Protocol #1

1. A total of _65_ column “E” guinea pigs were utilized in this study.

2. Painful procedure:

Animals are exposed to organophosphorus nerve agents, sulfur mustard and carfentanil. 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:

The goal of the research in Experiments 1 and 2 is to evaluate decontamination procedures and materials to prevent the lethal and injurious effects of nerve agents. The toxicity of nerve agents includes fasciculation, tremors, salivation, lacrimation, bronchoconstriction, dyspnea, broncho- secretions, seizures, motor convulsions and respiratory paralysis. Nerve agent exposure is thought to cause some pain and/or distress from the intense physiological changes produced by these toxicants. Thus, subjecting the animals to levels of chemical agent exposure that reliably elicit these toxic effects is essential for the goals of this protocol. Anesthetics and analgesics including non-steroidal anti-inflammatory drugs (NSAIDS) cannot be used in Experiments 1 and 2 because anesthetics and many analgesics produce respiratory depression or have other pharmacologic effects that could interfere with the response of the animals to agents. Respiratory depression is a principal sequelae of nerve agent intoxication, and conducting these experiments under anesthesia or analgesia could lead to faulty interpretation of the toxicity data and/or the effectiveness of the countermeasures because of the synergistic respiratory depressant effects of these drugs with the agents.

4. No federal regulations mandate this procedure.

Protocol #2

1. A total of _6__ 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 and physiological parameters. 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 #3

1. A total of _29___ 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 evaluate the toxicity of these agents and the efficacy of pretreatment, treatment, decontamination procedures. In addition it allows monitoring of behavioral performance after exposure, pre-treatment, and treatment. 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 analgesic 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 #4

1. A total of _4__ column “E” nonhuman primates were utilized in this study.

2. Painful procedure:

This protocol requires exposures in unanesthetized and anesthetized subjects.

3. Justification:

This protocol requires the analysis of acute and chronic toxic signs. We cannot pre-treat the animals with any medication as this would compromise the results of the study in determining the exposure parameters that lead to physiological and behavioral changes.

4. No federal regulations mandate this procedure.

Protocol #5

1. A total of _9___ column “E” nonhuman primates were utilized in this study.

2. Painful procedure:

All animals were originally placed in Cat E. The aerosol inhalation animals were all sedated while placed in the chair and helmet. Sedation was reversed once they were in the exposure room. They were then exposed to scopolamine and returned to their home cages. The scopolamine caused mydriasis, ataxia, tremors and even convulsions. While these effects may not be painful they were most likely distressful to the animals so they remain in Cat. E.

3. Justification:

We elected to err on the side of caution and preliminarily place all animals into Cat E, although we anticipate minimal toxicity at lower doses. The goal of the study is to determine a LCT50 of scopolamine and exposure to high doses of scopolamine may induce CNS effects that could be distressful to the animals.

4. No federal regulations mandate this procedure.

Protocol #6

1. A total of _21___ column “E” pigs were utilized in this study.

2. Painful procedure:

Nerve agent exposure may lead to convulsions followed by potential pain from muscle fasciculations and convulsions. See protocol for more information.

3. Justification:

Exposures to GD potentially can cause some pain and/or distress as a result of the intense physiological changes (potential seizures and muscle pain that follows convulsions, gastrointestinal distress, etc.). Subjecting the animals to levels of GD that reliably elicit these toxic effects is essential for the goals of this protocol to develop a model for evaluating medical countermeasures to alleviate these effects and to protect the brain from damage. Anesthetics (e.g., barbiturates, inhalation anesthetics) and analgesics (for example, anti-inflammatory drugs) for relief of pain or distress are known to exhibit protective effects on brain function. Some anesthetics are effective anticonvulsants and could block seizures on their own. Many analgesics can interact with the drugs to be tested and/or the toxicity of the nerve agent (e.g. by causing respiratory depression) and thus can complicate the outcome and interpretation of the results, particularly when death is a potential experimental endpoint. Since parameters such as the frequency and intensity of seizure activity and the time of death after GD exposure are experimentally essential observations for the research described in this protocol, use of anesthetic or analgesic compounds to alleviate GD induced pain/distress (which could either accelerate or delay the timing of these outcomes) would compromise the quality and utility of the results obtained.

4. No federal regulations mandate this procedure.

Protocol #7

1. A total of _24___ column “E” pigs were utilized in this study.

2. Painful procedure:

Exposure to phosgene and the development of pulmonary edema.

3. Justification:

Interfering with the natural progression of phosgene-induced injury would compromise our ability to use the model to assess medical countermeasures and countermeasure strategies. Alleviation of pain via use of analgesics is very likely to influence the same physiological mechanisms as phosgene and any potential therapeutics. Any administration of analgesics or anti-inflammatory drugs to reduce discomfort will confound experimental results and potentially mask the true outcomes of experimental countermeasure strategies. Administration of anesthetics or tranquilizers may also have respiratory depressant effects that would be contraindicated in this model.

4. No federal regulations mandate this procedure.
