

THREAT AGENT DEFEAT MODELING AND TESTING USING WMD SIMULANTS

Development Of Assays For Novel Reactivators Of Organophosphorus-inhibited Human Acetylcholinesterase

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The use of chemical warfare agents poses a great threat to both the warfighter and civilian populations. Organophosphorus nerve agents (OPNAs) inhibit acetylcholinesterase (AChE) via a covalent interaction in the active site, causing a buildup of excess acetylcholine (ACh) in the synaptic cleft. This excess ACh results in a systemic cholinergic crisis that clinically manifests as a conglomeration of adverse effects that can eventually lead to death if left untreated. In vitro assays have been established as a part of the Improved Nerve Agent Treatment System: New and Emerging Reactivator Development Screening (INATS NERDS) at the United States Army Medical Research Institute of Chemical Defense. These assays serve as a preliminary evaluation for potential reactivator compounds submitted to the INATS NERDS and the resulting data can also be used to inform the development of subsequent novel drug candidates. The employment of several generations of liquid handling robotic systems over the years has contributed to the evolution of these assays. In conclusion, these assays allow for the rapid, high throughput evaluation of not only the efficacy of novel reactivator compounds but also several biochemical parameters.