Policy on Conduct of Human Subjects Research Activities during COVID-19 Operations

In support of our mission to protect our patients and clinical and research community, we have been working with Dartmouth-Hitchcock Health (D-HH) leadership to develop our approach to the continued conduct of human subjects research in our clinical health environment. Effective immediately we are implementing the following requirements regarding human subjects research conducted in our D-HH facilities and D-HH research sites.

Points of Contact for Questions:
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Included in this document:

A. Policy on Conduct of Human Subjects Research including Clinical Trials

- Ongoing activities may continue only if they are commensurate with the D-HH Telecommuting or Remote Work Policy – Employees (Policy ID: 2064) and/or Telecommuting Policy – Laboratory (Policy ID: 2685) regarding staffing and remote work requirements. These activities cannot violate current D-HH policy for research staffing.
- These requirements apply regardless of the IRB that oversees the ethical and regulatory conduct of these research activities (including D-HH, other institutional IRBs and commercial IRBs.) Researchers should also follow the policies and procedures of the IRB that oversees the ethical and regulatory requirements of their research regarding how to report changes or obtain approval for changes that are needed to comply with the requirements below.

1. Therapeutic Research (potential for direct benefit to subjects through therapeutic intervention)

a. Recruitment of new subjects may continue ONLY for the following:

i. Any novel coronavirus or COVID-19 research

ii. Research that has the potential to be life-saving or is disease-altering AND there are no appropriate alternative clinical treatments available for the patient. Do not enroll new subjects if there is risk they will have to come off of the therapeutic intervention due to lack of available supplies or staffing.

iii. Study-specific procedures to maintain safety of subjects can be continued (e.g. labs, exams etc.)

iv. Studies must also be conducted in accordance with the following:

1. The PI is available to maintain appropriate oversight for the study throughout the length of the study including in a remote capacity should that be required.
2. There are adequate and accessible supplies available to complete the study including the study treatment itself and all additional supplies to administer and monitor the study treatment.
3. There will be a sufficient number of trained study staff to support conduct of the study considering staff workloads and any requirement to work remotely or to support other D-HH needs.

b. Ongoing conduct of active therapeutic studies may continue for subjects already enrolled in the study under the following conditions:

i. The PI is available to maintain appropriate oversight throughout the length of the study including in a remote capacity should that be required.

ii. There are adequate and accessible supplies available to complete the study, including the study treatment itself, and all additional supplies to administer and monitor the study treatment.

iii. Study-specific procedures to maintain safety of subjects can be continued (e.g. labs, exams etc.)

iv. There will be a sufficient number of trained study staff to support conduct of the study considering staff workloads and any requirement to work remotely or

to support other D-HH needs.

Contact the D-HH Clinical Trials Office *if you need consultation or help in planning for the continuation of clinical therapeutic studies or planning for moving subjects from studies to clinical care. Contact* CTO@hitchcock.org

2. Non-Therapeutic Research (no direct benefit to subjects through therapeutic intervention)

a. Recruitment of new subjects may continue ONLY under the following conditions:
   1. Recruitment occurs completely remotely (e.g. by phone, videoconference) via an approved IRB protocol.
   2. No in-person interaction with potential subjects is required.
   3. The research staff is working remotely.
   4. All study activities are currently approved to be conducted remotely or may be transitioned to remote activities (e.g. an internet-based survey study).
   5. If recruitment and study activities can occur with both staff and potential subjects operating remotely, the following must also be in place for recruitment to continue:
      a. The PI is available to maintain appropriate oversight throughout the length of the study in a remote capacity.
      b. There will be a sufficient number of trained study staff to support the conduct of the study remotely considering staff workloads and any requirement to work remotely or to support other hospital and D-HH needs.

b. Ongoing conduct of non-therapeutic studies may continue for subjects already enrolled in the study under the following conditions:
   b. No in-person interaction with subjects is currently required or visits can be changed to occur remotely.
   c. Research staff can work remotely to conduct all study activities.
   d. The PI is available to maintain appropriate oversight throughout the length of the study in a remote capacity.
   e. There will be a sufficient number of trained study staff to support conduct of the study remotely and considering staff workloads and any requirements to work remotely or to support other hospital-HH needs.

3. Review of New Studies:

The IRB will continue to accept and review new study submissions (therapeutic or non-therapeutic) but plans to prioritize the following:

1. Any research on:
   - novel coronavirus or COVID-19, or
   - related to novel coronavirus or COVID-19.
2. Emergency Use requests or Single Patient Expanded Access requests; and
3. Studies that have federal funding and receive Just-In-Time (JIT) notice. *Researchers must include a copy of their JIT notice as an attachment to their IRB submission.*

Note: Any studies that were in the process of review with the IRB at the time of this notice will continue through the review process only as time allows considering other priorities. Studies that are approved are still required to follow the requirements above with regard to recruitment limitations and conduct of research.

B. Working with the IRB

1) Changes to the protocol which DO NOT require prior IRB review and approval
2) Changes to the protocol which DO require prior IRB review and approval
3) Emergency Use and Expanded Access Requests
4) Contingency planning
5) Home visits
6) Requesting priority review for novel coronavirus or COVID-19 research

1. Changes to the protocol which DO NOT require prior IRB review and approval

- **Implementing mandatory COVID-19 screening of human subjects prior to planned study visits.** All study teams should immediately implement the COVID-19 procedures to screen human subjects before any interaction and incorporate mandatory telephone screening prior to planned study visits.
    - If a subject already enrolled in a study becomes symptomatic, study visits should be deferred if possible and the subject referred to appropriate clinical screening and care for COVID-19. For additional information, please refer to D-HH policies and procedures (http://one.hitchcock.org/intranet/departments/high-threat-infections/policies-procedures-and-documents) for management of patients with potential or confirmed High threat Infections.
    - If a subject in recruitment/screening becomes symptomatic, they should be referred to appropriate clinical screening and care for COVID-19.

D-HH has provided specific procedures to conduct this mandatory screening. If you are at a facility that has not provided this information, please follow the procedures at these links:

Ambulatory Care Call Centers
Job Aid 12207: Screening Script for Ambulatory Care Call Centers - Job Aid - High Threat Infection

Ambulatory Care Reception
Job Aid 12208: Screening Script for Ambulatory Care Reception Desks - Job Aid - High Threat Infection

Algorithm for Positive Screening
Job Aid 12209: Algorithm for Positive Screening for a High Threat Infection - Job Aid

- **Changes to protocols to prevent an immediate hazard to human subjects.** The PI is responsible for making the assessment that there is a need for immediate action to protect the safety and

wellbeing of a subject. If there is a need, the PI may make the change without first obtaining IRB approval. Note this option is only available for changes that would impact subjects already enrolled in a study. It is not appropriate to make such a change in order to enroll a new subject (e.g. exceptions to inclusion/exclusion criteria.) Please use flexibility and judgment in a making these decisions in this challenging environment.

Follow the steps below if a change is made to prevent immediate hazard without prior IRB review and approval:

- Execute the "Report New Information" activity via D-HH eIRB to submit the RNI within 5 working days of the change.
- The change and rationale for making it should be clearly documented in your research records (e.g. in a note to file) for each subject that it applies to.
- This change may apply to one subject or a group/all subjects in the research study.

- **Protocol deviations which do not have the potential to negatively impact subject safety or integrity of study data (ability to draw conclusions from the study data), or affect subject's willingness to participate in the study.** Protocols deviations could include conducting a study visit by remote means or outside of a specified study window, omitting a specific research procedure or collecting questionnaire/assessment data by remote means. Please review each protocol to see what is specifically required and if a change to a study procedure would constitute a protocol deviation or if the protocol allows for flexibility. Protocol deviations (due to the action or inaction of the investigator or study staff) should be reported to the D-HH IRB as a New Information Report. Please note that protocol deviations not due to the action or inaction of the investigator or study staff, such as a missed study visit due to a participant not being able to come to the study site, would not be reportable to the IRB.

2. Changes to the protocol which DO require prior IRB review and approval

All other changes to the protocol and requests for protocol (including requests for protocol or subject exceptions), that may impact subject safety or the integrity of the study data require prior IRB review and approval. This may include dispensing study drug without performing a key safety lab or procedure, shipping study drug directly to participants for self-administration, or failure to capture endpoint assessment data. PI and study teams submitting Modifications related to on the novel coronavirus or COVID-19 may email the IRB helpdesk to request a priority review: **IRB@hitchcock.org. We also ask that Modifications clearly reference novel coronavirus or COVID-19 in the Modification description.**

3. Emergency Use and Expanded Access Requests

A. Emergency Use

Contact the IRB Office or IRB chair immediately to discuss the situation. If there is no time to make this contact, see HRP-322 - WORKSHEET - Emergency Use for the regulatory criteria allowing such a use and make sure these are followed. Use HRP-506 - TEMPLATE CONSENT DOCUMENT - Emergency or Compassionate Device Use to prepare your consent document.

You will need to submit a report of the use to the IRB within five working days of the use and for drugs and biologics, submit an IRB application for initial review within 30 days.
If you fail to submit the report within working five days or the IRB application for initial review within 30 days, you will be restricted from submitting new Human Research until the report and IRB application for initial review have been received.

Emergency use of an unapproved drug or biologic in a life-threatening situation without prior IRB review is "research" as defined by FDA, the individual getting the test article is a "subject" as defined by FDA, and therefore is governed by FDA regulations for IRB review and informed consent. Emergency use of an unapproved device without prior IRB review is not "research" as defined by FDA and the individual getting the test article is not a "subject" as defined by FDA. However, FDA guidance recommends following similar rules as for emergency use of an unapproved drug or biologic.

Individuals getting an unapproved drug, biologic, or device without prior IRB review cannot be considered a "subject" as defined by DHHS and their results cannot be included in prospective "research" as that term is defined by DHHS.

B. Expanded Access Requests

A licensed physician must submit Expanded Access Requests to the FDA as a protocol under a new IND. There are three request types:

- Non-Emergency Individual Patient IND (submitted prospectively)
- Emergency Use Individual Patient IND (submitted retrospectively)
- Intermediate-size Population IND (submitted prospectively)

See the FDA website for guidance and instruction for how to submit the appropriate IND to the FDA (https://www.fda.gov/news-events/expanded-access/expanded-access-how-submit-request-forms).

IMPORTANT: When completing FDA Form 3926 be sure to select box 10b to "Request Authorization to Use Alternate IRB Review Procedures" so the D-HH IRB can expedite the review of the Expanded Access Request.

Once complete, contact the IRB Office immediately to discuss the request. Using the "Report New Information" activity, submit the treatment protocol reviewed by the FDA, the consent form (using HRP-506 - TEMPLATE CONSENT DOCUMENT - Emergency or Compassionate Device Use to prepare your consent document), the eIND and completed FDA Form 3926.

Expanded access is a potential pathway for a patient with an immediately life-threatening condition or serious disease or condition to gain access to an investigational product for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available. The FDA does not consider Expanded Access to be "research" but does require IRB review and approval before treatment may begin (except for emergency access use when there is not sufficient time to secure prospective IRB review).

1. Contingency Planning

PI and research staff should begin planning now for potential disruptions, including:

- availability or accessibility of supplies,
- study visit schedules, and
- temporary reduction in research staff.

Research teams should also closely monitor:

- applicable regulatory guidance and requirements; and
- institutional policies, procedures, and clinical care job aides (including those put forth by D-HH)

to assess how such potential disruptions in research could impact safety and welfare of human subjects.

- **Investigational Drugs**: If human subjects are on investigational drugs, work with the research pharmacy and the study sponsor (as applicable) to develop a contingency plan if the investigational drug cannot be dispensed to the human subjects. If the investigational drugs cannot be dispensed to the human subjects, D-HH recommends that the PI should make plans to transition human subjects to the most appropriate clinically available treatments. This transition should include consultations with the investigational drug service, research sponsor(s) and the clinical team caring for the human subjects.

- **Research Procedures:** PIs need to assess whether any reduction in research staff makes it unsafe to complete the planned research activities (e.g. specimen collection may not be safe if the study does not have appropriately trained staff to conduct the specimen collection.)

- **Review of Research Data:** If research staff are not available, completion of research-required procedures such as reviewing lab results in a timely manner might not be possible and may require special attention under the direction of the study PI.

- **Conference Call/Video Conference**: If clinically appropriate, PI and research staff should consider alternative study visit options to allow subjects who cannot or do not want to come to the study site to complete study visits.

If you have specific questions on research contingency planning, please contact the D-HH IRB: **IRB@hitchcock.org.**

2. Home Visits

Any study that is currently approved to conduct home visits should suspend these visits. If you believe home visits are required to maintain the safety of subjects on therapeutic research as provided in Part A of this policy, please contact the IRB for consultation prior to visiting the home. (irb @hitchcock.org)

3. Requesting priority review for novel coronavirus or COVID-19 research

Any novel coronavirus or COVID-19 research needs to consider exposures to staff and clinical needs, and we recommend that you consult the your department section lead before drafting your protocol. Due to expected shortages in personal protective equipment (PPE), and to avoid exposure of staff, clinical care interactions for potential or confirmed patients with this high threat infection may be limited. In order for D-HH IRB to prioritize the review and consult on regulatory and ethical issues the PI should provide the following information by email (**IRB@hitchcock.org**) prior to submission the study in eIRB:

- PI Name
- Protocol No.
- Protocol Title
- Funding (if any)
- 1-2 sentence summary on the proposed work
- Identify any local agencies working on the study

C. Working with Sponsors

The PI and research staff are responsible for working with their sponsors to address changes needed to accommodate any potential disruptions in the approved research protocol. In the event that any study changes are requested or pursued that could impact the sponsor's contract or budget, the PI and research staff should reach out to the CTO for guidance.

The requirements set out in this policy as well as any other D-HH requirements take precedent over sponsor approaches unless the sponsor's changes result in more restrictive study requirements..

1. **Contact study sponsors** (e.g., federal, industry, private) and/or the coordinating center for study-specific information related to procedures to address the following:
    - Anticipated delays in recruitment for new subjects
    - How delayed or missed study contacts/visits for subjects may impact on-going study participation (e.g., whether a missed safety assessment might impact the ability of the subject to receive the next round of therapy)
    - If the sponsor anticipates any drug shortages or delays in shipping and the subsequent impact on study conduct
    - Any changes to biospecimen/sample storage and shipping requirements
    - Changes in any reporting requirements to the sponsor

2. **Changes in monitoring** (implementation of remote monitoring procedures.) All sponsor monitoring or audit visits must be conducted remotely or in accordance with current D-HH policies.

   The process for giving monitors access to EDH is already in place. Monitors can get access to patient charts via ROIconnect and study coordinators may facilitate this by emailing LebanonResearchandReviewAudit@hitchcock.org and request ROIconnect for Reseach. Study coordinators who have not already done so should submit a request on behalf of the monitor to set up the account via the ROIconnect process.

3. **Develop study-specific plans** for each active study including consideration of the following:
   - Sponsor provided information (from prior section)
   - Need for continuity of the research intervention during the study period
   - Feasibility of changing from protocol-mandated visits to home visits or telemedicine (or telephone visits)
   - Need for active assessment for Adverse Events (AEs)
   - Facility availability
   - Study team and clinical staff availability
   - Identify emergency contacts within the study team
   - Develop a communication plan with the study team and subjects (i.e., assure subjects are kept informed if clinic visits or administration of study intervention is canceled or delayed)
   - Orderly withdrawal of subjects if indicated or necessary

   Contact D-HH CTO (CTO@hitchcock.org) for contract or budget considerations on industry sponsored projects.

D. D-HH IRB FAQs

1. **Is my novel coronavirus or COVID-19-related project considered research?**

   It depends. In some cases, IRB approval may not be required for novel coronavirus or COVID-19-related activities. For example, the activities may consist solely of public health surveillance activities, clinical care, or diagnostic testing for which an FDA emergency authorization has been obtained. Contact Candi Loeb (candice.m.loeb@hitchcock.org) or Liam Harrison (william.r.harrison@hitchcock.org) for consult on this issue.

2. **Do I need IRB approval to communicate a pause in recruitment and study activities to human subjects?**

No. These messages to subjects do not require IRB approval. In addition, messages about changes to study visits, like administering questionnaires over the phone or video conferencing, do not require IRB approval.

3. **Based on D-HH requirements my study will pause to recruitment, is submission to the D-HH IRB required?**

   No.

4. **The PI has decided to suspend the ongoing study due to COVID-19, do I need to notify the IRB?**

   It depends. If this is a non-therapeutic or Minimal Risk study (expedited study) where the temporary suspension would not impact the safety or welfare of human subjects, this would not require prior approval by the IRB.

   If the study is a therapeutic study and More than Minimal Risk (Full Board study), submission of an Modification or RNI is required to the IRB and should contain information on contingency planning related to interruption or changes in investigational product and/or safety monitoring.

5. **My research study is reviewed by an external IRB of Record, do the restrictions apply to my study?**

   Yes. This D-HH policy and requirements regarding research restrictions applies to all research conducted in our D-HH facilities/sites, regardless of the IRB that oversees the ethical and regulatory conduct of these studies. You should consult with the external IRB to determine the IRB's reporting requirements.

6. **I am pausing recruitment and/or study procedures on a project reviewed by an external IRB of Record, should I notify that IRB?**

   It depends. You should follow the requirements of the IRB that oversees your research regarding reporting changes and whether any review/approval will be needed prior to resumption of study procedures.

7. **Do I have to submit a Modification to change an in-person visit to one conducted virtually or by remote means?**

   It depends. If the approved procedures to be conducted at that visit are described in the protocol in such a way that remote or virtual procedures can be done remotely without changes to the protocol and the safety of the human subject or the scientific validity of the

study are not impacted, this would not require prior approval by the IRB. However, if there are approved procedures are specific about in-person visits AND those procedures impact the safety of the subject or the scientific validity of the study, this should be submitted to IRB for prior approval as described above.

8. **Should informed consent forms be revised to include the risk of contracting novel coronavirus at the hospital or during a study visit?**

   No. Research teams should carefully consider the risks of subjects attending study visits in light of the factors discussed in this policy.

9. **Do I need to report risk of contracting coronavirus at time of continuing review in response to the question "Since the last continuing (or initial) review, have the risks to subjects changed?"**

   No. The PI should not include the risk of contracting coronavirus in the continuing review report.

10. **Do I need to report to the IRB if a subject or member of the research tests positive for COVID-19?**

    No. The PI and research teams should follow applicable D-HH policy for reporting all new COVID-19 infections. The IRB does not require New Information Reports for COVID-19 infections or deaths unless determined to be unexpected AND related to the protocol.

11. **Do I need to report to the IRB if a subject is hospitalized or dies due to COVID-19?**

    No. Unless the hospitalization or death is determined to be unexpected and related to the research protocol. Note that other applicable laws, regulations, and policies, including those around mandated reporting, may still apply.

12. **I am the Lead PI on a study where the D-HH IRB serves as the central IRB for external research sites. Do these requirements apply to the external sites?**

    It depends. The requirements apply to research conducted at D-HH sites/facilities and are based on the current situation in New Hampshire and Vermonth. External research sites may have different requirements based on the local situation. As the IRB of Record for research conducted at the external research site, we require the Lead PI assess whether the study can continue for recruitment and subjects already enrolled in the study under the following conditions:

    - The PI is available to maintain appropriate oversight.
    - There are adequate supplies available and accessible, including the treatment itself, and all additional supplies to administer and monitor the study treatment.

- Procedures to maintain safety of subjects can be continued (labs, exams etc.)
- There are a sufficient number of trained study staff to support conduct of the study considering staff workloads and any requirement to work remotely or to cover other responsibilities at their health care facility or institution.

13. How can I flag my Modification related to novel coronavirus or COVID-19 for priority review?

Email the IRB helpdesk (IRB@hitchcock.org) AND include novel coronavirus or COVID-19 in the description field in the Modification form.

14. **I am conducting FDA-regulated research for which I am the sponsor of an IND or IDE. Do I need to notify the FDA if I pause my study?**

Yes. The FDA will need to be notified as soon as feasible. Please contact Vijaya Chadaram at vijaya.chadaram@hitchcock.org.

15. I submitted an initial review to the IRB before the effective date of this policy, will the IRB still review my study?

Yes. The IRB will continue to review and approve submissions submitted before the effective date. For studies that are approvable but subject to additional D-HH restrictions on recruitment and study activities, the IRB will approve the study but explicitly note all research conducted at D-HH sites/facilities must comply with current restrictions on human subjects research.

16. Will the IRB continue to accept and review Modifications, Reports of New Information and Continuing Reviews?

Yes. The IRB will continue to review and approve these submissions. The IRB will approve submissions but explicitly note that all research conducted at D-HH facilities must comply with current restrictions on human subjects research.

17. My new study is assigned to an upcoming IRB meeting, will it still be reviewed?

It depends. The IRB is prioritizing research related to novel coronavirus or COVID-19 and last minutes changes may be made to accommodate essential research.

18. Has the process for emergency use been changed?

No. The procedure for Emergency Use of an experimental drug or device remains the same during the COVID-19 operations.

19. Is the IRB office still functioning?

Yes. The D-HH IRB is fully functioning, and the research community is encouraged to contact the team with any questions:
Tel: 603-650-1846
Email: IRB@hitchcock.org