Column E Explanation

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1. Registration Number: **51-F-0019 (Edgewood Chemical Biological Center)**

2. Number **48** of animals used in this study.

3. Species (common name) **guinea pigs** of animals used in the study.

4. Explain the procedure producing pain and/or distress.

   Guinea pigs were exposed, via head-only inhalation, as well as intravenous and subcutaneous or intraperitoneal injections, of military grade chemical agents. These agents caused toxic signs such as respiratory distress and ocular effects in forty-eight (48) guinea pigs.

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.)

   The novel pharmaceutical compound was pre-administered as an experimental pain alleviation treatment for the animals, to examine the effectiveness of the compound as a pain treatment to riot control agents. Any other administration of analgesics or anesthetics could not be used, as their analgesic/sedative effects may have been mistaken for analgesia due to the novel compound. Any effect of the novel compound would then have been indistinguishable from the effect of the additional analgesic and/or anesthetic.

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):

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1. Registration Number: **51-F-0019 (Edgewood Chemical Biological Center)**

2. Number **218** of animals used in this study.

3. Species (common name) **guinea pigs** of animals used in the study.

4. Explain the procedure producing pain and/or distress.

   Guinea pigs were exposed, via nose-only and whole-body inhalation, to lethal and moderately sub-lethal concentrations of a military grade chemical agent. This compound caused toxic signs such as gasping and bronchoconstriction in two hundred eighteen (218) guinea pigs.

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.

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):

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1. Registration Number: **51-F-0019 (Edgewood Chemical Biological Center)**

2. Number **6** 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, dermally, to military grade chemical agents. These compounds caused toxic signs such as respiratory distress and convulsions in six (6) 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.)

   No anesthetics or analgesics were administered to the animals because the investigator needed to observe and describe all toxic effects produced by the test compounds.

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):

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1. Registration Number: **51-F-0019 (Edgewood Chemical Biological Center)**

2. Number **3** 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 three (3) 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 ECt_{50} (time to effects data), ED_{50} (dose to effects data), and LD_{50} (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):

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1. Registration Number: **51-F-0019 (Edgewood Chemical Biological Center)**

2. Number **299** 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, both dermally and intravenously, to lethal concentrations of military grade chemical agents. These compounds caused toxic signs such as respiratory distress and convulsions in two hundred ninety-nine (299) 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 ECt_{50} (time to effects data), ED_{50} (dose to effects data), and LD_{50} (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):

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1. Registration Number: **51-F-0019 (Edgewood Chemical Biological Center)**

2. Number **167** 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 sixty-seven (167) 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.

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):

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