Optional Column E Explanation Form

93R0440

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.

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1. **Registration Number:** 93-R-0440 (formerly 93-R-044I)

2. **Number** 18 **of animals used in this study.**

3. **Species (common name)** Rabbit **of animals used in this study.**

4. **Explain the procedure producing pain and/or distress.**
   Two procedures could produce pain or distress in the animals. I) Aortic valve catheterization is performed via a cut-down over the right neck. However, general and local anesthesia are provided prior to and during the procedure, which is also performed in Category B animals. As the period of discomfort is brief and animals suffer no ill effects from it, additional analgesia has not been deemed necessary. II) The experimental infection that is produced with Staphylococcus aureus in this animal model may cause distress to a small proportion of the animals. Signs of infection appear at 18-24h after inoculation. Untreated, control rabbits are euthanized approximately 24h after inoculation, which minimizes the distress in these animals. Signs of infection abate with institution of antimicrobial agents in treated animals and generally resolve in two to three days. During the first two days of the experiment, supplemental fluid is administered to provide fluid replacement and some calories until the appetite returns. If fluid intake remains poor thereafter, fluid supplements are continued as needed. Food supplements such as carrots, lettuce, and greens are provided to encourage food intake and to help maintain normal flora.

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 question 6 below)
   Analgesics are not be used during the period of infection for the following reasons. 1) They are not necessary. Pain is not a prominent symptom of endocarditis. The chapter in Mandel's "Principles and Practice of Infectious Diseases" lists pain in association with endocarditis that occurs at various locations at a frequency of 10-15%. Pain is a more prominent feature of tricuspid valve (or right-sided) endocarditis, but the model is aortic valve endocarditis. Based on my experience with several hundred cases of endocarditis in humans, analgesics are rarely needed in the management of left-sided endocarditis. Also the protocol includes use of fluid supplementation and antimicrobial therapy, which ameliorate signs of the disease. 2) Analgesics also may alter the natural course of the disease, lead to over-sedation or respiratory depression, and thereby contribute to mortality, or have unanticipated interactions with antimicrobials. Administration of agents other than antimicrobials in a model of this type would be highly questionable scientifically and analgesic agents are not employed by any investigators using this model of infection.

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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1. **Registration Number:** 93-R-0440 (formerly 93-R-044I)

2. **Number** 32 **of animals used in this study.**

3. **Species (common name)** Rabbit **of animals used in this study.**

4. **Explain the procedure producing pain and/or distress.**
   The Committee on Animal Research (UCSF's IACUC) requested that these rabbits be categorized as Column E usage because they were exposed to tobacco smoke. This determination was based on the discomfort felt by humans in the room in which these rabbits are housed during the period of the exposure to second-hand smoke. However, it is not clear that this causes any physical distress to the rabbits. They are exposed to tobacco smoke for 8 hours per day, 5 days per week, for 10 weeks, and otherwise breathe clean air. Their food intake is the same as controls and their weight gain is the same as controls. They also have a drug placed in their drinking water which does not seem to cause any distress. Their water intake is the same as the controls. Thus, neither of the above appear to produce any distress and therefore no countermeasures appear necessary. Blood samples are drawn twice during the whole 10 week period. This is done by withdrawing blood from an ear vein with the rabbits in a restraining box for a short time. Again, there does not appear to be evident stress with the blood drawing.

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 question 6 below)
   Because the purpose of the study is to determine the comparative effects of angiotensin converting enzyme inhibitors and angiotensin receptor blockers on vascular function and atherosclerosis in cholesterol-fed rabbits exposed to second-hand smoke, additional fresh air would eliminate the exposure required to measure the effects. It is unclear that any pain or distress is caused by exposure to tobacco smoke or by drinking water with drug dissolved in it

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**_____