# Human Subject Protection Issues Related to COVID-19
# Frequently Asked Questions

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1. **Is R&D Committee approval required for all types of expanded access protocols or uses of investigational medical products, to include single patient, intermediate population, and treatment protocols?**

   Answer: No. R&D Committee approval is not required for any emergency use of an investigational medical product (drug, biologic, or medical device) as described in FDA's expanded access regulations in 21 CFR §56.104. However, R&D Committee prospective approval is required for any non-emergency use of investigational medical products under FDA's regulations. VA adheres to FDA's expanded access regulations, which includes the different categories of single patient, intermediate-size population, and wide-spread treatment protocols or uses for investigational drugs and biologics. FDA's expanded access categories for unapproved medical devices are emergency use, compassionate (for single patient or intermediate-size population), and wide-spread treatment protocols or uses.

   The R&D Committee can choose to use a designated review process as described in VHA Directive 1200.01, Paragraph 9e(5) to provide initial approval for all non-emergency expanded access protocols or uses involving investigational medical products following approval by the IRB. Emergency use of an investigational medical product under FDA's expanded access regulations do not require R&D Committee approval.

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2. **If I am permanently changing my study procedures as a result of the pandemic, is an amendment necessary?**

   Answer: Yes. If you are changing the conduct of the protocol permanently, please submit an amendment. This should be done in accordance with local IRB policies and procedures after initiating the change to eliminate immediate hazards to subject safety. If this is not a permanent change and only a temporary modification to eliminate immediate hazards to subject safety, an amendment is not required. If you are making changes to study procedures that not related to eliminating immediate hazards to subject, an amendment is necessary.

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3. **If I am only changing my study procedures temporarily, to eliminate immediate hazards to subject safety, do I have to notify the IRB?**

   Answer: Yes. You must notify the IRB whenever you are making any change in the IRB-approved protocol. You do not have to wait to obtain IRB approval when making changes to eliminate immediate hazards to subject safety to implement those changes, but you must notify the IRB of the changes that were made, in the manner and timeframe required by written local policy. In addition, you must notify any other applicable parties or individuals if required. For example, if the protocol was an industry-sponsored clinical trial, and the protocol stated that any modifications in the IRB-approved protocol require notification to the sponsor, reporting to the sponsor is required.

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4. **If my non-ORD sponsor notifies me that they are suspending the whole trial due to the pandemic, do I have to notify the IRB?**

   Answer: Yes. This represents a change in the IRB-approved research procedures of which the IRB must be informed. As required by VHA Directive 1058.01, Paragraph 6.i., the IRB must be notified, in writing, within 5 business days after becoming aware of any suspension or termination of VA research by, or at the direction of, any entity external to the facility

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5. **Do I have to change my consent form or reconsent my subjects after I implement changes to eliminate immediate apparent hazards?**

   Answer: The IRB determines whether changes in the IRB-approved informed consent form or reconsenting of subjects is required. As part of the IRB approval criteria in 38 CFR§16.111(a)(4), the IRB is responsible for both the process and documentation of informed consent, including any revisions in either the process or documentation after the research is initially approved by an IRB. ORD wishes to reinforce that IRB approval is not required for an Investigator to implement changes to eliminate immediate hazards to subjects.

   If the IRB determines that previously enrolled subjects and/or currently enrolled subjects require reconsenting, the IRB may require reconsenting or other means of conveying the information to the subjects, such as notifying the subjects by written communication or other forms of communication defined by the IRB and

requiring the investigator to document when the communication occurred.

However, information is not to be withheld from subjects if changes are implemented immediately to eliminate apparent hazards to human subjects. For example, if an Investigator changed a study visit required for monitoring the safety of the subject at the Investigator's VA Medical Center to a telephone study visit, the Investigator must inform the subject to not come to VA Medical Center and that monitoring will occur through a non-physical contact study visit; the Investigator does not need to wait for the IRB to evaluate whether an informed revision is necessary.

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6. **Can an Investigator make a change in the IRB-approved method of documenting informed consent prior to obtaining IRB approval in order to eliminate immediate apparent hazards to human subjects?**

   Answer: No. The IRB has regulatory authority over both the process and documentation of informed consent in a non-exempt human subjects study as described in 38 CFR§16.111(a)(4). Any changes in how informed consent documentation is obtained must be approved prospectively by the IRB.

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7. **How can written informed consent be obtained from VA research subjects who are in COVID-19 isolation?**

   Answer: ORD and ORO have consulted with other federal agencies, including the Office for Human Research Protections (OHRP) and FDA, on obtaining written informed consent from research subjects who are in COVID-19 isolation. As stated in FDA's guidance released on March 20, 2020 and updated on March 27, 2020, ORD is in alignment with FDA's guidance titled: FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic located: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-pandemic

   As referenced in FDA's guidance, the following options are available to satisfy documentation requirements as approved by the IRB for written informed consent for patients in COVID-19 isolation who consent to be in VA research studies.

   A. Electronic methods of obtaining consent

   B. When it is not possible to obtain informed consent electronically, the

following steps can be considered:

1. An unsigned consent form is provided to the patient by a heath care worker who has entered the room

2. If direct communication with the patient in isolation is not feasible or safe, the investigator or delegated research staff obtains the patient's phone number and arranges a three-way call or video conference with:
    a. the patient,
    b. an impartial witness,
    c. and if desired and feasible, additional participants requested by the patient, e.g. next of kin.

3. To ensure that patients are approached in a consistent fashion, a standard process should be used that will accomplish the following:
    a. Identification of who is on the call
    b. Review of the informed consent with the patient by the investigator (or their designee) and response to any questions the patient may have
    c. Confirmation by the witness that the patient's questions have been answered
    d. Confirmation by the investigator that the patient is willing to participate in the trial and sign the informed consent document while the witness is listening on the phone
    e. Verbal confirmation by the patient that they would like to participate in the trial and that they have signed and dated the informed consent document that is in their possession.

If the signed informed consent document will not be able to be collected from the patient's location and included in the study records, the following two options are acceptable to provide documentation that the patient signed the informed consent document:

**Option #1:** Attestations by the witness who participated in the call and by the investigator that the patient confirmed that they agreed to participate in the study and signed the informed consent,

Note: ORD recommends that the documented verbal confirmation include information on the version of the IRB-approved informed consent document that was used, such as IRB-approved informed consent dated 03/30/2020, Version 1.0, or other type of designation such as IRB-approved on 03/30/2020.

**Option #2**: A photograph of the informed consent document with attestation by the person entering the photograph into the study record

that states how that photograph was obtained and that it is a photograph of the informed consent signed by the patient.

A copy of the informed consent document signed by the investigator and witness should be placed in the patient's trial source documents, with a notation by the investigator of how the consent was obtained, e.g. telephone. The trial record at the investigational site should document how it was confirmed that the patient signed the consent form (i.e., either using attestation by the witness and investigator or the photograph of the signed consent). The note should include a statement of why the IC document signed by the patient was not retained, e.g., due to contamination of the document by infectious material.

If the patient is unable to provide informed consent and there is a legally authorized representative, investigators should obtain consent from the participant's legally authorized representative if the IRB approved that informed consent could be obtained from the subject's legally authorized representative.

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**8. How can written HIPAA authorization be obtained from VA research subjects who are in COVID-19 isolation?**

Answer: As a response to the COVID-19 health pandemic, HHS Office of Civil Rights (OCR) is exercising enforcement exceptions that apply to health care provider activities beyond treatment and would cover research-related care or treatment, such as with clinical trials. Please note that HHS OCR guidance is not expanding or otherwise altering the HIPAA Privacy and Security Rules but simply provides that HHS OCR will use its enforcement discretion to not issue penalties for violations by covered entities responding to the COVID-19 public health emergency.

Research HIPAA Authorizations, VA Form 10-0493 may also obtained remotely by the following:

- Subject signs VAF 10-0493 at home and send to VHA via fax or take a digital image to send via MyHealtheVet secure messaging. ORD is not recommending instructing the subject to send back the signed document by mail. VHA accepts an image of a signed authorization the same as the original.

In addition, the IRB may approve to waive the HIPAA authorization requirement due to challenges of obtaining authorization during the COVID-19 crisis as outlined in Question#9 below.

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**9. Can a waiver or alteration of HIPAA authorization be used to disclose protected health information (PHI) when written HIPAA authorization cannot be obtained from VA research subjects who are in COVID-19 isolation?**

Answer: VHA does not permit alterations of authorizations, so IRBs or Privacy Boards cannot grant an alteration of authorization eliminating the requirement for signatures or dates of the subject or the subject's personal representative. However, if a written authorization cannot be obtained from the subject who is in COVID-19 isolation or subject's personal representative because he or she is unable to enter the hospital because of isolation precautions, the IRB or Privacy Board may approve a waiver of the requirementsof written HIPAA Authorization provided the research meets the criteria for waiverof authorization in 45 CFR 164.512(i)(2)(ii). This will permit VHA to use and disclose PHI outside of VHA for research purposes under the HIPAA Privacy Rule. As a reminder, when disclosing PHI outside of VHA for research purposes authority under the other applicable federal privacy laws is required in addition to the waiver.

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**10. If my ORD-funded protocol just received approval and I am now ready to start, can I still begin if I received my ACOS/R&D letter to initiate the study?**

Answer: Yes, if your study involves critical interactions as defined in the CRADO memorandum dated March 17, 2020, then:

a. Please ensure that you have adequate study staff and resources before you begin conducting the study.
b. Please consider delaying enrollment if your study procedures may be impacted by the pandemic.

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