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Explanation of procedures being done at Category E

Efficacy studies to evaluate oxime candidates, involve challenging animals with organophosphorous nerve agent (OPNA), followed by administration of atropine and an anticonvulsant, such as diazepam or midazolam, and the oxime of interest to reactivate inhibited acetylcholinesterase (AChE). More recently, midazolam has been used as the anticonvulsant of choice due to its rapid bioavailability and ease of administration (i.e. intramuscular, intranasal, sublingual).

The current standard of care uses AChE reactivator pralidoxime chloride (2-PAM Cl), however, this oxime does not readily cross the blood-brain barrier (BBB), limiting its ability to reactivate central nervous system AChE.

Analgesics/sedatives cannot be used as they may affect the binding of the OPNA to the cholinesterase or may bind to/affect the activity of the drugs (atropine/midazolam) and oxime. No relevant literature exists to demonstrate that an analgesic/sedative will not confound the results from this study. This study was designed with literature in mind to directly compare to other groups/oximes of interest.

69 Guinea Pigs