Ministry Guidance for COVID-19 Research Activities

We recognize the time and sacrifice of the clinical and support staff in responding to the current COVID-19 pandemic. In the course of clinical care activities, and in the absence of evidence based treatment protocols, many have recognized the need and opportunity to contribute to the pool of scientific knowledge surrounding COVID-19. Given the priority of clinical care demands, it is necessary to discern the value of COVID-19 related clinical data requests and potential research projects. Below are recommended guidelines for ministries, regarding the review and coordination of COVID-19 related research activities. Note that these research activities may take the form of interventional studies; clinical trials involving drugs, devices, and/or biologics; participation in research registries or biorepositories, as well as other data collection and review activities.

- If an investigator has a proposal for a research study, please ensure that local executive support (i.e. Institutional Official, VP/CMO role or higher, or local COVID-19 Incident Command structure, if applicable) is confirmed. If you are aware of any investigators from external entities who wish to collaborate with a local ministry investigator, please have them propose their research studies and obtain local executive support as well.

- Priority should be given to research activities based on scientific merit, community benefit, clinical and research mission of your ministry, and feasibility.

- Because resources will be needed to support research activities leading to dissemination and/or publication, it is recommended that each ministry establish a mechanism for identifying and prioritizing research protocols. This will ensure that local resources are available for execution of the research study, and that local efforts are coordinated.

- All research projects approved by ministry leadership must adhere to applicable federal and state research regulations, and the ministry’s internal policies and procedures, including applicable Institutional Review Board (IRB) requirements. Note that for investigator-initiated
research studies involving an investigational new drug, biologic or device, the investigator must fulfill the legal and regulatory responsibilities of both Principal Investigator (PI) and Sponsor. Appendix A of this Guidance provides an overview of the responsibilities of Sponsor-Investigators.

- All research activities require a PI who is responsible for the overall conduct of the execution of the research, as well as responsible for the documentation needed for IRB review and approval. Although the PI may delegate tasks to other individuals, he/she is responsible for the overall conduct of the research study (i.e., execution of the protocol). It is important to note that considerable time is required to fulfill the PI responsibilities.

- For research activities that involve sharing data externally, the PI should contact their Regional Security Officials (contact information available at: https://intranet.trinity-health.org/web/enterprise-information-security/contact-us) to determine whether an assessment of the external party's data security measures is required. This typically involves working with Enterprise Information Security (EIS) to complete a security assessment on all information systems that will create, receive, store, transmit, or view protected health information of confidential information of Trinity Health, or that will connect to the Trinity Health Network. If EIS determines a security assessment is needed, this assessment must be completed prior to the sharing of research data.

Please note that system level research activities, which are defined as involving 3 or more ministries or are led/sponsored by a system office colleague, are approved through Trinity's system level research approval process. This involves submission to Trinity Health's Scientific and Operations Review Committee (SORC). SORC approval is required prior to submission to the Trinity IRB of Record. For more information on the approval process for system level research, contact Dawn Pedinelli, Trinity Health's Director of Research at dawn.pedinelli@trinity-health.org
APPENDIX A

Responsibilities of Sponsor-Investigators

As defined in FDA regulations (21 CFR 312.3 and 812.3(o)), a Sponsor-Investigator is an individual who both initiates and conducts a Clinical Investigation (as such term is defined under FDA regulations), and under whose immediate direction a Test Article (i.e. an investigational drug, device, or biologic) is administered, dispensed or used. The requirements of a Sponsor-Investigator include both those applicable to an Investigator and those applicable to a Sponsor. Links to the FDA guidance as well as a complete list of FDA Regulations are located at the end of this Appendix A under the subheadings References and List of Regulations.

The Sponsor-Investigator is responsible for ensuring that the Clinical Investigation is conducted according to:

- sound research design and generally acceptable scientific methods;
- all terms of contracts and/or signed agreement(s);
- the obligations specified in the signed Form FDA 1572, if applicable;
- the Clinical Investigation plan (otherwise known as the Protocol) as approved by the IRB; and
- all applicable regulations and laws.

Specific responsibilities of a Sponsor-Investigator ("SI") include:

1) Selecting qualified study team personnel, including a research coordinator, who have appropriate training and expertise to assist in the conduct of the proposed research according to regulatory requirements. This coordinator would need to be familiar with the Ministry’s processes for subject registration/enrollment, tracking visits to ancillary departments, and proper billing procedures for study-related services as they occur;

2) Providing study team member(s) with the necessary information and training to conduct the Clinical Investigation. All study team members must be trained by the Sponsor-Investigator on the methods detailed in the Protocol including but not limited to, the method of obtaining consent, process of reporting adverse events, data collection and data monitoring plan. The Sponsor-Investigator is responsible for submitting evidence of the required education and training for all study team members to the IRB as required by its Ministry’s IRB Policies;

3) Prior to initiation of the Clinical Investigation, a Medicare Coverage Analysis (MCA) will need to document research charges, standard of care and non-covered standard of care charges and confirm that according to Centers for Medicare and Medicaid it is a qualifying trial. The MCA will document whom or what entity will bear the costs that will be incurred during the Clinical Investigation such as through a subject’s insurance and what will be paid for as part of the research. This is required by Centers for Medicare and Medicaid and must be signed by the Sponsor-Investigator. Proper tracking, coding and billing milestones will need to be documented to ensure timely and accurate billing to the payor, the study subject, or another funding mechanism, as determined in the research budget.

4) Personally conducting or supervising the proposed Clinical Investigation, including:

   (a) Conducting the Clinical Investigation in accordance with agreements, contracts, the Protocol, as filed with the FDA and IRB and any other applicable FDA regulations, and conditions of approval imposed by the reviewing IRB and the Ministry where the Clinical Investigation is being conducted;
(b) Supervising the use of the Test Article at their site and administering the Test Article only to subject's under the SI's personal supervision or under the supervision of a person whom the SI has formally delegated that authority to in the delegation log; and

(c) Obtaining the legally effective informed consent of the subject or the subject's legally authorized representative prior to the administration of a Test Article;

(d) Protecting the rights, safety, and welfare of subjects under the Investigator's care;

(e) Understanding FDA guidance on FDA expectations regarding supervision and task delegation to other research team members;

5) Ensuring IRB approval is obtained before the Clinical Investigation activities begin, and again prior to the expiration of IRB approval (at the time of each periodic continuing IRB review of the research);

6) Preparing, submitting and maintaining an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE) application to FDA, as applicable, and that these regulatory documents are also maintained by the IRB as part of the submission processes;

7) Registering and maintaining the Clinical Investigation on Clinicaltrials.gov and obtaining the NCT number prior to beginning the Clinical Investigation that will be used in billing procedures;

8) Ensuring compliance with all applicable FDA labeling requirements, as applicable;

9) Maintaining adequate records of the disposition of the Test Article, including dates, quantity, and use by subjects; return of the unused supplies of the Test Article to the manufacturer or other disposition of unused supplies, and complying with any other applicable record-keeping and retention requirements for the Test Article, as set forth by the FDA.

10) The Sponsor-Investigator and the institution are required to permit and facilitate monitoring and auditing, at reasonable times, by the IRB, its designee, funding agencies, and federal and state regulatory agencies as appropriate;

11) For research involving more than minimal risk to subjects, the Sponsor-Investigator is responsible for submitting a Data and Safety Monitoring Plan or standard operating procedures to the IRB describing how the Sponsor-Investigator will fulfill all the requirements of a Sponsor, and ensuring proper monitoring of the Clinical Investigation in accordance with the plan submitted to the IRB; and

12) The Sponsor-Investigator must ensure prompt reporting of any unanticipated problem involving risk to subjects or others to the IRB, appropriate Institutional Officials and State and Federal regulatory agencies as appropriate in keeping with the IRB’s policy on Problems or Events that Require Prompt Reporting to the IRB.

REFERENCES:

For sponsor-investigator guidance when applying to the FDA for an IND, refer to Information for Sponsor-Investigators Submitting Investigational New Drug Applications (INDs): http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm071098.htm#form1571

Clinical investigators either conduct a clinical trial or are the responsible party of a team of investigators. See 21 CFR 312.3 and 812.3(i). The clinical investigator is responsible for protecting the rights, safety,


In addition, supplemental guidance on the use of computerized systems in clinical investigations is available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070266.pdf

LIST OF REGULATIONS:

In addition to the requirements of 21 CFR 312 and 21 CFR 812, investigators who hold an IND or IDE must also meet all regulatory requirements pertaining to sponsors, appearing in other FDA parts, as applicable, as listed but may not be limited to:

**For Drugs or Devices:**
- □ 21 CFR 11 (Electronic records and electronic signature)
- □ 21 CFR 54 (Financial Disclosure by Clinical Investigators)

**For Drugs and Biologics:**
- □ 21 CFR 210 (Current Good Manufacturing Practice in Manufacturing, Processing, Packing, or Holding of Drugs; General)
- □ 21 CFR 211 (Current Good Manufacturing Practice for Finished Pharmaceuticals)
- □ 21 CFR 312 (Investigational New Drug Application)
- □ 21 CFR 314 (Drugs for Human Use)
- □ 21 CFR 320 (Bioavailability and Bioequivalence Requirements)
- □ 21 CFR 330 (Over-The-Counter (OTC) Human Drugs Which Are Generally Recognized as Safe and Effective and Not Misbranded)
- □ 21 CFR 601 (Biologics Licensing)

**For Devices:**
- □ 21 CFR 807 (Establishment Registration and Device Listing for Manufacturers and Initial Importers of Devices)
- □ 21 CFR 812 (Investigational Device Exemptions)
- □ 21 CFR 814 (Premarket Approval of Medical Devices)
- □ 21 CFR 820 (Quality System Regulation)
- □ 21 CFR 860 (Medical Device Classification Procedures)

**Centers for Medicare and Medicaid:**
National Coverage Determination (NCD) for Routine Costs in Clinical Trials (310.1)