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COVID-19 Update: Guidance for Institutions and Researchers

HRP is providing the following information as part of its ongoing responsibility to assist clients in navigating their research programs through the COVID-19 pandemic. This information is intended to supplement the information previously provided in HRP's document "Management of Ongoing Human Subjects Research During COVID-19."

First, given the ever-changing landscape in which we are working to continue to ensure the safety of our research subjects during this time, HRP recommends adding to your HRPP policies and procedures/SOPs a statement concerning HRPP operations under emergency situations. Sample language is as follows:

> *In the event of an emergency or disaster (e.g., public health or weather-related), the procedures in these SOPs may be modified as appropriate for the situation. Such modifications may include alternative meeting procedures, alternative procedures for the submission and review of modifications, alternative procedures for prompt reporting, and any other changes necessary to ensure appropriate ongoing oversight and conduct of research. Because procedural modifications may vary based on the nature of the event, these cannot be anticipated and described in these SOPs. Instead, such procedural modifications will be recorded in an addendum to the SOPs, note-to-file, or other appropriate means of documentation and communicated to the research community. This documentation will be maintained in accordance with applicable record retention requirements.*

Inclusion of a statement acknowledges that policies and procedures may need to be modified in an emergency and provides you the flexibility to ensure that your emergency procedures "fit" the situation.

As always, be sure to review your SOPs/policies and procedures to ensure that Institution-specific requirements are also addressed and adapted if needed (e.g., internal approvals, etc.).

HRP has (and is) assisting several clients with developing and refining their interim procedures and researcher guidelines during COVID-19. We can also provide remote support for your IRB office operations. Please don't hesitate to reach out if we can assist you.

I. Guidance from FDA for Conducting Clinical Trials

> *"The U.S. Food and Drug Administration today [March 18, 2020] issued a guidance for industry, investigators and institutional review boards conducting clinical trials during the coronavirus (COVID-19) pandemic.*
>
> *The FDA recognizes that the COVID-19 pandemic may impact the conduct of clinical trials of medical products, including drugs, devices and biological products. Challenges may arise, for example, from quarantines, site closures, travel limitations, interruptions to the supply chain for the investigational product, or other considerations if site personnel or trial subjects become infected with SARS-CoV-2, the virus that causes COVID-19. These challenges may lead to difficulties in conducting the clinical trials. The FDA is aware that protocol modifications may be required, and that there may be unavoidable protocol deviations due to COVID-19. Although the impact of COVID-19 on trials will vary depending on many factors, including the nature of disease under study, the trial design and in what region(s) the study is being conducted, the FDA outlines considerations to assist sponsors in assuring the safety of trial*

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participants, maintaining compliance with good clinical practice and minimizing risks to trial integrity. Considerations recommended include, among others, sponsors evaluating alternative methods for assessments, like phone contacts or virtual visits and offering additional safety monitoring for those trial participants who may no longer have access to investigational product or the investigational site."

For the guidance, please see https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-pandemic.

In addition, FDA provides the following website for relevant updates that you may wish to regularly monitor: https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/coronavirus-disease-2019-covid-19

II. A Few Tips and Lessons Learned for Clinical Research

If you haven't already done so:

- Begin to prepare communications for researchers with information and instructions for a rapid ramp-down of research and for if a shelter-in-place order is placed
- Define essential research and essential research activities to help people understand which research activities may and may not continue in these circumstances
- Provide information about which essential services will remain available for research activities and any relevant changes (e.g., investigational pharmacy, phlebotomy and laboratory services, imaging, infusion suites)
- Include information about COVID-19 screening prior to and upon arrival when in-person visits are essential to the health and well-being of participants; and information about what to do when the screening indicates that the subject may have COVID-19
- Be careful about absolute prohibitions on new studies and new study enrollments particularly for clinical trials. Establish rules or a process for exceptions when the enrollment is the patient's only or best medical option, when access to the investigational product is not available outside of the research, and when the study can be safely implemented in a manner that minimizes exposure risks for subjects and staff
- Consider consulting with the local or state Department of Public Health or COVID-19 Response Center about all of the above so that clinical research is on their radar and so that they are aware of your plans and can provide input
- Be clear about restrictions being applicable regardless of who the IRB of record is and the need to communicate with the IRB of record as well as communicating with sponsors, granting agencies, and the FDA (when holding an IND or IDE)
- Provide instructions for:
    - reporting changes to research made without IRB approval to eliminate apparent immediate hazards to the subject(s)
    - requesting modifications to research, including modifications to consent, subject information/materials, and procedural changes to minimize risk
    - reporting unanticipated problems involving risks to subjects or others
- Provide information about procedures for expanded access and emergency use

- Update your information as the situation evolves and make it easy to find (e.g., dedicated web page)

III. Access to Remdesivir, an Experimental Antiviral

According to the pharmaceutical company, Gilead, who is testing Remdesivir:

> *"Remdesivir has demonstrated in vitro and in vivo activity in animal models against the viral pathogens MERS and SARS, which are also coronaviruses and are structurally similar to COVID-19. The limited preclinical data on remdesivir in MERS and SARS indicate that remdesivir may have potential activity against COVID-19.*
>
> *This is an experimental medicine that has only been used in a small number of patients with COVID-19 to date, so Gilead does not have an appropriately robust understanding of the effect of this drug to warrant broad use at this time."*

While Gilead is working on increasing supply and it's own clinical trials (currently enrolling in Asia and Washington State), the company and FDA are approving expanded access uses of Remdesivir in the U.S. on a case by case basis, for hospitalized individuals with a confirmed diagnosis and significant clinical manifestations. Gilead is also providing study drug at no charge for a NIAID trial with several U.S. sites.

While emergency use is still an available option under the regulations, HRP reminds you that FDA has updated their requirements so that single-patient expanded access (EA) can be approved by the IRB Chair (or another Chair-designated IRB member with appropriate expertise) instead of the convened IRB. This option is only available for single-patient use of investigational drugs when the physician has requested "Alternative IRB Review Procedures" in their application to the FDA by checking the box at 10.b. on Form FDA 3926, or by including a written request with Forms FDA 1571 and 1572. FDA does not routinely specify approval for alternative IRB review procedures; it can be presumed approved when an expanded access application that includes the request is approved.

- Gilead has information about COVID-19 and access to Remdesivir on a dedicated webpage: https://www.gilead.com/purpose/advancing-global-health/covid-19
- Information on the current Remdesivir trials is available on clinicaltrials.gov: https://clinicaltrials.gov/ct2/results?cond=&term=remdesivir&cntry=&state=&city=&dist=
- Information on FDA's requirements and procedures for expanded access is available here: https://www.fda.gov/news-events/expanded-access/expanded-access-information-physicians

IV. Guidance from the National Institutes of Health

NIH issued the below Guidance for NIH-funded Clinical Trials and Human Subjects Studies Affected by COVID-19. While much of the guidance is about grants management issues, it does include some information relevant to human subjects protections, which HRP has highlighted for you.

Notice Number: NOT-OD-20-087
Key Dates

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Release Date: March 16, 2020
Related Announcements
NOT-OD-20-082
NOT-OD-20-083
NOT-OD-20-086
Issued by
National Institutes of Health (NIH)

Purpose

The purpose of this notice is to provide guidance outlining the flexibilities available to recipients conducting NIH-funded clinical trials and human subject studies, that are impacted by the declared public health emergency for COVID-19. NIH recognizes the significant effects that this emergency is having on NIH-funded clinical trials and other human subjects studies. First and foremost, NIH is concerned about the safety and welfare of human subject participants and research staff. Institutions should take all steps necessary to ensure the safety of all human participants and research staff involved in NIH-funded clinical trials and human subjects studies.

At this time, NIH encourages recipients to consult with their IRB and institutions about potential measures to protect participants and research staff. Examples of such measures are:

- Limiting study visits to those needed for participant safety or coincident with clinical care.
- Conducting virtual study visits
- Arranging flexibilities for required laboratory tests or imaging needed for safety monitoring to occur at local laboratories or clinics
- Canceling large gatherings of 50 or more people
- Limiting or suspending unnecessary travel

Recipients will likely encounter delays to ongoing research based on the effects of COVID-19. As outlined in NOT-OD-20-086, recipients may submit late financial and progress reports, if research is delayed due to COVID-19, and may carryover unobligated balances on active grants without requesting prior approval.

Below are additional details related to current and expanded flexibilities.

Delays in Research Progress:

As outlined in the NIH Grants Policy Statement 8.1.1.3, recipients may extend the final budget period of the approved project on active grants one time for up to 12 months without requesting prior approval from NIH.

To support participant health and safety, and continuity of research during this public health emergency, NIH will allow for additional extensions, including mid-project period extensions, for awards supporting NIH-funded clinical trials and human subjects research. Recipients should contact the awarding Institute or Center (IC) to provide details on the effects of COVID-19, and the need for an extension. NIH is committed to working with its recipients during this public health emergency.

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Typically, project periods for NIH awards supporting clinical trials and other human subjects research are limited to seven years. NIH will allow project periods to extend beyond the 7-year timeframe for extensions related to COVID-19.

Unanticipated Costs

As a result of COVID-19, recipients may incur unanticipated costs. For example:

- Costs incurred to arrange for participants to receive care at their local sites or virtually, rather than the study site, for required visits.
- Supply chain disruptions
- Personnel disruptions due to illness or closure of facilities
- Additional lab testing (e.g. for COVID-19)
- Increased transportation costs

If unanticipated costs are identified due to impacts of COVID-19, and unobligated balances are not available to rebudget, recipients may request administrative supplements from the funding ICs (see PA-18-591 Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp Clinical Trial Optional). ICs will make funding decisions on a case by case basis in an effort to support the safety and welfare of participants and sustain research during any delays.

Additional NIH resources related to COVID-19 are available here which includes FAQs that include, but are not limited to, human research and clinical trials specific questions. NIH is continuing to monitor the situation and will publish any additional information regarding this ongoing public health emergency in the NIH Guide.

Inquiries

Please direct all inquiries to:

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