

**PHASE 1 RAMP-UP GUIDELINES REGARDING HUMAN SUBJECT RESEARCH ACTIVITIES AT UTHSC FOR
NON-COVID-19 STUDIES**

Updated 6/1/2020

Given the rapidly developing COVID-19 pandemic across the world, clinical research is likewise affected. The risk/benefit calculus for research subjects have fundamentally changed across the research landscape given the increased risk of contracting and being impacted by the COVID-19 pandemic. As such, for each trial, consideration must be given to continue patients receiving benefit from experimental therapies while minimizing exposure to the virus for both participants, caregivers, and medical staff. As such, the following guidelines for UTHSC have been developed to attempt to navigate the changing nature of the pandemic. These guidelines are intended to supplement but not replace the current guidance document entitled “Continuity of Research Operations at: <https://uthsc.edu/research/covid-19-notice.php>

The following guidance applies only to trials that do not attempt to study or modify the COVID-19 pandemic. All studies relating to the COVID-19 pandemic, whether observational or interventional, should be prioritized and conducted preferentially.

These guidelines have been updated to reflect the “ramp-up” of clinical research activities that is occurring effective June 1, 2020. To see previous versions of these guidelines that were effective from April 7, 2020 to May 31, 2020, see the following link: <https://uthsc.edu/research/covid-19-notice.php>.

These current guidelines will be in effect until Phase 2 Ramp-up guidelines supersedes them, which will in turn be based on COVID-19 cases and deaths in Shelby County and Tennessee as well as the policies of partner hospitals.

Sections:

- 1. Observational Studies**
- 2. Biospecimen Only Studies**
- 3. Phase I Studies**
- 4. Phase II/III Studies**
 - a. Participants Currently On Study**
 - b. New Enrollments**
- 5. Phase IV Studies**
- 6. Risk Mitigation During Study Visits**
- 7. New Studies**
- 8. Study Monitoring**
- 9. Data Entry**
- 10. Policy Sharing and Communication with Sponsors and IRBs**
- 11. Conflicting Policies**
- 12. Summary**

1. Observational Studies:

Prospective observational enrollments or visits may be conducted in person going forward on a case by case basis at the discretion of the PI or in the event that the PI is not a health care provider, at the discretion of a health care provider (MD, DMD, DNP, or equivalent) who is PI’s designee. Effective April 7,

**PHASE 1 RAMP-UP GUIDELINES REGARDING HUMAN SUBJECT RESEARCH ACTIVITIES AT UTHSC FOR
NON-COVID-19 STUDIES**

2020, all observational visits for patients already on observational studies were to be moved to telephone or video visits. New participants enrolled on observational studies are encouraged to maintain social distancing and limit in-person interactions whenever possible.

If remote enrollment is a possibility, consideration should be given prior to enrolling new participants to ensure the participant and study team have the ability to comply with the protocol given no in-person assessments. Should tele-health consents be possible, unless IRB approval is specifically obtained for electronic consenting, the participant should sign the consent form (wet-ink) and send their signed copy by mail or electronically to study staff, whereby study staff will witness. All signed copies of the consent form obtained by study staff should be stored in the study binder.

Retrospective observational studies not requiring patient participation or consent can continue for as long as access to necessary databases and records is maintained.

Sponsors have, as a rule, been compliant with recent FDA guidance and have been amenable to deviations from the protocol or rapid amendments to allow for these types of assessments. The following should be done for each procedure on observational research that deviates from the protocol:

- A. Good records of actions and interactions with participants, third-party providers, and the study sponsor should be kept.
- B. Be in contact with all current study participants to inform them of the change to virtual visits and give them the opportunity to withdraw from the observational trial.
- C. All potential new patients to be enrolled on the studies should be informed of the new policy, where it does not correspond to the current language in the consent form, and this should be specifically documented. Relevant IRBs should be informed should their policies mandate.

2. Biospecimen Only Studies:

New enrollments on biospecimen studies may resume effective the date of the most recent version of these guidelines. Participants currently on biospecimen studies that require further biospecimen collection or further visits may also resume as of the date of these guidelines. Continuation should not place an undue burden on facilities or staff or interfere with other ongoing studies. IRBs and sponsors should be informed as to this policy change. Refer to Section 6 (Risk mitigation) for appropriate protection for interactions between research participants and study personnel.

3. Phase I Studies:

Phase I trials utilizing healthy volunteers may resume at the discretion of the primary investigator and with appropriate risk mitigation as detailed in Section 6. Healthy volunteers currently enrolled on these trials should be informed of the increased risk during the COVID-epidemic and given the opportunity to withdraw. Consideration should be given to stop healthy-volunteer studies altogether or postpone visits, and this decision is to be made by the responsible investigator.

**PHASE 1 RAMP-UP GUIDELINES REGARDING HUMAN SUBJECT RESEARCH ACTIVITIES AT UTHSC FOR
NON-COVID-19 STUDIES**

Phase I studies with an element of therapeutic intent, are to be treated as Phase II/III trials below.

4. Phase II/III Studies (Participants Currently on Study and New Enrollments)

In general, trial participants should stay on study and receive their medical treatments. Staff should stay in contact with study participants to keep up with any safety concerns and changes in subject willingness to remain on trial. When the PI and the Medical Director of the Research Office determine that the risk/benefit ratio is not significantly affected, patients should have key safety and efficacy procedures completed (such as labs and scans) as per protocol. When possible, these procedures should be performed on a day in which the patient was otherwise going to be treated or seen by their health care provider. Telehealth visits for follow-up will be allowed when appropriate. Good records should be kept for each time-point regarding deviations from the protocol.

A. Participants Currently On Study:

Highest priority should be given to ensure that participants actively receiving therapy on Phase II/III studies continue to receive investigational product and therapy during the pandemic. Non-therapeutic visits (for scans, labs, etc.) should be limited when possible or combined into visits where treatment or medical care is already being performed. Telehealth visits for follow-up will be allowed when appropriate. In some instances, this will require a protocol deviation. Sponsors will be informed of this policy. Additionally, participants on study should be informed as to the risks of COVID-19 and given the opportunity to withdraw should they wish to do so. IRBs should be consulted regarding how best to make changes to protocols, communicate changes to participants, and the policy for modifications prior to IRB approval. For UTHSC-Memphis, refer to the guidance document at: <https://uthsc.edu/research/compliance/irb/covid-19.php>

B. New Enrollments:

Generally, persons who sign up for research studies may be doing so because the research study could represent the best possible care opportunity. However, there are instances in which this is not the case, and these cases are often nuanced and complicated. As such, after initial coordinator screening but prior to consent for each new interventional study, specific permission from the Medical Director of the Research Office overseeing enrollment on the trial *or* the study site Primary Investigator is required as to whether the person's risk/benefit ratio is commensurate with that person going onto a study. Only after this permission has been granted may consent occur.

5. Phase IV studies:

Generally, Phase IV studies test accepted or standard therapies with additional safety and efficacy measurements and monitoring. Enrollment may continue on Phase IV studies after a determination by the study PI that any in-person visits occurring only due to participation in the study are minimized (research-only laboratory measurements, CT scans, etc.)

**PHASE 1 RAMP-UP GUIDELINES REGARDING HUMAN SUBJECT RESEARCH ACTIVITIES AT UTHSC FOR
NON-COVID-19 STUDIES**

6. Risk Mitigation During Study Visits

When in-person visits are required for patients enrolling or currently enrolled in clinical trial, the most recent guidelines regarding pre-screening personnel and participants for COVID-19 symptoms should be utilized. Personal protective equipment should be utilized as per the most updated guidelines from the US Centers for Disease Control (CDC). These guidelines can be found at

<https://www.cdc.gov/coronavirus/2019-ncov/infection-control/infection-prevention-control-faq.html>.

At a minimum, the following protocols should be enforced at all research clinics:

- A. Within 24 hours prior to check-in, either by phone or at the time of check-in, the participant's temperature should be recorded and the following questions answered
 - a. Have you had a fever in the last 48 hours?
 - b. Have you experiencing a cough, shortness of breath, or a sore throat?
 - c. Have you tested positive for COVID-19?
 - d. Has anyone in your household been ill in the last 48 hours or tested positive for COVID-19.
 - e. Have you experienced a recent loss of taste or smell?

Should the participant have a fever of greater than 100.0 degrees or above the normal range of the temperature taking mechanism, whichever is lower, or should the participant answer yes to any of the above questions, the participant should be advised to receive testing for COVID-19 and should not return to the research clinic until the test is documented to be negative. Should a participant appear acutely ill, the participant should be referred for appropriate medical care.

- B. All participants must wear masks at all times while in the research clinic. Acceptable masks include facemask, cloth face covering, or N95 masks.
- C. All participants are to perform hand hygiene both before and after interaction with study personnel
- D. All research staff should wear face masks while in any patient area or while interacting with a study participant. N95 masks, eye protection, gloves, and gowns should be used if there is more than minimal risk for the likelihood of aerosolization of material from research participants.
- E. All staff must perform hand hygiene using alcohol based hand-rub with 60-95% alcohol or by washing hands with soap and water for at least 20 seconds both before and after each participant interaction.
- F. All study participants must maintain social distancing, defined as 6 feet from any other person, in any common area of the clinic and should maintain social distancing with study personnel whenever not necessary for direct medical or study assessment.
- G. Increased vigilance should be taken by the research team in their interactions with study participants from populations at specifically higher risk for COVID-19 morbidity and mortality, including, but not limited to, adults over the age of 60 and those with underlying cardiac or

**PHASE 1 RAMP-UP GUIDELINES REGARDING HUMAN SUBJECT RESEARCH ACTIVITIES AT UTHSC FOR
NON-COVID-19 STUDIES**

pulmonary disease. For these participants, research staff should apply a low threshold for COVID-19 testing, should be especially strict regarding personal protective equipment utilization, with additional precautions utilized as per the study PI or designee.

7. New Studies:

New interventional studies may begin enrollment effective the date of these guidelines. This is in line with guidance received from study sponsors, experts in the field, and the FDA. Study start-up activities may continue for studies to which a CDA has been signed. For new trial opportunities, study activities should be limited to those that can be done either at home or in line with the University's work policy.

8. Study Monitoring:

Some Clinical Research Offices allow remote monitoring where access to the EMR is required. Care should be taken to maintain data and participant confidentiality should remote monitoring be implemented. Monitors may request periodic calls with staff to maintain appropriate study oversight during this time. Given the current increased demands on staff and the possible reduction of staff levels, each Clinical Research Office will consider these requests on a case by case basis to determine if they are able to entertain such calls at their requested frequency. Effective the date of this policy, UTHSC will resume on-site monitor visits until such time as it is deemed safe to host external sponsor/CRO employees at our facilities. Online or remote monitoring may continue based on the sponsor's request.

9. Data Entry:

All attempts to ensure timely and accurate data entry will be made, as this directly impacts participant safety for those on clinical trials.

10. Policy Sharing and Communication with Sponsors and IRBs

As per the FDA guidance of 3/18/20, this plan is to be shared with all CRAs. IRB/IBCs will be informed of this policy on a study-by-study basis when deemed appropriate by the regulatory staff of each Clinical Research Office. IRBs should be consulted regarding how best to make changes to protocols, communicate changes to participants, and the policy for modifications prior to IRB approval. For UTHSC-Memphis, refer to the guidance document from 3/20/2020 at: <https://uthsc.edu/research/compliance/irb/covid-19.php>

All attempts should be made to secure COVID-19 related deviation submissions free of charge from the IRB of record. Where this is not possible, sponsors should be informed as to the added costs incurred and attempts should be made to obtain compensation for these submissions. CRAs should be used as a sponsor point of contact for this policy and for individual study deviations.

11. Conflicting policies

Some study sponsors have provided additional guidance/requirements for their studies (such as forbidding further enrollment without access to remote monitoring). Where a sponsor's policy is stricter than this policy, the sponsor's policy takes precedence. Where the sponsor's policy is less strict than this policy, the UTHSC Guidelines takes precedence.

**PHASE 1 RAMP-UP GUIDELINES REGARDING HUMAN SUBJECT RESEARCH ACTIVITIES AT UTHSC FOR
NON-COVID-19 STUDIES**

Some individual Clinical Research Offices affiliated with UTHSC have policies already in place for Clinical Trials during the COVID epidemic. Where those policies are stricter than this process document, those policies should take precedence. Where those policies are less strict than these guidelines, these guidelines should take precedence.

12. Summary

Wherever possible, participants should continue to receive effective therapy on clinical trials while minimizing risks related to exposure to healthcare environments unnecessarily. Study deviations may and should occur to meet the above goals, and communication with IRBs, sponsors, and internally is paramount. The situation is fluid and the above guidelines may change at any time. We look forward to resuming normal operations in the near future.

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