Effective Date: 4/7/2020

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.

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. Guideline Sharing and Communication with Sponsors and IRBs
11. Conflicting Guidelines
12. Summary

1. Observational Studies:

No prospective observational enrollments or visits are to be conducted in person going forward. Effective the above date, all observational visits for patients already on these studies are to be moved to telephone or video visits. New patients enrolled on observational studies are to be limited only to those studies that have provisions for online or telephonic enrollment. 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. 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 guidelines where they do not correspond to the current language in the consent form, and this should be specifically documented.

2. Biospecimen Only Studies:

New enrollments on biospecimen studies (with the exception of COVID-19 related studies) are to halt effective April 7, 2020. Participants currently on biospecimen studies that require further biospecimen collection or further visits should be postponed until the shelter in place orders have been rescinded. IRBs and sponsors should be informed as to this policy change. In instances where a biospecimen study with significant disease-related scientific importance is already established and measures have been taken to greatly reduce or eliminate risks from COVID-19 to study personnel and participants, new recruitment and specimen collection may continue with approval by the IRB and the Medical Director of the clinical research site in consultation with the PI(s) and sponsor. Continuation should not place an undue burden on facilities or staff or interfere with other ongoing studies.

3. Phase I Studies:

Phase I trials utilizing healthy volunteers are to stop enrollment as of the above effective date. 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 until the shelter in place orders are rescinded, and this decision is to be made by the responsible investigator.

Phase I studies on participants, with a degree of therapeutic intent, are to be treated as Phase II/III trials below.

4. Phase II/III Studies

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 physician. 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 these guidelines. 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 guidelines for modifications prior to IRB approval. For UTHSC-Memphis, refer to the updated guidance document from 3/20/2020 at:


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 in consultation with the study 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.)

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

7. New Studies:

While the guidelines for enrollment of participants on existing studies already open to enrollment are covered in Section 4.B., this section is to address the initiation of studies not yet open to enrollment. No new interventional studies that have not yet opened to enrollment at the site (other than COVID-19 related studies) should activate and begin enrollment until further notice. 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. New trial opportunities may have CDA’s signed but study activities should be limited to ones that can be done at home while the shelter in place orders are in effect.

8. Study Monitoring:

Effective the above date, UTHSC will discontinue on-site monitor visits until such time as it is deemed safe to host external sponsor/CRO employees at our facility. 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 we are able to entertain such calls at their requested frequency.

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. Guidelines Sharing and Communication with Sponsors and IRBs

As per current FDA guidance (https://www.fda.gov/media/136238/download), these guidelines are to be shared with all CRAs. IRB/IBCs will be informed of this guideline 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 guidelines for modifications prior to IRB approval. For UTHSC-Memphis, refer to the updated guidance document 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 these guidelines and for individual study deviations.

11. Conflicting guidelines

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 these guidelines, the sponsor’s policy takes precedence. Where the sponsor’s policy is less strict than these guidelines, the UTHSC Guidelines take precedence.

Some individual Clinical Research Offices affiliated with UTHSC have internal policies already in place for Clinical Trials during the COVID epidemic. Where those policies are stricter than these guidelines, those internal 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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*On behalf of The UTHSC Clinical Trials Governance Board*