To
IRB
The Children's Hospital of Philadelphia

Subject: Determination for COVID 19 Clinical Registry for COVID 19 Associated Cardiac Rhythm Disorders

Since its emergence from Wuhan, China, in late 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for coronavirus disease 2019 (COVID-19), has already infected approximately 4.8 million people world-wide claimed the lives of more than 300,000 individuals worldwide. With the number of COVID-19 cases and deaths increasing with each passing day, there is perhaps no more pressing need in medicine than to minimize the spread of infection, identify patient population at risk, and identify safe and efficacious therapies to prevent and treat SARS-CoV-2 infections as well as to attenuate the severity of the resulting COVID-19 illness.

The CDC has estimated that < 2.5% the pediatric population was infected with the COVID-19 virus. The predominant signs and symptoms of COVID-19 reported to date among all patients are similar to other viral respiratory infections, including fever, cough, and shortness of breath Recently, reports of multisystem inflammatory syndrome in children (MIS-C) including cardiac involvement and cardiac arrest associated with COVID-19. As we begin to discover that children may have clinical manifestations that differ from those typically described with in adults with COVID 19 infections, it is critically important to determine if there are cardiac electrical changes and rhythm abnormalities associated with COVID-19 infection in children with and without underlying cardiac conditions. This is especially true for children with underlying congenital heart disease and inherited cardiac arrhythmias such as long QT syndrome.

Although there are no proven US Food and Drug Administration (FDA)–approved drugs to prevent or treat COVID-19, a number of promising novel (e.g. remdesivir) and repurposed (eg, hydroxychloroquine, potentially together with azithromycin) pharmacological agents, reported to inhibit the growth of SARS-CoV-2 in vitro, are being evaluated in randomized clinical trials. The proclivity of many promising COVID-19 pharmacotherapies—specifically antimalarial agents such as hydroxychloroquine—to prolong the QTc, thereby increasing the risk of drug-induced serious arrhythmias such as torsades de pointes (DI-TdP) and drug induced-sudden cardiac death (DI-SCD). While most of the patients who receive these drugs are adults, and the risk to children especially those with underlying cardiac conditions and cardiac arrhythmias is unknown.

Given the gaps in knowledge about COVID 19 in pediatrics and how the virus as well as its treatment affects the cardiac electrical system, we propose to create a multi-center international clinical registry of all pediatric COVID 19 cases < 21 years of age with a focus on documenting cardiac manifestations that include electrocardiographic (ECG) and rhythm

abnormalities. Dr. Maully Shah will create and maintain the registry with a de-identified data collection via a CHOP RedCap data base and patients will be enrolled through The Pediatric and Congenital Electrophysiology Society (PACES) which is an international society of Pediatric electrophysiologists (www.pediatricepsociety.org). Data collection will continue until such time when the CDC has determined that the COVID 19 Pandemic has ended. At the present time there is no research intent for this registry. If the direction of the clinical registry changes, we will submit an IRB proposal to conduct research. Please see the attached CRF for the clinical registry.