51F0006
10/27/99

Protocol 3

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

2. Painful procedure: Guinea pigs will receive a convulsive dose of the nerve agent soman, which is thought to cause some pain and/or distress due to the intense physical activity caused by the seizure.

3. Justification: The use of anesthetics and/or analgesics would result in misleading information regarding the role of mast cell mediated anaphylactoid reactions/mast cell degranulation in acute organophosphorous poisoning. Anesthetics/analgesics also have profound effects on brain function that can interact with the toxicity of the nerve agent and thus complicate interpretation of the results.

4. No federal regulations mandate this procedure.

51F0006
12/21/99

1. A total of 231 column "E" guinea pigs were utilized in this study.

2. Painful procedure: Both species receive a convulsive dose of nerve agent which is thought (but not documented) to cause some pain and/or distress due to the intense physical activity caused by the seizure. There is a potential for the pain and/or distress to be relieved to some extent by the administration of one of the test drugs that successfully terminates the seizure.

3. Justification: Anesthetics and analgesics are known to have profound effects on brain function that can interact with the drugs of interest (Marshall and Wollman, 1985), the synthesis and release of brain neurotransmitters (Beleslin and Polak, 1965; Ngai *et al.*, 1978; Hanin, 1978), and/or the toxicity of the nerve agent (Clement, 1984) and thus complicate interpretation of the results. This is especially so since the purpose of the study is to model the pharmacological intervention a human nerve agent casualty would receive.

4. No federal regulations mandate this procedure.