

**SELECT AGENT RESEARCH/BIOHAZARDS. No select agent research.**

**Agents:** SARS-related bat coronaviruses (SARSr-CoV), like WIV1, WIV16 and SHC014. These bat viruses are distantly related to the epidemic human SARS-CoV which emerged in 2003 and caused 8,000 cases and 800 deaths worldwide. While the epidemic human SARS-CoV is a BSL3 select agent, the SARSr-CoV are BSL3 pathogens in the US and not select agents. The proposal will use a SARSr-CoV molecule clone designated WIV1 during the course of these studies, which is NOT a select agent. This strain has not been shown to cause human disease or be transmissible between humans. All recombinant DNA work will use the bat SARSr-CoV WIV1 molecular clone. At the University of North Carolina (US Government select agent certified laboratory), some virus growth studies will be conducted in primary human airways, comparing wildtype SARS-CoV, WIV1 and various SARSr-CoV WIV1 chimeric virus growth kinetics. Wildtype SARS-CoV strain research will not be conducted at the Wuhan Institute of Virology.

**Registration status of all entities where select agent(s) will be used.** Wildtype SARS-CoV is a select agent. UNC-Chapel Hill is currently registered with the CDC for select agent use, including SARS-CoV, as required by select agent regulations (42 CFR 73). The UNC SARS select agent laboratories are routinely inspected by the environmental health and safety department at UNC and by the CDC. Workers receive select agent and BSL3 training focused on SARS-CoV safety, procedures and protective clothing/PAPR training each year.

**Introduction and Background.** SARS-CoV caused outbreaks with significant case fatality rates, and there are no vaccines available for this agent. SARS-CoV is classified as a BSL-3 select agent. Wildtype SARS-CoV is currently thought extinct in the wild. The work proposed in this application will involve two aspects: field work and laboratory work, focusing on distantly SARS-like bat coronaviruses (SARSr-CoV). Fieldwork involves the highest risk of exposure to SARSr-related or other bat CoVs, while working in caves with high bat density overhead and the potential for fecal dust to be inhaled. There is also some risk of exposure to pathogens or physical injury while handling bats, civets, rodents or other animals, their blood samples or their excreta. The Co-PIs and field team have extensive experience and certification working with wildlife species and high-biosecurity pathogens (Nipah virus, ebolavirus, SARS), and great care will be taken in the field to limit the risk of accidental exposure to known or unknown animal pathogens. We have strict procedures for handling bats and working with samples from them as they are secured in the field and transported to the lab. Field team members handling animals will be trained to utilize personal protective equipment (PPE) and practice proper environmental disinfection and biosafety techniques. This includes wearing coveralls or dedicated clothing, nitrile gloves, eye protection, and a P95 or P100 respirator during bat handling and sampling. Fully Tyvek suits and HEPA-filtered Powered Air Purifying and Supplied Air Respirator Systems (PAPRs) will additionally be worn in cave systems where there is a higher risk of contact with aerosolized bat feces. All field clothing and equipment will be disinfected using Virkon disinfectant. All biological waste from field surveys will be disposed of in the appropriate container (sharps box or an autoclave bag) and will be autoclaved at local hospitals or university labs. All personnel will be vaccinated against rabies and have a neutralizing antibody titer, in accordance with WHO and CDC recommendations. Field teams will carry rabies boosters in the field and will receive a booster in the event of a potential rabies exposure.

**Field safety protocol:** Our procedures to deal with bites, needle-sticks etc. are as follows: The wound is washed thoroughly with soap and water to clean away dirt and debris, then vigorously scrubbed with a sterile gauze bandage and benzalkonium chloride for 5 minutes. If bleeding, pressure is applied with a sterile bandage for until bleeding has stopped. If the wound continues to bleed, medical attention at the nearest hospital is sought. The bat from which the bite or exposure originated is identified, and the samples collected from it labeled on the data sheet that these were involved in an exposure. Our procedures require that the person potentially exposed reports to a major hospital within 24 hours to