



MEMORANDUM

DATE: March 23, 2020

TO: Principal Investigators and Operations/Statistics Offices of NCI CTEP-Supported Clinical Trials Networks & Consortia and DCP-Supported NCI Community Oncology Research Program (NCORP) Research Bases

FROM: Meg Mooney, MD, Associate Director, CTEP, DCTD, NCI
Worta McCaskill-Stevens, MD, Director, NCORP, DCP, NCI

SUBJECT: Additional Guidance Regarding Alternative Procedures for Clinical Trials Supported by the NCI Cancer Therapy Evaluation Program (CTEP) and NCI Community Oncology Research Program (NCORP) Affected by the Spread of the Novel Coronavirus

Interim Guidance [[link](#)] was provided to CTEP and NCORP Principal Investigators and Operations/Statistics offices on March 13, 2020 that addressed:

- transfer of a patient's care to a different participating study site for a trial
- continuity of care provided by non-research staff
- administration of oral and injectable investigational agents and other investigational interventions

This memorandum provides **additional guidance** to address alternative procedures that may be implemented to maintain the safety and continuity of care for patients enrolled on ongoing clinical trials supported by CTEP and the NCORP that are being affected by the spread of the novel coronavirus.

This guidance lays out a general framework, in conjunction with the NCI Central Institutional Review Board (NCI CIRB), for consideration of alternative procedures as necessary/unavoidable deviations to protocol-specific requirements due to emergency public health measures enacted to control the spread of the novel coronavirus and/or treat COVID-19 illness.

For CTEP or NCORP trials not under the purview of the NCI CIRB, investigators and institutions would need to consult with their local IRB of record.

Alternative Procedures for Ongoing Trials – Minor Protocol Deviations:

Alternative procedures that do not impact patient safety, compromise the overall integrity of the study data (ability to draw conclusions from the study data), or affect the willingness of the patient to participate in the trial would be considered minor protocol deviations. These minor deviations would

need to be documented in the medical record by the Responsible Investigator with the reason for the deviation (e.g., mandatory or precautionary travel restrictions to prevent exposure to the virus) and brief justification for why the deviation was considered to be minor (e.g., routine follow-up on patient no longer on active therapy). These minor protocol deviations only need to be reported to the organization leading the trial (i.e., Lead Protocol Organization or LPO) so that the LPO can report them to the NCI CIRB at the time of continuing review for the trial. Examples of alternative procedures that could be considered minor protocol deviations are listed below.

- **Study Visits:** Study visits conducted by phone or videoconferencing technology (i.e., “virtual” or “telemedicine” visits) including adverse event assessments for patients could be substituted for protocol-required in-person visits if the Responsible Investigator determines that the phone/virtual visit is adequate to achieve the central purpose of the visit and assure the safety of the patient.

Study visits could also be delayed or missed if in the judgment of the Responsible Investigator the benefit of delay/omission of a visit outweighs the risks of exposure of the patient to the virus by coming in for an in-person visit and an alternative method (phone or virtual visit) is not possible. Likewise, scheduled data collections for secondary objectives such as optional quality of life or other sub-studies embedded in a cancer treatment trial could be delayed or missed.

- **Laboratory and/or Imaging Tests:** Special protocol-required laboratory tests and/or imaging could also be delayed if these tests/imaging are not available because healthcare resources have been diverted for emergency purposes due to control measures for COVID-19 and the Responsible Investigator believes it is in the best interests of the patient to continue trial treatment without those tests/safety assessments (e.g., the patient has been on therapy for a prolonged period without any safety signals) given the potential direct benefit of the therapy.
- **Treatment Delays:** Delays in treatment that the Responsible Investigator believes are minimal and do not impact patient safety or compromise the study integrity can be made to avoid potential patient exposure to the virus or because of mandatory travel restrictions.
- **Biospecimen Collection:** Depending on the nature of biospecimen collections specified in the protocol (e.g., mandatory vs optional, real-time processing vs staged processing requirements) and the status of the participating site to store specimens locally, if the central biorepository is not operating at full capacity, alterations to the procedures for handling biospecimen collections may or may not constitute minor protocol deviations.

Biorepositories will be updating participating sites on general guidelines for biospecimen collections on ongoing trials and alternative procedures for collection of biospecimens that are not mandatory/integral to the study or do not requiring real-time processing. Trial specific information will be made available for other laboratories specific for the trial by the organization leading the study – this information may be made available on the protocol page for the study on the members side of the Cancer Trials Support Unit (CTSU). If information is not available yet, the Responsible Investigator should contact the organization leading the trial or biorepository, as appropriate. The CTEP/NCORP Program Director for the clinical trials

network program that oversees the trial could also be contacted about issues related to program biorepositories for trials.

For documentation, the Responsible Investigator can simply note in the medical record that any general or specific guidelines issued by the organization leading the trial on alternative procedures for biospecimen collection due to the public health emergency were followed.

All study visits, laboratory tests, imaging, treatment schedules as specified in the protocol should resume as soon as emergency public health control measures for COVID-19 are no longer needed in the patient's location to confirm patient safety. It is understood that significant delays of protocol-required study visits, laboratory tests, imaging, treatment delays, and inability to obtain mandatory tissue essential to achieve the study endpoint would result in discontinuation of the patient's participation in the clinical trial if appropriate safety monitoring can no longer be maintained or the study integrity is compromised.

Alternative Procedures for Ongoing Trials – Major Protocol Deviations:

Alternative procedures that impact on patient safety, substantially alter risks to the patient, compromise the overall integrity of the study data (ability to draw conclusions from the study data), or affect the willingness of the patient to participate in the trial are considered major protocol deviations. Given the current public health emergency, alternative procedures may be unavoidable and result in major deviations (e.g., more than a minimal delay in study treatment due to mandatory travel restrictions). The Responsible Investigator must determine with input from the trial Study Chair and Sponsor, if applicable, whether it is reasonable for the patient to continue participation in the trial depending on the nature of the protocol deviation.

In all cases the Responsible Investigator must document the major protocol deviation in the medical record along with the reason for the deviation and the rationale for the decision to continue or discontinue the patient's participation on study. The major protocol deviation must also be reported to the NCI CIRB in an expedited manner using the standard procedures/algorithms to determine serious or continuing non-compliance (SCNC). It is not anticipated that unavoidable major protocol deviations would necessarily lead to a protocol amendment or a corrective action plan if the deviation was directly due to the current public health emergency.

Alternative Procedures for Auditing/Monitoring of Trials:

Planned on-site monitoring/auditing visits are being re-scheduled as needed because of emergency measures being enacted by institutions due to public health control measures for COVID-19. Central monitoring already included in specific trials is being supported without interruption. Remote auditing can be considered and implemented if a site is able to provide a secure access portal to its electronic medical record (EMR) system to the CTEP Clinical Trials Monitoring Branch (CTMB) staff and auditors for the specific clinical trials program.

Alternative Procedures for Informed Consent for Trials:

If possible, the informed consent process should be combined with other pre-study testing and patient assessments that require an in-person visit to the institution/participating site so that the patient's potential exposure to the novel coronavirus is limited (e.g., avoid having a patient go to the healthcare facility only to sign an informed consent). The informed consent for the trial can be signed before all screening components are completed; however, the protocol-specified intervention/tests would only be started after all eligibility criteria, including the informed consent process, are completed.

The NCI CIRB can support "remote" informed consent (i.e., telephone/teleconferencing **discussion in conjunction with** an informed consent document that can be sent to the patient, signed, and transmitted back to the participating site research team and signed by the consenting physician/healthcare provider before any research procedures begin). This "remote" informed consent can be used due to COVID-19 control measures (e.g., travel restrictions) and would not be considered a protocol deviation. Information on the NCI CIRB's support for "remote" informed consent for sites using the NCI CIRB as the IRB of record will be available on the NCI CIRB website at www.ncicirb.org later this week or sites can contact the NCI CIRB at ncicirbcontact@emmes.com. It is anticipated that this type of consenting may be especially useful for patients already on study who are proceeding to a next step on the trial that requires additional informed consent.

Procedures for Clinical Services, Testing, and Screening Related to COVID-19:

Clinical services, testing, and screening related to COVID-19 that need to be performed for patients enrolling on clinical trials or those already on trial do not need IRB approval prior to initiation since these procedures would be considered usual care for patients outside of the research environment. If a patient develops COVID-19 illness while on study, complications related to infection would be reported through the trial's existing adverse event reporting system. However, if the data are being collected as a new research objective within the trial, a protocol amendment would be required.

CTEP and the NCORP will continue to monitor closely the studies being conducted across all its clinical trials network programs to address emerging issues due to the COVID-19 illness and/or COVID-19 control measures. Any recommendations about reasonable alternative procedures for specific trials that become available will be posted on the protocol page for the trial on the members side of the Cancer Trials Support Unit (CTSU).