CCRP Product Development Support Services - Preclinical Efficacy Evaluation Resources: Soman Neurotoxicity Model

Background

The goal of NIH Chemical Countermeasures Research Program (CCRP) centralized Product Development Support Services (PDSS) - Preclinical Efficacy Evaluation Resources (PEER) is to assist applicants with acquisition of pilot proof-of-principle efficacy data of candidate MCM(s) against the lethal and/or non-lethal effects of chemical threat agents in established or new models of chemical intoxication. PDSS resources are limited and not intended to sustain the entire spectrum of chemical MCM discovery, research, and development and should not be the sole source of support.

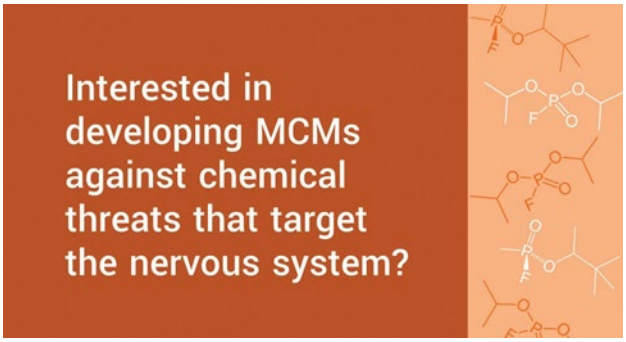
All information provided will be treated as confidential. Participants will retain custody of and have primary rights to the data developed, subject to Government rights of access consistent with current HHS, PHS, and NIH policies.

If approved, studies are performed at **no cost** to the applicant. Investigators seeking these services receive no funding from NIAID, but instead receive products or information generated by NIH-funded contractors on their behalf. NIH will deliver a final study report to the investigator at the end of the study.

PDSS Soman (GD) Neurotoxicity Model

Organophosphate (OP)-induced seizures result from overstimulation of susceptible brain circuits by abnormally high levels of the excitatory neurotransmitter acetylcholine, which rapidly builds up after inhibition of the enzyme acetylcholinesterase by an OP nerve agent. The seizure rapidly progresses to a condition known as *status epilepticus* (SE); a medical emergency only treatable with a subset of known anticonvulsant drugs.

The current MCM approach to treat OP-induced seizures includes administration of a benzodiazepine-based anticonvulsant such as midazolam along with atropine and pralidoxime chloride. Although this treatment is efficacious to an extent, overall improvements in both mortality and morbidity outcomes are highly desired. The goal of the GD neurotoxicity model is to identify novel therapeutics that may be administered with standard-of-care treatments in a civilian first-responder setting to suppress SE activity more effectively and/or mitigate long-term neuropathology after OP exposure.



What We Offer -

The GD neurotoxicity model employs an *in vivo* rodent GD-induced electrographic SE approach that utilizes up to 24-hour of electroencephalographic (EEG) recordings to determine the efficacy of investigational compounds in suppressing electrographic SE along with Fluoro-Jade B (FJB) staining-based histopathology to evaluate the potential neuroprotective effects of the test compound(s).

The proposed pilot study will be limited in scope and aim to facilitate initial characterization of candidate MCM(s) efficacy. Preliminary evidence of therapeutic efficacy, i.e., biological response (preferably *in vivo*) against the actual threat agent OR an acceptable surrogate injury model is required. Applicants seeking label-expansion indications of already FDA-approved medications and /or those further along in the exploratory or validation stage for a conventional indication are highly encouraged to apply.

Applicant Eligibility Criteria

Utilization of PDSS resources is available to any domestic U.S.-based applicant with promising MCM candidates (and appropriate supporting preliminary data) responsive to the CCRP mission

Who to Contact

To learn more or request preparation instructions for a study pre-proposal, please contact **Dave Yeung, Ph.D.** (Deputy Director, CCRP); dy70v@nih.gov