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 persons* as *well* as *scientists.*

1. Registration Number: **74-R-0012**

2. Number of animals used in this study: **4**

3. Species (common name) of animals used in the study: **New Zealand White Rabbits**

4. What is the purpose of this study?
To feed ticks for the purpose of: (1) maintain tick colonies, (2) generate tick tissue, protein, DNA, and RNA specimens, and (3) testing the anti-tick vaccine efficacy of candidate recombinant tick vaccine antigens.

5. Describe what pain and/or distress occurred; and explain the procedure producing pain and/or distress:

The potential pain and/or distress associated with this study is due to the rabbits developing an immunological (allergic) response to the tick proteins which results in skin irritation and itching. This normally occurs after repeated tick feeding episodes. During tick infestation, Elizabethan collars are used to prevent rabbits from scratching off the tick containment apparatus. Repeatedly infested rabbits can develop immunity to tick saliva proteins. In severe cases this can cause skin irritation and itching. The formation of these reactions is limited by only having two tick feeding periods per animal.

6. 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:

The central goal of the research is to understand how ticks evade the host defense mechanism to allow the ticks to feed. By determining these mechanism we will be able to find important tick proteins that can be used to develop anti-tick vaccines. Artificial feeding of the ticks would not be a suitable alternative since we need an intact host immune system to determine the role of the tick proteins. Animals could be prevented from developing a resistance to tick feeding by injecting them with immune-suppressants; however this would compromise the results as determining how the tick proteins affect the host immune system is the point of the research. An Elizabethan collar is placed on the rabbits to prevent them from scratching their ears excessively and removing the protective stockinet. In addition, the rabbits are monitored twice daily to observe any unusual or excessive reaction to the ticks or the collars.

7. 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): **None**

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1. Registration Number: **74-R-0012**

2. Number of animals used in this study: **13**

3. Species (common name) of animals used in the study: **Guinea Pigs**

4. What is the purpose of this study?

   Coxiella burentii, the etiologic agent of Q fever, is a highly transmissible pathogen with significant risk for use as a biological agent of terrorism. Currently, there are no vaccines available for widespread use in the US, and those that are available in other countries may cause severe adverse reactions and require time-consuming testing prior to vaccination. A new vaccine is therefore needed that is both effective in preventing Q fever and safe for routine use. Recombinant proteins and soluble fractions from C. burnetii strain will be produced and used to immunize animals. Animals will subsequently be challenged with virulent C. burnetii and the safety and protectiveness of vaccine candidates will be determined.

5. Describe what pain and/or distress occurred; and explain the procedure producing pain and/or distress:

   Guinea pigs infected with Coxiella burentii can develop clinical disease and will experience fever, respiratory difficulty, and weight loss. Clinical disease is necessary to determine the effectiveness of vaccine candidates. All vaccination preps will be tested in mice prior to testing in guinea pigs. Guinea pigs will be monitored daily after infection for fever. Once animals have fever they will be monitored daily for fever, weight loss, and respiratory difficulties and scored using Karnofsky's scale designed for disease progression and stress in Guinea pigs infected with C. burnetii.

6. 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:

   The aims of the study are to analyze immune responses elicited from vaccination and the protection afforded after challenge. Administration of analgesics would compromise the experimental design by altering the immune response in these animals. Guinea pigs develop clinical disease and will be monitored daily after infection for fever. At the first signs of fever the animals will be classified as ill and will then have respiratory rates and weight taken on a daily basis. Animals will be removed from the study if their total Karnofsky score is equal/greater than 6 or if they have a score of 4 in any one category.

7. 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): **None**

30 NOV 2018

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1. Registration Number: **74-R-0012**

2. Number of animals used in this study: **7**

3. Species (common name) of animals used in the study: **Pigs**

4. What is the purpose of this study?
   Effect of sepsis on protein metabolism. The Primary significance of this project is the development of a new approach to nutritional support in sepsis that will promote and preserve muscle mass and have no adverse physiological effects.

5. Describe what pain and/or distress occurred; and explain the procedure producing pain and/or distress:

   Sepsis is induced by IV infusion of *Pseudomonas aeruginosa*. During induction of sepsis (1st 6 hrs.), pigs will develop a fever and may show clinical signs (chills, malaise, lethargy). Sepsis recovery begins after 6 hours by giving antibiotics and pain relief to mimic the human clinical condition.

6. 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:

   This sepsis/recovery model needs to be clinically relevant in order to translate the metabolic changes that we are studying to human situations. In most human clinical sepsis situations, treatment (including pain relief) is started 6 hours of the start of the septic condition (when typical symptoms are diagnosed.) Therefore, we do not give pain relief in the first 6 hours of the sepsis.

7. 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): **None**

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1. Registration Number: **74-R-0012**

2. Number of animals used in this study: **10**

3. Species (common name) of animals used in the study: **Pigs**

4. What is the purpose of this study?
To investigate the efficacy of new drug candidates for the treatment of an intestinal parasite (Cryptosporidium) that inhibits a protein called AccD6 within the parasite. Cryptosporidium is commonly found in contaminated water sources worldwide in both developing and highly developed countries. Cryptosporidium causes diarrhea in both humans and livestock and is the leading cause of waterborne disease among humans in the United States. It can be lethal in individuals with weakened or compromised immune system such as children, elderly, and AIDS patients. Currently, there are no fully effective drugs to treat this parasitic infection so if our novel drugs prove effective, they may be able to save lives.

5. Describe what pain and/or distress occurred; and explain the procedure producing pain and/or distress:

Animals challenged with cryptosporidium may exhibit self-limiting diarrhea and fever.

6. 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:

We are looking for signals of efficacy and those include the length of time the animal exhibits signs of clinical illness, fecal inconsistency, and oocyte shedding.

7. 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): **None**

30 NOV 2018