

CAT E justification for protocol IS00008056 for hamsters –FY21- USDA 58R0015- University of South Florida

The objective of this project is to utilize the hamsters to evaluate the efficacy of candidate vaccines against *Clostridium difficile* infection, and additionally evaluate the efficacy of specific vaccine candidates via a specified route of delivery. Vaccines function by stimulating the immune system. The immune system comprises many parts. It is very difficult to predict which portion(s) of the immune system are necessary for the function of a particular vaccine. Thus, for evaluation of vaccines the entire immune system is required.

*C. difficile* strains are expected to induce diarrhea. As a result, these hamsters may also become weak and dehydrated. In addition, hamsters infected with *C. difficile* may become moribund. All of the potential adverse effects that may be seen are related to *C. difficile* infection. The only means by which to abrogate development of the expected adverse effects is to administer antibiotics (metronidazole, vancomycin) to which *C. difficile* is susceptible. This will eliminate the *C. difficile* infection. Given that the basis of this study relies on *in vivo* infection with these *C. difficile* strains and evaluation of the efficacy of vaccines, therapeutic agents and host immune response to infection, administration of such antibiotics would obviate the purpose of this study.

Administration of anti-diarrheal drugs or analgesics would be expected to eliminate the diarrhea and/or abdominal/gastrointestinal pain associated with this diarrhea. Given that one of the goals of this study is to evaluate the effect of *C. difficile*-associated virulence factors, reduction or elimination of these clinical signs would inhibit our ability to assess the establishment of this model and to evaluate the effect of the virulence factors.