device.
			3. Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.
		3. Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. Such records must include:
			1. Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent.
			2. Documentation that informed consent was obtained prior to participation in the study.
			3. All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
			4. A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.
		4. The protocol, with documents showing the dates of and reasons for each deviation from the protocol.
		5. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.
	4. Inspections[[15]](#footnote-14)
		1. Entry and inspection: A sponsor or an investigator who has authority to grant access must permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept).
		2. Records inspection: A sponsor, IRB, or investigator, or any other person acting on behalf of such a person with respect to an investigation, must permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.
		3. Records identifying subjects: An investigator must permit authorized FDA employees to inspect and copy records that identify subjects, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.
	5. Prepare and submit the following complete, accurate, and timely reports[[16]](#footnote-15)
		1. Unanticipated adverse device effects. An investigator must submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.
		2. Withdrawal of IRB approval. An investigator must report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.
		3. Progress. An investigator must submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
		4. Deviations from the investigational plan:
			1. An investigator must notify the sponsor and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency.
			2. Such notice must be given as soon as possible, but in no event later than 5 working days after the emergency occurred.
			3. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and IRB also is required.
		5. Informed consent. If an investigator uses a device without obtaining informed consent, the investigator must report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.
		6. Final report. An investigator must, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB.
		7. Other. An investigator must, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.
11. Additional Requirements for Clinical Trials (ICH-GCP)
12. Investigator's Qualifications and Agreements
	1. The clinical trial should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practice and the applicable regulatory requirements.
	2. The investigator should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirements, and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB, and/or the regulatory authorities.
	3. The investigator should be thoroughly familiar with the appropriate use of the investigational product, as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.
	4. The investigator should be aware of, and should comply with, GCP and the applicable regulatory requirements.
	5. The investigator/institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authorities.
	6. The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.
13. Adequate Resources
	1. The investigator should be able to demonstrate (e.g., based on retrospective data) a potential for recruiting the required number of suitable subjects within the agreed recruitment period.
	2. The investigator should have sufficient time to properly conduct and complete the trial within the agreed trial period.
	3. The investigator should have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.
	4. The investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product, and their trial-related duties and functions.
14. Medical Care of Trial Subjects
	1. A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions.
	2. During and following a subject's participation in a trial, the investigator/institution should ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the trial. The investigator/institution should inform a subject when medical care is needed for intercurrent illnesses of which the investigator becomes aware.
	3. It is recommended that the investigator inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.
	4. Although a subject is not obliged to give his/her reasons for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reasons, while fully respecting the subject's rights.
15. Communication with IRB
	1. Before initiating a trial, the investigator/institution should have written and dated approval opinion from the IRB for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects.
	2. As part of the investigator's/institution’s written application to the IRB, the investigator/institution should provide the IRB with a current copy of the Investigator's Brochure. If the Investigator's Brochure is updated during the trial, the investigator/institution should supply a copy of the updated Investigator’s Brochure to the IRB.
	3. During the trial the investigator/institution should provide to the IRB all documents subject to review.
16. Compliance with Protocol
	1. The investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authorities and which was given approval opinion by the IRB. The investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.
	2. The investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval opinion from the IRB of an amendment, except where necessary to eliminate an immediate hazards to trial subjects, or when the changes involves only logistical or administrative aspects of the trial (e.g., change in monitors, change of telephone numbers).
	3. The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol.
	4. The investigator may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard to trial subjects without prior IRB approval opinion. As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendments should be submitted: a) to the IRB for review and approval opinion, b) to the sponsor for agreement and, if required, c) to the regulatory authorities.
17. Investigational Product
	1. Responsibility for investigational product accountability at the trial site rests with the investigator/institution.
	2. Where allowed/required, the investigator/institution may/should assign some or all of the investigator's/institution’s duties for investigational product accountability at the trial site to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator/institution.
	3. The investigator/institution and/or a pharmacist or other appropriate individual, who is designated by the investigator/institution, should maintain records of the product's delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused product. These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product and trial subjects. Investigators should maintain records that document adequately that the subjects were provided the doses specified by the protocol and reconcile all investigational product received from the sponsor.
	4. The investigational product should be stored as specified by the sponsor and in accordance with applicable regulatory requirements.
	5. The investigator should ensure that the investigational product are used only in accordance with the approved protocol.
	6. The investigator, or a person designated by the investigator/institution, should explain the correct use of the investigational product to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.
	7. Randomization Procedures and Unblinding: The investigator should follow the trial's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the trial is blinded, the investigator should promptly document and explain to the sponsor any premature unblinding (e.g., accidental unblinding, unblinding due to a serious adverse event) of the investigational product.
18. Informed Consent of Trial Subjects
	1. In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirements, and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the trial, the investigator should have the IRB's written approval opinion of the written informed consent form and any other written information to be provided to subjects.
	2. The written informed consent form and any other written information to be provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject’s consent. Any revised written informed consent form, and written information should receive the IRB's approval opinion in advance of use. The subject or the subject’s legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject’s willingness to continue participation in the trial. The communication of this information should be documented.
	3. Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial.
	4. None of the oral and written information concerning the trial, including the written informed consent form, should contain any language that causes the subject or the subject's legally acceptable representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence.
	5. The investigator, or a person designated by the investigator, should fully inform the subject or, if the subject is unable to provide informed consent, the subject's legally acceptable representative, of all pertinent aspects of the trial including the written information and the approval opinion by the IRB.
	6. The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the subject or the subject's legally acceptable representative and the impartial witness, where applicable.
	7. Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the subject or the subject's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the subject or the subject's legally acceptable representative.
	8. Prior to a subject’s participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion.
	9. If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to subjects, is read and explained to the subject or the subject’s legally acceptable representative, and after the subject or the subject’s legally acceptable representative has orally consented to the subject’s participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject’s legally acceptable representative.
	10. Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following:
		1. That the trial involves research.
		2. The purpose of the trial.
		3. The trial treatments and the probability for random assignment to each treatment.
		4. The trial procedures to be followed, including all invasive procedures.
		5. The subject's responsibilities.
		6. Those aspects of the trial that are experimental.
		7. The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.
		8. The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
		9. The alternative procedures or courses of treatment that may be available to the subject, and their important potential benefits and risks.
		10. The compensation and/or treatment available to the subject in the event of trial related injury.
		11. The anticipated prorated payment, if any, to the subject for participating in the trial.
		12. The anticipated expenses, if any, to the subject for participating in the trial.
		13. That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.
		14. That the monitors, the auditors, the IRB, and the regulatory authorities will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.
		15. That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject’s identity will remain confidential.
		16. That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.
		17. The persons to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.
		18. The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.
		19. The expected duration of the subject's participation in the trial.
		20. The approximate number of subjects involved in the trial.
	11. Prior to participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated written informed consent form and any other written information provided to the subjects. During a subject’s participation in the trial, the subject or the subject’s legally acceptable representative should receive a copy of the signed and dated consent form updates and a copy of any amendments to the written information provided to subjects.
	12. When a clinical trial (therapeutic or non-therapeutic) includes subjects who can only be enrolled in the trial with the consent of the subject’s legally acceptable representative (e.g., minors, or patients with severe dementia), the subject should be informed about the trial to the extent compatible with the subject’s understanding and, if capable, the subject should sign and personally date the written informed consent.
	13. Except as described above, a non-therapeutic trial (i.e. a trial in which there is no anticipated direct clinical benefit to the subject), should be conducted in subjects who personally give consent and who sign and date the written informed consent form.
	14. Non-therapeutic trials may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled: a) The objectives of the trial cannot be met by means of a trial in subjects who can give informed consent personally. b) The foreseeable risks to the subjects are low. c) The negative impact on the subject’s well-being is minimized and low. d) The trial is not prohibited by law. e) The approval opinion of the IRB is expressly sought on the inclusion of such subjects, and the written approval opinion covers this aspect. Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.
	15. In emergency situations, when prior consent of the subject is not possible, the consent of the subject's legally acceptable representative, if present, should be requested. When prior consent of the subject is not possible, and the subject’s legally acceptable representative is not available, enrolment of the subject should require measures described in the protocol and/or elsewhere, with documented approval opinion by the IRB, to protect the rights, safety and well-being of the subject and to ensure compliance with applicable regulatory requirements. The subject or the subject's legally acceptable representative should be informed about the trial as soon as possible and consent to continue and other consent as appropriate should be requested.
19. Records and Reports
	1. The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
	2. Data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.
	3. Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained); this applies to both written and electronic changes or corrections. Sponsors should provide guidance to investigators and/or the investigators' designated representatives on making such corrections. Sponsors should have written procedures to assure that changes or corrections in CRFs made by sponsor's designated representatives are documented, are necessary, and are endorsed by the investigator. The investigator should retain records of the changes and corrections.
	4. The investigator/institution should maintain the trial documents as specified in Essential Documents for the Conduct of a Clinical Trial and as required by the applicable regulatory requirements. The investigator/institution should take measures to prevent accidental or premature destruction of these documents.
	5. Essential documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period however if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained.
	6. The financial aspects of the trial should be documented in an agreement between the sponsor and the investigator/institution.
	7. Upon request of the monitor, auditor, IRB, or regulatory authority, the investigator/institution should make available for direct access all requested trial-related records.
20. Progress Reports
	1. The investigator should submit written summaries of the trial status to the IRB annually, or more frequently, if requested by the IRB.
	2. The investigator should promptly provide written reports to the sponsor, the IRB and, where applicable, the institution on any changes significantly affecting the conduct of the trial, and/or increasing the risk to subjects.
21. Safety Reporting
	1. All serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The immediate reports should be followed promptly by detailed, written reports. The immediate and follow-up reports should identify subjects by unique code numbers assigned to the trial subjects rather than by the subjects' names, personal identification numbers, and/or addresses. The investigator should also comply with the applicable regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authorities and the IRB.
	2. Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.
	3. For reported deaths, the investigator should supply the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports).
	4. Premature Termination or Suspension of a Trial If the trial is prematurely terminated or suspended for any reason, the investigator/institution should promptly inform the trial subjects, should assure appropriate therapy and follow-up for the subjects, and, where required by the applicable regulatory requirements, should inform the regulatory authorities. In addition:
		1. If the investigator terminates or suspends a trial without prior agreement of the sponsor, the investigator should inform the institution where applicable, and the investigator/institution should promptly inform the sponsor and the IRB, and should provide the sponsor and the IRB a detailed written explanation of the termination or suspension.
		2. If the sponsor terminates or suspends a trial, the investigator should promptly inform the institution where applicable and the investigator/institution should promptly inform the IRB and provide the IRB a detailed written explanation of the termination or suspension.
		3. If the IRB terminates or suspends its approval opinion of a trial, the investigator should inform the institution where applicable and the investigator/institution should promptly notify the sponsor and provide the sponsor with a detailed written explanation of the termination or suspension.
22. Final Reports by Investigator: Upon completion of the trial, the investigator, where applicable, should inform the institution; the investigator/institution should provide the IRB with a summary of the trial’s outcome, and the regulatory authorities with any reports required.
23. Additional Requirements for Department of Defense (DOD) research
24. When appropriate, research protocols must be reviewed and approved by the IRB prior to the Department of Defense approval. Consult with the Department of Defense funding component to see whether this is a requirement.
25. Civilian researchers attempting to access military volunteers should seek collaboration with a military researcher familiar with service-specific requirements.
26. Employees of the Department of Defense (including temporary, part-time, and intermittent appointments) may not be able to legally accept payments to participate in research and should check with their supervisor before accepting such payments. Employees of the Department of Defense cannot be paid for conducting research while on active duty.
27. Service members must follow their command policies regarding the requirement to obtain command permission to participate in research involving human subjects while on-duty or off-duty.
28. Components of the Department of Defense might have stricter requirements for research-related injury than the DHHS regulations.
29. There may be specific educational requirements or certification required.
30. When assessing whether to support or collaborate with this institution for research involving human subjects, the Department of Defense may evaluate this institution’s education and training policies to ensure the personnel are qualified to perform the research.
31. When research involves U.S. military personnel, policies and procedures require limitations on dual compensation:
	1. Prohibit an individual from receiving pay of compensation for research during duty hours.
	2. An individual may be compensated for research if the participant is involved in the research when not on duty.
	3. Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to $50 for each blood draw.
	4. Non-Federal persons may be compensated for research participating other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.
32. Surveys performed on DOD personnel must be submitted, reviewed, and approved by the DOD Information Management Control Officer (IMCO) after the research protocol is reviewed and approved by the IRB. When a survey crosses DOD components, additional review is required. Consult with the Department of Defense funding component to coordinate this review.
33. When research involves large scale genomic data (LSGD) collected on DOD-affiliated personnel, additional protections are required:
	1. Additional administrative, technical, and physical safeguards to prevent disclosure of DoD-affiliated personnel’s genomic data commensurate with risk (including secondary use or sharing of de-identified data or specimens)
	2. Research will apply an HHS Certificate of Confidentiality
	3. DoD Component security review
34. Data or information sent to a DOD component under a pledge of confidentiality for exclusively statistical purposes must be used exclusively for statistical purposes and may not be disclosed in identifiable form for any other purpose, except with the informed consent of the respondent.
35. When conducting multi-site research, a formal agreement between institutions is required to specify the roles and responsibilities of each party.
36. The following must be reported to the applicable DOD Component Office of Human Research Protections within 30 days:
	1. When significant changes to the research protocol are approved by the IRB or EC:
		1. Changes to key investigators or institutions.
		2. Decreased benefit or increased risk to participants in greater than minimal risk research.
		3. Addition of vulnerable populations as participants.
		4. Addition of DOD-affiliated personnel as participants.
		5. Change of reviewing IRB.
	2. When the organization is notified by any federal body, state agency, official governing body of a Native American or Alaskan native tribe, other entity, or foreign government that any part of an HRPP is under investigation for cause involving a DOD-supported research protocol.
	3. Any problems involving risks to participants or others, suspension or termination of IRB approval, or any serious or continuing noncompliance pertaining to DOD-supported human participant research.
	4. The results of the IRB’s continuing review, if required.
	5. Change in status when a previously enrolled participant becomes pregnant, or when the researcher learns that a previously enrolled participant is pregnant, and the protocol was not reviewed and approved by the IRB in accordance with 45 CFR 46, Subpart B.
	6. Change in status when a previously enrolled participant becomes a prisoner, and the protocol was not reviewed and approved by the IRB in accordance with 32 CFR 219, Subpart C.
	7. Closure of a DOD-supported study.
37. For human participant research that would not otherwise be approved but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates, written approval from the DOD Office for Human Research Protections must be obtained through the DOD Component Office of Human Research Protections prior to research starting.
38. Other specific requirements of the Department of Defense research be found in the “Additional Requirements for Department of Defense (DOD) Research” section in the IRB’s HRP-318 - WORKSHEET - Additional Federal Agency Criteria.
39. Additional Requirements for Department of Energy (DOE) Research

(See DOE Order 443.1C)

1. Research that involves one or more of the following must be submitted to the appropriate IRB for human subjects research review and determination :
	1. Study of humans in a systematically modified environment. These studies include but are not limited to intentional modification of the human environment:
		* Study of human environments that use tracer chemicals, particles or other materials to characterize airflow.
		* Study in occupied homes or offices that:
			1. Manipulate the environment to achieve research aims.
			2. Test new materials.
			3. Involve collecting information on occupants’ views of appliances, materials, or devices installed in their homes or their energy-saving behaviors through surveys and focus groups.
	2. Use of social media data.
	3. Human Terrain Mapping (HTM).
	4. All exempt HSR determinations must be made by the appropriate IRB and/or IRB office.
2. Personally identifiable information collected and/or used during HSR projects must be protected in accordance with the requirements of DOE Order 206.1, Department of Energy Privacy Program, current version. The Central DOE IRBs require submission of DOE’s HRP- 490-CHECKLIST-Reviewing Protocols that use Personally Identifiable Information (PII) if your research includes PII.
3. You must report the following to the DOE human subjects research Program Manager (and, when an NNSA element is involved, the NNSA HSP Program Manager) prior to initiation of any new human subjects research project, even if it meets the regulatory definition of exempt human subjects research as outlined in 10 CFR Part 745.104, involving:
	1. An institution without an established Institutional Review Board (IRB);
	2. A foreign country;
	3. The potential for significant controversy (e.g., negative press or reaction from stakeholder or oversight groups);
	4. Research subjects in a protected class (prisoners, children, individuals with impaired decision making capability, or DOE/NNSA federal or DOE/NNSA contractor employees as human subjects, who may be more vulnerable to coercion and undue influence to participate) that is outside of the reviewing IRB’s typical range/scope; or
	5. The generation or use of classified information.
4. The IRB must be notified immediately and the DOE HSP Program Manager (and, when an NNSA element is involved, the NNSA HSP Program Manager) must be notified within 48 hours and consulted regarding planned corrective actions if any of the following occur:
	1. Adverse events. Notify the IRB for all adverse events and the DOE/NNSA HSP Program Manager if the IRB determines them to be significant, as defined in DOE Order 443.1C.
	2. Unanticipated problems and complaints about the research.
	3. Any suspension or termination of IRB approval of research.
	4. Any significant non-compliance with HSP Program procedures or other requirements.
	5. Any finding of a suspected or confirmed data breach involving PII in printed or electronic form. Report immediately to the IRB, the DOE/NNSA HSP Program Manager(s), and the DOE-Cyber Incident Response Capability, in accordance with the requirements of the CRD associated with DOE O 206.1.
	6. Serious adverse events and corrective actions taken must be reported immediately to the IRB and the DOE/NNSA HSP Program Manager(s). The time frame for “immediately” is defined as upon discovery.
5. Requirements for human participant protections for classified research apply to all classified research conducted or supported by the DOE and its national laboratories, including contracts, and including Human Terrain Mapping research.
6. Researchers conducting human subjects research in any other country or on citizens or other individuals residing in that country must be cognizant of country-specific human subjects research requirements and consult the IRB regarding applicability of such requirements.
7. No human subjects research conducted with DOE funding, at DOE institutions (regardless of funding source), or by DOE or DOE contractor personnel (regardless of funding source or location conducted), whether done domestically or in an international environment, including classified and proprietary research, may be initiated without both a Federalwide Assurance (FWA) or comparable assurance (e.g., Department of Defense assurance) of compliance and approval by the cognizant Institutional Review Board (IRB) in accordance with 10 CFR §745.103. Human subjects research involving multiple DOE sites (e.g., members of the research team from more than one DOE site and/or data or human subjects from more than one DOE site) must be reviewed and approved by one of the Central DOE IRBs prior to initiation, or if authorized by the DOE and/or NNSA HSP Program Manager, other appropriate IRB of record. In all cases, an IRB Authorization Agreement (IAA) or Memorandum of Understanding (MOU) must be in place between the organization(s) conducting the HSR and the organization responsible for IRB review.
8. Human subjects research that involves DOE Federal and/or contractor employees must first be reviewed and approved by the appropriate DOE IRB (the DOE site IRB or one of the Central DOE IRBs), or if deemed more fitting by the Federally assured DOE site or Headquarters, other appropriate IRB of record, in accordance with an IAA or MOU negotiated between the DOE site or Headquarters and the organization responsible for IRB review.
9. Classified and unclassified human subjects research that is funded through the Strategic Intelligence Partnership Program (SIPP) must be reviewed and approved by the Central DOE IRB-Classified.
10. If applicable, federally funded HSR must comply with the requirements of the Paperwork Reduction Act.
11. Other specific requirements of the DOE research can be found in the “Additional Requirements for Department of Energy (DOE) Research” section in the IRB’s HRP-318 - WORKSHEET - Additional Federal Agency Criteria.
12. Additional Requirements for Department of Justice (DOJ) Research

### Additional Requirements for DOJ Research conducted in the Federal Bureau of Prisons

1. Implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.
2. The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.
3. The research design must be compatible with both the operation of prison facilities and protection of human subjects.
4. Investigators must observe the rules of the institution or office in which the research is conducted.
5. Any investigator who is a non-employee of the Bureau of Prisoners must sign a statement in which the investigator agrees to adhere to the requirements of 28 CFR §512.
6. The research must be reviewed and approved by the Bureau Research Review Board.
7. Incentives cannot be offered to help persuade inmate subjects to participate. However, soft drinks and snacks to be consumed at the test setting may be offered. Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research subjects who are both: No longer in Bureau of Prisons custody. Participating in authorized research being conducted by Bureau employees or contractors.
8. A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency.
9. Except as noted in the consent statement to the subject, you must not provide research information that identifies a subject to any person without that subject’s prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertain.
10. Except for computerized data records maintained at an official Department of Justice site, records that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system.
11. If you are conducting a study of special interest to the Office of Research and Evaluation but the study is not a joint project involving Office of Research and Evaluation, you may be asked to provide Office of Research and Evaluation with the computerized research data, not identifiable to individual subjects, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.
12. Required elements of disclosure additionally include:
	1. Identification of the investigators.
	2. Anticipated uses of the results of the research.
	3. A statement that participation is completely voluntary and that the subject may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable).
	4. A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, an investigator may not guarantee confidentiality when the subject indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the subject is an inmate, indicates intent to leave the facility without authorization.
	5. A statement that participation in the research project will have no effect on the inmate subject's release date or parole eligibility.
13. You must have academic preparation or experience in the area of study of the proposed research.
14. The IRB application must include a summary statement, which includes:
	1. Names and current affiliations of the investigators.
	2. Title of the study.
	3. Purpose of the study.
	4. Location of the study.
	5. Methods to be employed.
	6. Anticipated results.
	7. Duration of the study.
	8. Number of subjects (staff or inmates) required and amount of time required from each.
	9. Indication of risk or discomfort involved as a result of participation.
15. The IRB application must include a comprehensive statement, which includes:
	1. Review of related literature.
	2. Detailed description of the research method.
	3. Significance of anticipated results and their contribution to the advancement of knowledge.
	4. Specific resources required from the Bureau of Prisons.
	5. Description of all possible risks, discomforts, and benefits to individual subjects or a class of subjects, and a discussion of the likelihood that the risks and discomforts will actually occur.
	6. Description of steps taken to minimize any risks.
	7. Description of physical or administrative procedures to be followed to: Ensure the security of any individually identifiable data that are being collected for the study.
	8. Destroy research records or remove individual identifiers from those records when the research has been completed.
	9. Description of any anticipated effects of the research study on institutional programs and operations.
	10. Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules.
16. The IRB application must include a statement regarding assurances and certification required by federal regulations, if applicable.
17. You must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor.
18. At least once a year, you must provide the Chief, Office of Research and Evaluation, with a report on the progress of the research.
19. At least 12 working days before any report of findings is to be released, you must distribute one copy of the report to each of the following: the chairperson of the Bureau Research Review Board, the regional director, and the warden of each institution that provided data or assistance.
20. You must include an abstract in the report of findings.
21. In any publication of results, you must acknowledge the Bureau's participation in the research project.
22. You must expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.
23. Prior to submitting for publication the results of a research project conducted under this subpart, You must provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.
24. Other specific requirements of the Department of Justice (DOJ) Research Conducted within the Federal Bureau of Prisons (BOP) can be found in the “Additional Requirements for Department of Justice (DOJ) Research Conducted within the Federal Bureau of Prisons (BOP)” section in the IRB’s HRP-318 - WORKSHEET - Additional Federal Agency Criteria.

### Additional Requirements for DOJ Research Funded by the National Institute of Justice

1. The project must have a privacy certificate approved by the National Institute of Justice Human Subjects Protection Officer.
2. All investigators and research staff are required to sign employee confidentiality statements, which are maintained by the responsible investigator.
3. The confidentiality statement on the consent document must state that confidentiality can only be broken if the subject reports immediate harm to subjects or others.
4. Under a privacy certificate, investigators and research staff do not have to report child abuse unless the subject signs another consent document to allow child abuse reporting.
5. A copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, or other relevant research materials.
	1. At least once a year, the researcher shall provide the Chief, Office of Research and Evaluation, with a report of the progress of the research.
	2. At least 12 working days before any report of findings is to be released, the researcher shall distribute one copy of the report to each of the following: the chairperson of the Bureau Research Review Board, the regional director, and the warden of each institution that provided data or assistance. The researcher shall include an abstract in the report of findings.
	3. In any publication of results, the researcher shall acknowledge the Bureau's participation in the research project.
	4. The research shall expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.
	5. Prior to submitting for publication the results of a research project conducted under this subpart, the researcher shall provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons
6. Other specific requirements of the Department of Justice (DOJ) Research Funded by the National Institute of Justice can be found in the “Additional Requirements for Department of Justice (DOJ) Research” section in the IRB’s HRP-318 - WORKSHEET - Additional Federal Agency Criteria.
7. Additional Requirements for Department of Education (ED) Research
8. Each school at which the research is conducted must provide an assurance that they comply with the Family Educational Rights and Privacy Act (FERPA) and the Protection of Pupil Rights Amendment (PPRA).
9. Provide a copy of all surveys and instructional material used in the research. Upon request parents of children[[17]](#footnote-16) involved in the research[[18]](#footnote-17) must be able to inspect these materials.
10. The school in which the research is being conducted must have policies regarding the administration of physical examinations or screenings that the school may administer to students.
11. Other specific requirements of the Department of Education (ED) Research can be found in the “Additional Requirements for Department of Education (ED) Research” section in the IRB’s HRP-318 - WORKSHEET - Additional Federal Agency Criteria.
12. Additional Requirements for Environmental Protection Agency (EPA) Research
13. Research conducted, supported, or intended to be submitted to EPA is subject to Environmental Protection Agency Regulations.
14. Intentional exposure of pregnant women or children to any substance is prohibited.
15. Observational research involving pregnant women and fetuses are subject to additional DHHS requirements for research involving pregnant women (45 CFR §46 Subpart B) and additional DHHS requirements for research involving children (45 CFR §46 Subpart D.)
16. Research involving children must meet category #1 or #2.
17. Other specific requirements of the Environmental Protection Agency (EPA) Research can be found in the “Additional Requirements for Environmental Protection Agency (EPA) Research and Research Intended to be Submitted to the Environmental Protection Agency” section in the IRB’s HRP-318 - WORKSHEET - Additional Federal Agency Criteria.
18. Additional Requirements for Veterans Administration (VA) Research
* VA research is research that is conducted by researchers (serving on VA compensated, WOC, or IPA appointments) while on VA time or on VA property. The research may be funded by VA, by other sponsors, or be unfunded. VA research must have Research and Development (R&D) Committee approval before it is considered VA Research and before it can be initiated. All research activities approved by the R&D Committee are considered VA Research.
	+ VA-affiliated nonprofit research and education corporations (NPC) are authorized by Congress under 38 U.S.C. 7361-7366 to provide flexible funding mechanisms for the conduct of research and education at one or more VA facilities. Research approved by a facility R&D Committee are considered to be a VA research project or a VA education activity respectively, regardless of the source of funding, the entity administering the funds, or the research or education site (see VHA Handbook 1200.17, Department of Veterans Affairs Nonprofit Research and Education Corporations Authorized by Title 38 U.S.C. Sections 7361 Through 7366, dated April 27, 2016 and revised May 9, 2017).
	+ VA research includes VA-approved research conducted at international sites not within the United States, its territories, or Commonwealths; and includes research where human tissues are sent outside the United States.
* The investigator must give first priority to the protection of research subjects, uphold professional and ethical standards and practices, and adhere to all applicable VA and other federal requirements, including the local VA facility’s policies and procedures, regarding the conduct of research and the protection of human subjects. The investigator must hold a current VA appointment to conduct VA research.
* The responsibilities of the investigator may be defined in the protocol or IRB application. Specifically, the principal investigator’s and local site investigator’s responsibilities include, but are not limited to
	+ Qualifications to Conduct Human Subjects Research. VA investigators must have the appropriate training, education, expertise, and credentials to conduct the research according to the research protocol.
	+ PIs must ensure that all research staff are qualified (e.g., including but not limited to appropriate training, education, expertise, and credentials) to perform procedures assigned to them during the course of the study.
	+ Investigators and their staff conducting human subjects research must be credentialed and privileged as required by current local and VA requirements (see VHA Handbook 1100.19 and VHA Directive 2012-030, Credentialing of Health Care Professionals, or successor policy). Investigators and their research staff may only perform those activities in a research study for which they have the relevant credentials and privileges.
	+ Investigators and co-investigators must be identified on the IRB application and must provide credentials, conflict of interest statements or other documentation required by VA and local facility policies.
	+ All individuals involved in conducting VA human subjects research are required to complete training in ethical principles on which human subjects research is to be conducted. Specific requirements regarding the type and frequency of training are found on ORD’s Web site at: <http://www.research.va.gov/pride/training/options.cfm>. All other applicable VA and VHA training requirements at the local and national level must be met (e.g., privacy and information security training).
	+ Investigators must prospectively document their research with their supervisor in writing.
	+ Investigators must submit exempt protocols that require limited IRB review to the IRB for limited IRB review/approval.
	+ Research Protocol. The investigator must develop and submit a research protocol that is scientifically valid, describes the research objectives, background and methodology, provides for fair and equitable recruitment and selection of subjects, minimizes risks to subjects and others, and describes a data and safety monitoring plan consistent with the nature of the study. The research must be relevant to the health or welfare of the Veteran population. When relevant, the protocol must include the following safety measures:
	+ The type of safety information to be collected including AEs;
	+ Frequency of safety data collection;
	+ Frequency or periodicity of review of cumulative safety data;
	+ Statistical tests for analyzing the safety data to determine if harm is occurring; and
	+ Conditions that trigger an immediate suspension of the research, if applicable.
	+ Approvals. The investigator must submit the protocol for initial review and obtain written approvals from the IRB, other applicable committees, and from the R&D Committee. In addition, the investigator must receive written notice from the ACOS/R&D that the research may commence before initiating the research.
	+ An investigator may not self-certify that a study is exempt.
	+ Once approved by the IRB, the protocol must be implemented as approved. All modifications to the approved research protocol or consent form must be approved by the IRB prior to initiating the changes except when necessary to eliminate apparent immediate hazards to the subject.
	+ The investigator must also obtain continuing review and approval at a frequency established by the IRB, but not less than once every year and is expected to submit all materials required for continuing review in sufficient time to assure approval prior to the expiration date. No research activities may be conducted at any time without a currently valid IRB approval.
	+ Conflict Of Interest. The investigator must disclose to the IRB any potential, actual, apparent, or perceived conflict of interest of a financial, professional, or personal nature that may affect any aspect of the research, and comply with all applicable VA and other federal requirements regarding conflict of interest.
	+ Initial Contact. During the recruitment process, members of the research team must make initial contact with potential subjects in person or by letter prior to initiating any telephone contact, unless there is written documentation that the subject is willing to be contacted by telephone about the study in question or a specific kind of research as outlined in the study. (NOTE: This does not apply to situations where a Veteran calls in response to an advertisement. If existing information from sources such as a medical record or database, research or non-research, are used to identify human subjects, , there must be an IRB approved HIPAA waiver for this activity in the new protocol.)
	+ Any initial contact by letter or telephone must provide a telephone number or other means that the potential subject can use to verify that the study constitutes VA research.
	+ If a contractor makes the initial contact by letter, the VA investigator must sign the letter.
	+ Informed Consent for Research. The investigator must obtain and document legally effective informed consent of the subject or the subject's LAR prospectively (i.e., no screening or other interaction or intervention involving a human subject can occur until after the IRB-approved informed consent requirements have been met) that is in alignment with ethical principles that govern informed consent for research. The only exceptions are if the IRB determines the research is exempt, or approves a waiver of the informed consent process, or approves a waiver of the signed informed consent document.
	+ If the investigator does not personally obtain informed consent, the investigator must delegate this responsibility in writing (e.g., by use of a delegation letter) to research staff sufficiently knowledgeable about the protocol and related concerns to answer questions from prospective subjects, and about the ethical basis of the informed consent process and protocol.
		- If the investigator contracts with a firm, e.g., a survey research firm, to obtain consent from subjects, collect private individually identifiable information from human subjects, or are involved in activities that would institutionally engage the firm in human subjects research, the firm must have its own IRB oversight of the activity. In addition, the PO must determine that there is appropriate authority to allow the disclosure of individual names and other information to the contracted firm.
		- The investigator must ensure that all original signed and dated informed consent documents are maintained in the investigator’s research files, readily retrievable, and secure.
	+ HIPAA Authorization. The investigator or designee must obtain HIPAA authorization for the use and disclosure of the subject’s PHI, or obtain an IRB-approved waiver of HIPAA authorization unless there is a limited data set and appropriate DUA. The written HIPAA authorization may either be a standalone document or combined with the research informed consent approved by the IRB. If a standalone document is used as the written HIPAA authorization, VA Form 10-0493: Authorization for Use and Release of Individually Identifiable Health Information Collected for VHA Research, must be used to document the authorization.
	+ Reporting. The investigator is responsible for reporting unanticipated problems involving risks to subjects or others, serious unanticipated problems involving risks to subjects or others, apparent serious or continuing noncompliance, any termination or suspension of research; and privacy or information security incidents related to VA research, including: any inappropriate access, loss, or theft of PHI; noncompliant storage, transmission, removal, or destruction of PHI; or theft, loss, or noncompliant destruction of equipment containing PHI, in accordance with local facility or IRB SOPs and VHA Handbook 1058.01.
	+ VA personnel must ensure that the appropriate IRB of Record is notified, in writing, within five (5) business days after becoming aware of any apparent serious and/or continuing noncompliance with applicable laws, regulations, policies, and agreements pertaining to non-exempt human participants research. This includes, but is not limited to, serious or continuing noncompliance with the Common Rule, local VA medical facility policies and SOPs related to human participants research, if developed, IRB-approved protocols, and the requirements or determinations of the IRB.
	+ In the event of a local research participant death, VA personnel must ensure that the appropriate IRB of Record is notified:
		- Immediately (i.e., within one hour) upon becoming aware of any local research death of a human participant that is believed to be both unexpected and related or possibly related to participating in a VA non-exempt human participant study. VA personnel must also provide follow-up written notification to the IRB within one (1) business day.
	+ In the event of any apparent UPIRTSO, VA personnel must ensure that the appropriate IRB of Record is notified, in writing, within five (5) business days after becoming aware of any apparent UPIRTSO.
	+ Research Records. All written information given to subjects must be in the investigator’s research file along with the consent form(s). All records regardless of format (paper, electronic, electronic systems) must be managed per NARA approved records schedules found in VHA RCS 10-1 and therefore must be retained until disposition instructions, as approved by NARA, are published in VHA RCS 10-1. NOTE: Once the disposition schedule is determined, records should be disposed in accordance with VHA RCS 10-1. If the investigator leaves VA, all research records must be retained by the VA facility where the research was conducted.
	+ VHA Health Record. A VHA health record must be created or updated, and a progress note created, 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 nursing homes). Informed consent and HIPAA authorization documents are not required to be in the health record. The name and contact information of the researcher conducting the study should be included.
	+ Investigational Drugs and Devices. The investigator must conduct VA human subjects research involving investigational drugs and devices in accordance with all applicable VA policies and other federal requirements including, but not limited to: VHA Directive 1200.05, VHA Handbook 1108.04, and applicable FDA regulations. The storage and security procedures for test articles used in research must be reviewed and approved by the IRB and follow all applicable federal rules.
	+ The PI or Local Site Investigator (LSI) must provide the Pharmacy Service with the following:
		- Written approval letter signed by the ACOS for R&D that all relevant approvals have been obtained and that the study may be initiated at the site (VHA Directive 1200.01);
		- An IRB approval letter;
		- A copy of the approved study protocol;
		- A copy of VA Form 10-9012, when appropriate;
		- An IB, when appropriate;
		- Any sponsor-provided documents relating to the storage, preparation, dispensing, and accountability of the investigation products;
		- Copies of all correspondence addressed to the Researcher from the FDA specific to the investigational drugs as appropriate;
		- A copy of the consent document for each participating participant with all appropriate signatures;
		- Protocol revisions, amendments, and updates after IRB approval and after the IRB approved the amendment;
		- Updates and changes to authorized prescribers after IRB approval;
		- Documentation of IRB continuing review approval;
		- Notice to the Chief, Pharmacy Service, the research pharmacy when applicable and the IRB in writing and the Research and Development Committee when a study involving investigational drugs has been suspended, terminated, or closed.
	+ The PI or LSI must provide Pharmacy Service and/or the Research Service Investigational Pharmacy, investigational drug information on each patient receiving an investigational drug through the electronic medical record or other locally-approved means. This documentation is to include allergies, toxicities, or adverse drug events related to the investigational drug, or the potential for interaction with other drugs, foods, or dietary supplements (herbals, nutriceuticals).
	+ The PI must comply with all dispensing and documentation requirements and the dispensing log must be made accessible to the investigational drug pharmacist upon request.
	+ Initiation of Research Projects. IRB approval is for a specified time period based on the degree of risk of the study, not to exceed 1 year except for research subject to the 2018 Requirements where continuing review is not required. The IRB determines the expiration date based upon its date of review and communicates that date to the investigator in the written approval letter. The investigator must not initiate the IRB approved research protocol until all applicable requirements in VHA Directive 1200.01 have also been met including obtaining R&D Committee approval.
	+ Expiration of IRB Approval. There is no provision for any grace period to extend the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur on or before the date when IRB approval expires. If approval expires, the investigator must:
	+ Stop all research activities including, but not limited to, enrollment of new subjects, analyses of individually identifiable data, and research interventions or interactions with currently participating subjects, except where stopping such interventions or interactions could be harmful to those subjects; and
	+ Immediately submit to the IRB Chair a list of research subjects who could be harmed by stopping specified study interventions or interactions. The IRB Chair must determine within 2 business days whether or not such interventions or interactions may continue.
	+ Documentation of Informed Consent
		- * When documentation of informed consent is not waived by IRB, the investigator or designee must ensure that the informed consent document is signed and dated by the subject or the subject’s legally authorized representative,
		- If consent is obtained electronically, the following must be met:
			* Authentication controls on electronic consent provide reasonable assurance that such consent is rendered by the proper individual; and
			* The subject dates the consent as is typical or that the software provides the current date when signed.
* Vulnerable Subjects
	+ The following populations are considered categorically vulnerable and have specific VA requirements for their inclusion in research:
		- Pregnant Women, Human Fetuses and Neonates
		- Prisoners
		- Children
		- Subjects who Lack Decision-making Capacity.
* Research Involving Prisoners
	+ Research involving prisoners cannot be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities unless a waiver has been granted by the CRADO.
	+ Waiver requests must be submitted electronically to the CRADO by the VA medical facility Director with the following documents:
	1. A letter from the VA medical facility Director supporting the conduct of the VA study involving prisoners;
	2. Rationale for conducting the research involving prisoners to include additional ethical protections taken by the proposed research for prisoners to make voluntary and uncoerced decisions whether or not to participate as subjects in research;
	3. Documentation of the VA investigator’s qualifications to conduct the research involving prisoners, such as a biosketch and a list of all research team members;
	4. Location of institutions where the research is proposed to be conducted;
	5. A copy of the IRB approval letter specifically documenting its review determinations according to 45 CFR 46.305(a);
	6. A copy of the IRB minutes approving the research with documentation that at least one member of the IRB included a prisoner or a prisoner representative for the review of the research;
	7. A copy of the IRB-approved research study;
	8. A copy of the IRB-approved informed consent document; and
	9. A copy of the written HIPAA authorization.
	+ If such a waiver is granted, the research must comply with the requirements of 45 CFR 46.301 - 46.306.
* Research Involving Children
	+ Research involving children must not present greater than minimal risk.
	+ The VA medical facility Director must approve participation in the proposed research that includes children.
	+ Research involving biological specimens or data obtained from children is considered to be research involving children even if de-identified. If the biological specimens or data were previously collected, they must have been collected under applicable policies and ethical guidelines.
	+ The IRB must have the appropriate expertise to evaluate VA research involving children and must comply with the requirements of 45 CFR 46.401 - 46.404 and 46.408.
* Research Involving Pregnant Women, Human Fetuses and Neonates as Subjects
	+ Neonates: Interventional research enrolling neonates cannot be conducted by VA investigators while on official duty, or at VA facilities, or at VA approved off-site facilities. VA investigators may conduct research involving noninvasive monitoring of neonates if the research is determined by the IRB to be minimal risk. Prospective observational and retrospective record review studies that involve neonates or neonatal outcomes are permitted. The VA medical facility Director must certify that the medical facility has sufficient expertise in neonatal health to conduct the proposed research.
	+ Pregnant Women: The VA medical facility Director must certify that the medical facility has sufficient expertise in women's health to conduct the proposed research if the research includes interventional studies or invasive monitoring of pregnant women as subjects.
	+ Research that involves provision of in vitro fertilization services can be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities. This includes prospective and retrospective research involving provision of or the enhancement of FDA-approved methods of in vitro fertilization for studies involving consenting subjects, both male and female, undergoing or who have undergone in vitro fertilization for the treatment of certain forms of human infertility. In vitro fertilization is any fertilization of human ova that occurs outside the body of a female, either through a mixture of donor human sperm and ova or by any other means.
	+ Prospective and retrospective studies that enroll or include pregnant subjects who conceived through in vitro fertilization or other artificial reproductive technologies are permitted.
	+ Research that uses human fetal tissue or that focuses on either a fetus, or human fetal tissue, in-utero or ex-utero cannot be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities. Use of stem cells shall be governed by the policy set by NIH for recipients of NIH research funding.
* Research Involving Persons Who Lack Decision-Making Capacity
	+ The protocol must include a plan, that it is appropriate given the population and setting of the research, for how investigators will determine when a legally authorized representative will be required to provide informed consent. In general, the research staff must perform or obtain and document a clinical assessment of decision-making capacity for any subject suspected of lacking decision-making capacity.
	+ When the potential subject is determined to lack decision-making capacity, investigators must obtain consent from the LAR of the subject (i.e., surrogate consent). NOTE: Investigators and IRBs have a responsibility to consult with the Office of General Counsel (OGC) regarding state or local requirements for surrogate consent for research that may supersede VA requirements.
	+ The following persons are authorized to consent on behalf of persons who lack decision-making capacity in the following order of priority:
		- (1) Health care agent (i.e., an individual named by the subject in a Durable Power of Attorney for Health Care);
		- (2) Legal guardian or special guardian;
		- (3) Next of kin: a close relative of the patient 18 years of age or older, in the following priority: spouse, child, parent, sibling, grandparent, or grandchild; or
		- (4) Close friend.
	+ If feasible, the investigator must explain the proposed research to the prospective research subject even when the legally authorized representative gives consent. Although unable to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may a subject be forced or coerced to participate in a research study even if the LAR has provided consent.
	+ Legally authorized representatives must be told that their obligation is to try to determine what the subjects would do if able to make an informed decision. If the potential subjects’ wishes cannot be determined, the legally authorized representatives must be told they are responsible for determining what is in the subjects’ best interest.
* Research Involving Certificates of Confidentiality
	+ If information about the subject’s participation will be included as part of the VHA medical record that information must be given to the prospective subject as part of the informed consent process that information regarding study participation will be included in the medical record.
	+ In instances where a written informed consent form is used, inclusion of a statement that the study has been issued a CoC is required.
	+ Investigators should work with the research office in their facility to assure that when Veterans are enrolled in a study protected by a Certificate of Confidentiality, they are not simultaneously enrolled in other interventional studies unless it is absolutely clear that this enrollment does not raise safety issues.
* Collaborative Research
	+ This addresses collaborations between VA and non-VA investigators. Collaboration is encouraged when VA investigators have a substantive role in the design, conduct, and/or analysis of the research. VA may also serve as a Coordinating Center for collaborative studies. NOTE: Collaborative studies do not include studies conducted under a CRADA with pharmaceutical companies or other for-profit entities.
	+ IRB of Record Approval. Each institution is responsible for safeguarding the rights and welfare of human subjects and providing oversight of the research activities conducted at that institution.
		- Each collaborating institution engaged in human subjects research must obtain approval from its IRB of Record and hold a FWA or another assurance acceptable to VA, e.g. DoD assurance.
		- VA investigators must submit a protocol or other documentation to their VA IRB of Record that delineates which research activities will be conducted by VA.
		- Each institution engaged in the collaborative research must use the informed consent document and HIPAA authorization required by their respective institutional policies for subjects recruited from that institution, or procedures requiring participation of the subject at that institution. The informed consent document may contain information on the project as a whole as long as the document clearly describes which procedures will be performed at VA and which will be performed at other institutions.
			* The VA informed consent document must clearly state when procedures mentioned at other institutions are part of the VA’s portion of the study.
			* The informed consent document and HIPAA authorization must be consistent and include information describing the following:
				+ PHI to be collected and/or used by the VA research team;
				+ PHI to be disclosed to the other institutions; and
				+ Purpose for which the PHI may be used.
		- Waivers. PHI obtained in research for which the IRB of Record has waived the requirements to obtain a HIPAA authorization and a signed informed consent document may not be disclosed outside VA unless the VA facility Privacy Officer ensures and documents VA’s authority to disclose the PHI to another institution. A waiver of HIPAA authorization is not sufficient to fulfill the requirements of other applicable privacy regulations such as the Privacy Act of 1974 (5 U.S.C. 552a).
	+ Research Data. The protocol, addendum, and/or IRB of Record application must describe the data to be disclosed to collaborators, the entity(ies) to which the data are to be disclosed, and how the data are to be transmitted. This includes data from individual subjects as well as other data developed during the research such as the analytic data and the aggregate data.
		- Each VA facility must retain a complete record of all data obtained during the VA portion of the research in accordance with privacy requirements, the Federal Records Act, and VHA Records Control Schedule (RCS) 10-1.
		- All disclosures and data transmission must meet privacy and security requirements per VA Directive 6500, VHA Handbook 6500, and VHA Handbook 1605.1.
	+ Written agreements. Collaborative research involving non-VA institutions may not be undertaken without a signed written agreement (e.g., a CRADA or a Data Use Agreement (DUA)) that addresses such issues as the responsibilities of each party, the ownership of the data and the reuse of the data for other research. NOTE: Any reuse must be consistent with the protocol, the informed consent document, and the HIPAA authorization.
* Photography, Video and/or Audio Recording for Research Purposes
	+ The informed consent for research must include information describing any photographs, video, and/or audio recordings to be taken or obtained for research purposes, how the photographs, video, and/or audio will be used for the research, and whether the photographs, video, and/or audio will be disclosed outside the VA.
		- An informed consent to take a photograph, video, and/or audio recording cannot be waived by the IRB.
		- The consent for research does not give legal authority to disclose the photographs, video, and/or audio recordings outside the VA. A HIPAA authorization is needed to make such disclosures.
* International Research
	+ VA international research is defined as any VA-approved research conducted at international sites (i.e., not within the United States (U.S.), its territories, or Commonwealths), any VA-approved research using either identifiable or de-identified human biological specimens or identifiable or de-identified human data originating from international sites, or any VA-approved research that entails sending such specimens or data out of the U.S. This definition applies regardless of the funding source (funded or unfunded) and to research conducted through any mechanism of support including MOUs, CRADAs, grants, contracts, or other agreements. NOTE: Research conducted at U.S. military bases, ships, or embassies is not considered international research.
		- Sending specimens or data to individuals with VA appointments at international sites (e.g., a WOC appointment, a VA investigator on sabbatical at an international site) is considered international research. Remote use of data that is maintained on VA computers within the U.S. or Puerto Rico and accessed via a secure connection is not considered international research.
		- International research includes multi-site trials involving non-U.S. sites where VA is the study sponsor, a VA investigator is the overall study-wide PI, VA holds the Investigational New Drug (IND), or the VA manages the data collection and the data analyses.
		- International research does not include studies in which VA is only one of multiple participating sites where the overall study-wide PI is not a VA investigator (i.e., the PI for the study as a whole is not a VA investigator).
	+ Before approving international research involving human subjects research, the IRB must ensure that human subjects outside of the U.S. who participate in research projects in which VA is a collaborator receive equivalent protections as research participants inside the U.S. (see OHRP guidance at http://www.hhs.gov/ohrp/international/index.html). NOTE: The VA medical facility Director must approve participation in the proposed international research.
	+ All international research must also be approved explicitly in a document signed by the VA medical facility Director, except for Cooperative Studies Program activities which must be approved by the CRADO.
* Use Preparatory To Research
	+ VA investigators may use individually-identifiable health information to prepare a research protocol prior to submission of the protocol to the IRB for approval without obtaining a HIPAA authorization or waiver of authorization.
		- VA investigators must not arbitrarily review PHI based on their employee access to PHI until the investigator documents the following required information as “Preparatory to Research” in a designated file that is readily accessible for those required to audit such information (e.g., Health Information Manager or PO):
			* Access to PHI is only to prepare a protocol;
			* No PHI will be removed from the covered entity (i.e., VHA); and
			* Access to PHI is necessary for preparation of the research protocol.
		- Non-VA researchers may not obtain VA information for preparatory to research activities without appropriate VA approvals (see VHA Directive 1605.01).
		- During the preparatory to research activities the VA investigator:
			* Must only record aggregate data. The aggregate data may only be used for background information to justify the research or to show that there are adequate numbers of potential subjects to allow the investigator to meet enrollment requirements for the research study;
			* Must not record any individually identifiable health information; and
			* Must not use any individually identifiable information to recruit research subjects.
			* Preparatory activities can include reviewing database output (computer file or printout) containing identifiable health information generated by the database owner, if the investigator returns the database output to the database owner when finished aggregating the information.
	+ Contacting potential research subjects and conducting pilot or feasibility studies are not considered activities preparatory to research.
	+ Activities preparatory to research only encompass the time to prepare the protocol and ends when the protocol is submitted to the IRB.
* Posting of Clinical Trial Consent Forms
	+ For studies subject to the 2018 Requirements, if a VA research study is a clinical trial, one IRB-approved informed consent form used to enroll subjects, unless the IRB waived documentation of informed consent, must be posted by either the investigator or the Federal department or agency conducting or supporting the study. The informed consent form must be posted after the clinical trial is closed to recruitment and no later than 60 days after the last study visit by any subject as described in the IRB-approved protocol. For multi-site studies, it applies when the entire study has closed to subject recruitment. Any proprietary or personal information (such as names and phone numbers) must be redacted prior to posting the informed consent form.
		- For any ORD-funded clinical trial, the applicable ORD funding service will be responsible for posting the informed consent form.
		- For a clinical trial funded or supported by a Federal agency or department other than VA, the awardee is responsible for posting the informed consent form.
		- For a clinical trial funded or supported by a non-Federal agency or department (e.g., university, industry, nonprofit organization) or not funded, the VA Investigator conducting the clinical trial is responsible for ensuring that the informed consent form is posted. If the clinical trial includes multiple sites engaged in the clinical trial, an agreement must exist specifying who is responsible for posting the informed consent form.
* Other specific requirements of Veterans Administration (VA) research can be found in the “Additional Requirements for Veterans Administration (VA) Research” section in the IRB’s HRP-318 - WORKSHEET - Additional Federal Agency Criteria.
1. Single IRB Studies
2. That National Institutes of Health expects that all sites participating in multi-site studies involving non-exempt human subjects research funded by the NIH will use a single Institutional Review Board (sIRB) to conduct the ethical review required by the Department of Health and Human Services regulations for the Protection of Human Subjects at 45 CFR Part 46.
	1. This policy applies to the domestic sites of NIH-funded multi-site studies where each site will conduct the same protocol involving non-exempt human subjects research, whether supported through grants, cooperative agreements, contracts, or the NIH Intramural Research Program. It does not apply to career development, research training or fellowship awards.
	2. This policy applies to domestic awardees and participating domestic sites. Foreign sites participating in NIH-funded, multi-site studies will not be expected to follow this policy.
	3. Exceptions to the NIH policywill be made where review by the proposed sIRB would be prohibited by a federal, tribal, or state law, regulation, or policy. Requests for exceptions that are not based on a legal, regulatory, or policy requirement will be considered if there is a compelling justification for the exception. The NIH will determine whether to grant an exception following an assessment of the need.
3. The Office for Human Research Protections expects that all sites located in the United States participating in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research.

The following research is not subject to this provision:

* 1. Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or
	2. Research for which 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.
	3. For research not subject to paragraph (b) of this section, an institution participating in a cooperative project may enter into a joint review arrangement, rely on the review of another IRB, or make similar arrangements for avoiding duplication of effort.

1. Additional Requirements for Research Subject to EU General Data Protection Regulations (GDPR)

**What is the GDPR?**

The General Data Protection Regulation (GDPR) is a European law that went into effect on May 25, 2018 and establishes protections for privacy and security of "personal data" about individuals in European Economic Area (“EEA”)-based operations and certain non-EEA organizations that process personal data of individuals in the EEA.

Human Research involving “personal data” about individuals located in (but not necessarily citizens of) the following European Union member states, Norway, Iceland, Liechtenstein, and Switzerland are subject to EU General Data Protection Regulations.

Austria Belgium Bulgaria Croatia Cyprus

Czech Republic Denmark Estonia Finland France

Germany Greece Hungary Iceland Ireland

Italy Latvia Lichtenstein Lithuania Luxembourg

Malta Netherlands Norway Poland Portugal

Romania Slovakia Slovenia Spain Sweden

United Kingdom\*

\* UK update: <https://ico.org.uk/for-organisations/dp-at-the-end-of-the-transition-period/transition-period-faqs/>

**What is "personal data"?**

Under the GDPR, “**personal data**” refers to any information that relates to an identified or identifiable natural person (i.e., an individual, not a company or other legal entity), otherwise known as a “data subject.”

Examples of “personal data” include: a person’s name, email address, government-issued identification, or other unique identifier such as an IP address or cookie number, and personal characteristics, including photographs.

* ***Special categories of personal data***

The GDPR highlights some “special categories” of personal data which merit a higher level of protection due to their sensitive nature and risk for greater privacy harm.

This includes: information about a data subject’s health, genetics, race or ethnic origin, biometrics for identification purposes, sex life or sexual orientation, political opinions, religious or philosophical beliefs, or trade union membership.

* ***GDPR and Coded Data***

Importantly, the GDPR considers “pseudonymized data” (e.g., coded data) to be “personal data” even where one lacks access to the key-code/crosswalk required to link data to an individual data subject. *This is inconsistent with U.S. regulations protecting human subjects and, therefore, important for researchers to understand.*

* ***GDPR and Anonymized Data***

The GDPR *does not apply* to data that have been anonymized. Under the GDPR, in order for data to be anonymized, there can be **no key-code in existence to re-identify the data**. For example, if UMass Boston serves as the sponsor of a research study with a site located in the EEA and receives only coded data from the EEA site, such data from the EEA site remain “personal data." This holds true even when UMass Boston researchers have no access to the key-code/crosswalk required to link data to an individual data subject.

**What activities are subject to the GDPR?**

Activities involving identifiable information if personal data is being collected from one or more research participants ***physically located in the EEA*** at the time of data collection. Of note, the participant **does not need to be an EEA resident**.

Activities involving the transfer of personal data collected under the GDPR from an EEA country to a non-EEA country (like the U.S.).

Activities involving collection of identifiable personal data from individuals who are ***physically located within the U.S.*** at the time of data collection *-- even if the participant is an EEA citizen --* are not subject to the GDPR.

**How do I ensure that my study complies with the GDPR?**

* Collect only the absolute minimum personal/demographic data needed to complete the study. If your study can be completed using only de-identified data, then we strongly advise you to take this approach.
* Many online survey sites collect personal information, including IP addresses, by default. Ensure that you set up your study to receive **only** the information you are seeking. To the extent possible, verify that any third-party website or app being used for data collection is GDPR-compliant.
* Use an active (“opt-in”) informed consent. Under the GDPR, consent must be freely given, specific, informed, unambiguous, and explicit. A description of the data processing and transfer activities to be performed, if applicable, must be included in the informed consent document. Following an informed consent description, a “Click next to proceed to the survey” button or equivalent is sufficient for “active” consent for online data collection.
* Ensure that your consent form is in compliance with GDPR requirements (see below).
* For activities in which identifiable data is collected, you must have an executable plan to remove data in the event a participant requests to have his/her data removed.

**How is the consent documentation and process affected by GDPR?**

The good news is that many of the consent requirements under the GDPR are consistent with those that you already implement as part of standard consent processes and documentation. Below are the GDPR requirements:

* + - 1. Consent records, including time and date of consent, must be maintained for each subject. In the case of verbal, online, or any other type of undocumented consent, the Principal Investigator is responsible for maintaining a consent log indicating each subject (either by name or study ID number) and the date and time that consent was provided.
			2. Consent must be explicit. If the consent form or consent script serves multiple purposes (e.g., a consent form that is also the recruitment email), then the request for consent must be clearly distinguishable.
			3. Each subject has a right to withdraw consent at any time. Each subject must be informed of this right prior to giving consent. Withdrawal of consent must be as easy as giving consent.
			4. Consent must be an affirmative action. This means that opt-out procedures are not permitted.
			5. Consent information must be provided in clear and plain language in an intelligible and easily accessible format.
			6. Consent must be freely-given. Individuals in a position of authority cannot obtain consent, nor can consent be coerced. This means that faculty members or teachers cannot obtain consent from their own students.
			7. Consent forms must contain the following information:
		- The identity of the Principal Investigator;
		- The purpose of data collection;
		- The types of data collected, including listing of special categories: Racial or ethnic origin; Political opinions; Religious or philosophical beliefs; Trade union membership; Processing of genetic data; Biometric data for the purposes of unique identification; Health data; and/or Sex life or sexual orientation information;
		- The right to withdraw from the research and the mechanism for withdrawal;
		- Who will have access to the data;
		- Information regarding automated processing of data for decision-making about the individual, including profiling;
		- Information regarding data security, including storage and transfer of data;
		- How long data will be stored (this can be indefinite);
		- Whether and under what conditions data may be used for future research, either related or unrelated to the purpose of the current study.

**Other Considerations:**

* For all prospective Human Research subject to EU GDPR, contact institutional legal counsel or the institution’s Data Protection Officer to ensure that the following elements of the research are consistent with institutional policies and interpretations of EU GDPR:
	+ Any applicable study design elements related to data security measures.
	+ Any applicable procedures related to the rights to access, rectification, and erasure of data.
	+ Procedures related to broad/unspecified future use consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens.
* Where FDA or DHHS regulations apply in addition to EU GDPR regulations, ensure that procedures related to withdrawal from the research, as well as procedures for managing data and biospecimens associated with the research remain consistent with Appendices A-1 and A-2 above.
* In the event of a data breach, notify the University of Massachusetts IRB immediately so that appropriate steps can be taken.
1. Emergency/Disaster Preparedness Considerations for Investigators Conducting Human Research

Investigators conducting human research should be aware of the following additional considerations associated with managing Human Research during an emergency/disaster scenario (e.g., extreme weather events, natural disasters, man-made disasters, infectious disease pandemics, etc.) related to investigators’ ongoing interactions with research subjects and the institutional review board (IRB) in such cases.

**During Emergency/Disaster Scenarios: Deciding Whether a Study-Specific Risk Mitigation Plan for Ongoing Research Is Needed**

In general, investigators should develop a study-specific emergency/disaster risk mitigation plan for their research unless one of the following is true:

* Research does not involve in-person interaction with research subjects.
* Research can be conducted as written while adhering to additional institution-level and HRPP-level guidance and requirements regarding the emergency/disaster event.
* The research is externally sponsored, and the sponsor has developed a protocol-specific risk mitigation plan for the research.
* The research has been voluntarily placed on hold for recruitment and all research procedures (except for necessary follow-up procedures to be done consistently with additional institution-level and HRPP-level guidance and requirements regarding the emergency/disaster event).

**Tools and Resources for Developing Study-Specific Emergency/Disaster Risk Mitigation Plans for Ongoing Research**

Review “HRP-108 - FLOWCHART - Study-Specific Emergency-Disaster Risk Mitigation Planning” and “HRP-351 - WORKSHEET - Protocol-Specific Emergency-Disaster Risk Mitigation Plan” for general guidance on developing study-specific risk mitigation plans.

**Voluntary Holds on Human Research Activities**

Investigators may voluntarily elect to place all recruitment, enrollment and research procedures on temporary hold during emergency/disaster scenarios if doing so will better ensure the safety of research subjects and would not create any additional risks to the safety and welfare of research subjects. Such voluntary holds on research activity do not require IRB notification or review.

**Submitting Study-Specific Emergency/Disaster Risk Mitigation Plans for IRB Review**

If immediate modification of the research is necessary to eliminate an apparent immediate hazard to a subject, take action and notify the IRB within five business days following the standard pathway to submit reportable new information.

For all other study modifications made to ensure the ongoing safety of research subjects during emergency/disaster scenarios, submit a study amendment and all relevant new or modified study materials to the IRB.

**Other Reportable New Information Considerations During Emergency/ Disaster Scenarios**

The IRB’s list of reportable events includes two items for which additional clarification and guidance may be helpful during emergency/disaster scenarios:

* ***“Failure to follow the protocol due to the action or inaction of the investigator or research staff.”*** Emphasis on action or inaction of the investigator or research staff has been added because this requirement does not include action or inaction of the research subject. For example, study teams may notice an increase in the number of subjects who do not arrive for scheduled research visits under emergency/disaster circumstances. Failure of a research participant to appear for a scheduled research visit is not noncompliance due to action or inaction by the investigator or research staff, and therefore does not require reporting to the IRB.
* ***“Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject.”*** During emergency/disaster scenarios, there will be cases where there is sufficient time to receive IRB approval of any proposed modifications to previously approved research, and in such cases, investigators should follow standard IRB procedures for submitting modifications. However, there will be other cases where investigators must make more immediate changes to the protocol or investigational plan to minimize or eliminate immediate hazards or to protect the life and well-being of research participants. Such changes may be implemented without IRB approval, but are required to be reported to the IRB within five business days afterward in accordance with IRB policies and procedures for submitting reportable new information.
1. IRB Guidance on SONA

The UMass Boston Psychology Department and some UMass Boston investigators are using the SONA system which is a cloud-based subject pool software for universities to recruit students for participation in human research.

For questions regarding the SONA system, contact the SONA Administrator at sona@umb.edu.

For questions related to IRB submissions, contact irb@umb.edu or visit the IRB web site: <https://www.umb.edu/orsp/research_committees/irb>

**Pre-approval by the SONA Administrator is required BEFORE submitting applications using SONA to the IRB.**

* **Step 1:** Researcher receives pre-approval by the SONA Administrator. The SONA Administrator pre-reviews SONA-relevant materials to ensure they meet SONA system use guidelines. This is NOT an IRB review.
* **Step 2:** Researcher submits application (either new study or modification) to the IRB including the SONA pre-approval notice and all SONA recruitment materials. The IRB may have edits to the SONA materials. The IRB may also decide that a specific study is not appropriate for use with SONA (e.g., situations such as this are more likely to occur when the research poses more than minimal risk).

*If pre-approval for SONA is not included, the application may be withdrawn or placed on hold by the IRB until resolved.*

* **Step 3:** Researcher submits IRB approval notice and IRB-approved/finalized materials to the SONA Administrator.

**SONA Recruitment Materials**

All SONA recruitment listings/postings – like any research recruitment materials meant to be seen or heard by participants – need to be included in the IRB submission (as part of the initial “new” study application or via Modification) for review and approval by the IRB prior to use unless otherwise noted. Review [*“Advertisements WORKSHEET (HRP-315)”*](https://www.umb.edu/orsp/research_committees/irb/applying#Policies)for guidelines.

Please note that 18 years old may not be the legal age of an adult in the location from where the individual is participating in the research. Therefore, age requirements need to be considered when developing protocol inclusion/exclusion criteria and recruitment materials.

**Pre-screening**

Any study-specific prescreening materials used to assess eligibility criteria need to be submitted for IRB review.

**Course Credits**

Departments may use the SONA system and student subject pools for either course credit or extra credit research experience, which may be obtained by participating in IRB-approved studies conducted in the department under the supervision of faculty.

**Undue influence** occurs through an offer of an excessive or inappropriate reward or other overture in order to obtain compliance such as by over-payment or over-rewarding student participants. For example, participants may be unduly influenced to participate in Study A if it requires only 10 minutes when Study B requires 60 minutes to obtain the same credit.

Therefore, the amount of participant time estimated to complete a study should be consistent across protocols by department for the types of credit, incentive, or compensation offered by the Department. Credit is earned for the participant’s effort and not any specific research activity. If a one hour research credit is being awarded, the amount of effort should be one hour or close to it. If 10 points of extra credit is being awarded for participation in research, the effort to obtain the extra credit should be consistent from one project to another.

In addition, because research participation must be voluntary, an alternate method of fulfilling that academic requirement or extra credit opportunity must also be made available to students. Moreover, this alternate method must be equivalent in time and effort. If participating in a study for 30 minutes, for example, earns 2 points in extra credit, then the alternative cannot be writing a 5-page paper – it must be something that the student can do exerting no more effort than the research participation required.

**Protocol and Informed Consent**

The Protocol and Informed Consent form must reflect the availability of **alternatives** to course credit. They should also explain the process for **withdrawing** from an online study.

***Alternatives***

Indicate in the informed consent form that if students do not wish to participate in this study, there are other studies in which they can participate. They can also contact their instructor to learn more about an alternative way to fulfill the experimental participation requirement. **Include language such as the following in the informed consent:**

*“If you do not wish to participate in this study, there are other studies in which you can participate. You can also contact your instructor to learn more about an alternative way to fulfill the experimental participation requirement—e.g., through reading a short paper <give an example of alternative>.”*

SONA awards credit in .5 units; however, the department may choose how much time and effort each unit represents. Typically, one research credit or unit is equivalent to an hour. This needs to be clearly indicated to students participating in the pool.

Subject pools may also be used to recruit participants for research where monetary incentives are offered. Departments should decide on the best policy for managing recruitment for paying studies, i.e., whether such recruiting will be on the same platform as recruiting for participation credits in courses.

***Withdrawals***

Some departments may decide to compensate participants who choose to withdraw from an online study. SONA grants credit/s for online surveys through a redirect link (SONA > survey platform > SONA for credit), typically embedded in the End of Survey link. Thus, researchers in these departments will need to develop a plan for enabling participants to withdraw at multiple time points across the online survey, by providing multiple opportunities within the survey to redirect the participant back to the SONA system. The Psychology Department has suggested procedures for how to accomplish this, listed on their SONA website (for Qualtrics Survey System specifically). To notify participants of this option for credited withdrawal, **include language such as the following in the Voluntary Participation section of the Informed Consent**:

*“To withdraw from the study at any time, look for the item asking you whether you want to Continue or Exit the Survey. When you click to Exit the Survey, you will be asked whether you want your data to be included in the final dataset or removed from the final dataset. After you indicate your preference, you will be redirected to the SONA website and will receive full credit for your study involvement.”*

**“No Shows”**

Federal regulations indicate that research participants **must not be penalized** for a decision to withdraw from research at any time. **Coercion** occurs when an overt or implicit threat of harm is intentionally presented by one person to another in order to obtain compliance. Therefore, no department may penalize students for “no shows” when they have signed up for a study through the SONA system and then fail to attend the research session without cancelling the appointment in advance. Students who are ‘no shows’ may not be given a failing grade for the no-show or have the number of research participation credits increased as a penalty.

The regulations, however, do allow departments to set a maximum number of times that students can turn to the studies offered to fulfill their academic requirement. In other words, students may be informed that they have a maximum of four opportunities to participate in research to get the credit, and that, should they decide not to participate in a specific study, failure to cancel their appointment in a timely fashion (e.g., 24 hours in advance, midnight the night before the study, etc.) will count as one of those four opportunities. Any unfulfilled research credits will then have to be completed by an alternative research experience once those four opportunities have been used. These procedures, for each Department that uses the SONA System, should be clearly outlined and provided to students in writing in advance.

**Other Considerations**

* Non-participation in research studies should not impact the student’s educational experience.
* Consider when a general sample could be more representative or appropriate than recruiting from student pools to meet the objectives of the research study.
* If a study promises anonymity to the participants, the sign up system needs to be consistent (or the system should not be used for those studies where participation would otherwise be anonymous).
1. This document satisfies AAHRPP element I.1.A, I.1.C-I.1.E, I-3, I.4.C, I.5.C, I.5.D, I.6.B, I.7.A-I.7.C, I-9, II.2.A, II.2.C, II.2.G, II.2.E-II.2.E.2, II.2.F-II.2.F.3, II.2.I, II.3.C-II.3.C.1, II.3.E, II.3.F, II.3.G, II.4.A, II.4.B, II.5.A, II.5.B, III.1.A, III.1.B, III.1.D, III.1.E, III.1.F, III.2.A, III.2.C, III.2.D [↑](#endnote-ref-1)
2. <http://www.hhs.gov/ohrp/policy/subjectwithdrawal.html> [↑](#footnote-ref-1)
3. <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126489.pdf> [↑](#footnote-ref-2)
4. <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.7> [↑](#footnote-ref-3)
5. <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.60> [↑](#footnote-ref-4)
6. <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.61> [↑](#footnote-ref-5)
7. <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.62> [↑](#footnote-ref-6)
8. <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.64> [↑](#footnote-ref-7)
9. <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.66> [↑](#footnote-ref-8)
10. <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.68> [↑](#footnote-ref-9)
11. <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.69> [↑](#footnote-ref-10)
12. <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.100> [↑](#footnote-ref-11)
13. <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.110> [↑](#footnote-ref-12)
14. <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.140> [↑](#footnote-ref-13)
15. <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.145> [↑](#footnote-ref-14)
16. <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.150> [↑](#footnote-ref-15)
17. Children are persons enrolled in research not above the elementary or secondary education level, who have not reached the age or majority as determined under state law. [↑](#footnote-ref-16)
18. Research or experimentation program or project means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques. [↑](#footnote-ref-17)