Protocol 1

1. A total of 65 column "E" guinea pigs were utilized in this study.

2. Painful procedure:

Guinea pigs were exposed to organophosphorus nerve agents.

3. Justification:

The goal of this research is to evaluate the efficacy of novel bioscavenger enzymes in mitigating the consequences of nerve agent intoxication. Agent exposure potentially causes some pain and/or distress as a result of the intense physiological changes produced by these toxicants. Subjecting animals to levels of nerve agent exposure that reliably elicit these toxic effects is essential for the goals of this protocol. The use of anesthetics or analgesics would obscure the results, making it impossible to assess the efficacy of the candidate medical countermeasures.

4. No federal regulations mandate this procedure.

Protocol 2

1. A total of 284 column "E" guinea pigs were utilized in this study.

2. Painful procedure:

Animals are exposed to organophosphorus nerve agents and sulfur mustard. The toxicity of nerve agents includes fasciculations, tremors, salivation, lacrimation, bronchoconstriction, dyspnea, broncho-secretions, seizures, motor convulsions and respiratory paralysis. Agent exposure is thought to cause some pain and/or distress from the intense physiological changes produced by these toxicants. Sulfur mustard exposure induces skin lesions and systemic toxicity which are considered to cause pain/distress.

3. Justification:

Agent exposure potentially causes some pain and/or distress as a result of the intense physiological changes produced by these toxicants. Subjecting animals to levels of nerve agent exposure that reliably elicit these toxic effects is essential for the goals of this protocol. The use of anesthetics or analgesics would obscure the results, making it impossible to assess the efficacy of the candidate medical countermeasures.

4. No federal regulations mandate this procedure.

Protocol 3

1. A total of 71 column "E" guinea pigs were utilized in this study.

2. Painful procedure:

Animals are challenged with either the nerve agent sarin or VX at a dose that elicits electrographic seizure activity.

3. Justification:

The goal of the study is to utilize a guinea pig model to evaluate brain AChE activity and oxime therapy following nerve agent-induced exposure. Thus, subjecting the animals to nerve agent intoxication is essential to the goals of this protocol. EEG monitoring is essential to evaluate whether electrographical seizure activity is controlled by centrally active oxime therapy and how this relates to AChE activity. Anesthetics such as isoflurane, sevoflurane, halothane, flurothyl, propofol, or ketamine are known to interfere with seizure activity, causing either pro- or anti-convulsant effects. Analgesics can potentially interact with the toxicity of the agents because of their ability to enhance respiratory depression and thus complicate the interpretation of the results.

4. No federal regulations mandate this procedure.

Protocol 4

1. A total of 6 column "E" guinea pigs were utilized in this study.

2. Painful procedure:

Guinea pigs are exposed to organophosphorus nerve agents.

3. Justification:

The goal of this protocol is to develop a point-of-care in-vitro diagnostic device to give indication of exposure to chemical warfare nerve agents. Subjecting animals to levels of nerve agent intoxication that reliably elicit the toxic responses is essential to the goals of this protocol. Agent exposure potentially causes some pain and/or distress as a result of the intense physiological changes produced by these toxicants. The use of anesthetics or analgesics would obscure the results, making it impossible to assess the performance of this medical device during development.

4. No federal regulations mandate this procedure.

Protocol 5

1. A total of 26 column "E" nonhuman primates were utilized in this study.

2. Painful procedure:

Agent exposure

3. Justification:

This protocol requires exposure to potentially lethal doses of chemical agents in unanesthetized NHPs to be able to monitor behavioral performance. Agent exposure is thought to cause some pain and/or distress because of the intense physiological changes produced by these toxicants. We cannot pre-treat the animals with any medication as this would compromise the results of the study in determining the dose of the chemical agent that leads to behavioral deficits.

4. No federal regulations mandate this procedure.

Protocol 6

1. A total of 68 column "E" pigs were utilized in this study.

2. Painful procedure:

Nerve agent exposure

3. Justification:

This protocol requires exposure to otherwise convulsive or lethal doses of nerve agents in unanesthetized swine. Agent exposure is thought to cause some pain and/or distress because of the intense physiological changes produced by these toxicants. We cannot pretreat the animals with any medication as this would compromise the results of the study. The administration of anesthetics or analgesics to relieve pain or distress would lead to an erroneous evaluation of the toxicity of these agents and the efficacy of pretreatment, treatment, and decontamination procedures. Use of these anesthetics or analgesics would undermine the purpose of these experiments and may increase the number of animals needed to obtain statistical significance.

4. No federal regulations mandate this procedure.
