1 PURPOSE

1.1 This standard operating procedure (SOP) describes the process for:

1.1.1 Determining whether study-specific risk mitigation plans are needed to address additional research subject safety considerations associated with the COVID-19 pandemic.

1.1.2 Developing study-specific COVID-19 risk mitigation plans.

1.1.3 Communicating study modifications to the IRB.

1.1.4 Documenting any implemented modifications or deviations from the protocol in the research record.

1.2 The process begins when the investigator considers whether a study-specific risk mitigation plan is necessary during the COVID-19 pandemic.

1.3 The process ends when the investigator develops the risk mitigation plan or determines that no plan is necessary.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 POLICY

3.1 Until the COVID-19 pandemic is more effectively contained and managed, investigators should temporarily place recruitment and ongoing research procedures on voluntary hold for human research that requires direct contact with research subjects but does not offer direct benefit to participants (with the exception of a Phase I trial with no treatment alternatives).

4 RESPONSIBILITIES

4.1 Investigators are responsible for carrying out these procedures.

5 PROCEDURE

5.1 Determine whether a COVID-19 risk mitigation plan should be developed for each human research project the investigator is leading. A COVID-19 risk mitigation plan should be developed unless one of the following is true:

5.1.1 Research does not involve in-person interaction with research subjects.

5.1.2 Research can be conducted as written while adhering to social distancing requirements and institutional COVID-19 policies and requirements.

5.1.3 Research is externally sponsored, and the sponsor has already developed a COVID-19 risk mitigation plan for the research.

5.1.4 Research has been voluntarily placed on hold for recruitment, and all research procedures (with the exception of necessary follow-up procedures to be done consistently with social distancing requirements and institutional COVID-19 policies and requirements).

5.2 If an external sponsor has developed a COVID-19 risk mitigation plan for the research, skip to step 5.4.

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1 Social distancing recommendations include the following: that people stay at home as much as possible, going out only for critical needs like groceries and medicines, or to exercise and enjoy the outdoors in wide-open spaces. Other recommendations include avoiding gatherings of more than 10 people, no handshakes, regular handwashing and, when encountering someone outside of your immediate household, trying to remain at least 6 feet apart. (Source: NIH Director’s Blog, March 19, 2020)
5.3 For all other research involving in-person interactions with research subjects for which the research cannot otherwise be conducted in accordance with social distancing recommendations, develop a risk mitigation plan in consideration of the potential for direct therapeutic benefit associated with the research.

5.3.1 For research that does not offer potential for direct therapeutic benefit (and is not a Phase I trial with no treatment alternatives):
   5.3.1.1 Develop a plan to place study recruitment and study activities on voluntary hold.
   5.3.1.2 Notify the IRB if study recruitment and research activities cannot be placed on hold for any research requiring in-person interaction but offering no potential for direct therapeutic benefit.

5.3.2 For research that does offer potential for direct therapeutic benefit (or Phase I trial with no treatment alternatives):
   5.3.2.1 Determine whether the study should be voluntarily placed on hold to recruitment and/or study conduct, or
   5.3.2.2 Develop more detailed risk mitigation plan, considering the items included in Worksheet: Protocol-Specific COVID-19 Risk Mitigation Planning, based on the Food and Drug Administration’s (FDA) Guidance on Conduct of Clinical Trials of Medical Products During COVID-19 Pandemic.

5.4 Notify the IRB and applicable ancillary review committees (e.g., DSMB, DSMC, etc.) of the risk mitigation plan:
   5.4.1 If immediate modification of the research is necessary to eliminate an apparent immediate hazard to a subject, take action and notify the IRB following the standard pathway to submit reportable new information.
   5.4.2 For all other study modifications made to ensure the ongoing safety of research subjects during the COVID-19 pandemic, submit a study selecting a modification to “other parts of the study” in the SmartForm. Upload form “HRP-219 - FORM - COVID-19 Modification” in the “other attachments” section of the “local site documents” page of the study SmartForm.

5.5 Document mitigation plan details in the study record in accordance with sponsor and regulatory agency requirements, and in accordance with the information listed in “HRP-350 - Worksheet - Research-Specific COVID-19 Risk Mitigation Plan.”

6 MATERIALS
   6.1 HRP-219 - Form - COVID-19 Modification
   6.2 HRP-350 - Worksheet - Research-Specific COVID-19 Risk Mitigation Plan

7 REFERENCES
   7.1 Attached Appendix to SOP-092
   7.2 FDA Guidance on Conduct of Clinical Trials of Medical Products During COVID-19 Pandemic
Investigators conducting human research during the COVID-19 pandemic should be aware of the following additional considerations related to their ongoing interactions with the institutional review board (IRB).

**Deciding Whether a Study-Specific COVID-19 Risk Mitigation Plan for Ongoing Research Is Needed**

In general, investigators should develop a study-specific COVID-19 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 social distancing requirements and institutional COVID-19 policies/requirements.
- Research is externally sponsored, and the sponsor has developed a COVID-19 risk mitigation plan for the research.
- Research should be voluntarily placed on hold for recruitment and all research procedures (except for necessary follow-up procedures to be done consistently with social distancing requirements and institutional COVID-19 policies/requirements).

**Tools and Resources for Developing Study-Specific COVID-19 Risk Mitigation Plans for Ongoing Research**


**COVID-19 Screening Procedures: Is an IRB Modification Needed?**

COVID-19 screening procedures that may be mandated by the institution at which a clinical trial is being conducted do not need to be reported as modification to the protocol, even if done during clinical study visits, unless the sponsor is incorporating the data collected as part of a new research objective.

**Voluntary Holds on Human Research Activities**

Investigators may voluntarily elect to place all recruitment, enrollment and research procedures on temporary hold 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 COVID-19 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 as a reportable event (RNI). Investigators can send a list of accumulated events for each study.

For all other study modifications made to ensure the ongoing safety of research subjects during the COVID-19 pandemic, submit a study amendment and all relevant new or modified study materials to the IRB using “Form: Modification Due to COVID-19.”
Other Reportable New Information Considerations During the COVID-19 Pandemic

“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. 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.” It is recognized that during this pandemic 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 (e.g., to limit exposure to COVID-19). Such changes may be implemented without IRB approval, but are required to be reported to the IRB afterward in accordance with IRB policies and procedures for submitting reportable new information.

Expanded Access Requests

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).

A licensed physician must submit expanded access requests to the FDA as a protocol under a new investigational new drug (IND) application. 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 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-502h - Template Consent Document - Emergency or Compassionate Device Use to prepare your consent document), the eIND and completed FDA Form 3926.
**Decision Guide for Study-Specific COVID-19 Risk Mitigation Planning**

1. **Open/Active Human Research Study**
   - Does study involve in-person interactions with research subjects? **YES**
     - Can study be conducted as written while adhering to social distancing recommendations and applicable institutional policies? **YES**
       - No COVID-19 risk mitigation plan needed
     **NO**
     - Develop COVID-19 risk mitigation plan.
   **NO**
   - COVID-19 risk mitigation plan needed.

2. **Does the study have an external sponsor?** **YES**
   - Coordinate with sponsor to confirm COVID-19 risk mitigation plan.
   **NO**
   - No, or sponsor has no risk mitigation plan

3. **Does study offer potential for direct therapeutic benefit? (or Phase I trial with no treatment alternatives?)** **YES**
   - Develop plan to place study recruitment and study activities on voluntary hold.
   - Notify IRB if study recruitment and research activities cannot be placed on hold or modified for any research requiring in-person interaction but offering no potential for direct therapeutic benefit.
   **NO**
   - Notify IRB and applicable ancillary review committees (e.g., DMB, DSMC, etc.) of risk mitigation plan:
     - If time permits for mitigation plan to be reviewed/approved by IRB before implementation, submit a modification to the IRB.
     - If immediate action is needed to eliminate an apparent immediate hazard to a subject, take action and notify IRB using standard pathway for reportable new information.
   - Determine whether study should be voluntarily placed on hold to recruitment and/or study conduct.