

NOV 24 2015

### Column E Explanation

This form is intended as an aid to completing the Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay person as well as scientists.

1. Registration Number: **51-F-0019 (Edgewood Chemical Biological Center)**
2. Number **11** of animals used in this study.
3. Species (common name) **rabbits** of animals used in the study.
4. Explain the procedure producing pain and/or distress.

**Rabbits were exposed, intravenously, to lethal concentrations of new military grade chemical agents. These compounds caused toxic signs such as respiratory distress and convulsions in eleven (11) rabbits.**

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see item 6 below.)

**Anesthetics and analgesics were not used because their use could potentially mask or eliminate some of the toxic signs that must be observed to fully understand the toxicological aspects of the new compounds. Toxic signs and their severity, as well as time to death, had to be documented. The data had to be collected as accurately as possible to analyze the EC<sub>50</sub> (time to effects data), ED<sub>50</sub> (dose to effects data), and LD<sub>50</sub> (dose that is lethal to 50% of the animals tested).**

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency \_\_\_\_\_ CFR \_\_\_\_\_

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Obtained by Rise for Animals. Uploaded 07/04/2020

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1. Registration Number: **51-F-0019 (Edgewood Chemical Biological Center)**
2. Number **109** of animals used in this study.
3. Species (common name) **rabbits** of animals used in the study.
4. Explain the procedure producing pain and/or distress.

**Rabbits were exposed, via nose-only and whole-body inhalation, to lethal concentrations of military grade chemical agents. These compounds caused toxic signs such as gasping and bronchoconstriction to one hundred nine (109) rabbits.**

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see item 6 below.)

**During exposure, toxic signs were observed to determine a nose-only and whole-body concentration lethal to 50 percent of the population. Pre-treating the animals with analgesics was not an option because it could potentially affect the lethality or sub-lethal results through pre-exposure enhancement of liver metabolism. This potential metabolic enhancement is likely to shift the lethality or No Observable Adverse Effects Levels (NOAEL) results and render the study potentially invalid. Further, the progression of toxic signs was required to inform future studies investigating therapeutic compounds, as it allows for a definition of the therapeutic window. Analgesics will affect the timing and severity of onset of signs of exposure.**

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Agency \_\_\_\_\_ CFR \_\_\_\_\_