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: **93-R-0032**

2. Number of animals used in this study: **120**

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

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

   There is one protocol that uses rabbits for stroke research. The purpose of the research is to evaluate new therapeutics for the treatment of stroke. A minor surgery is performed under inhaled anesthesia to place a cannula into the common carotid artery near the internal carotid artery directed toward the brain. After the rabbit has recovered from surgery for 2-3 hours, it undergoes a conscious embolization procedure. Non-autologous blood clots are prepared from a donor rabbit. Small or large blood clots are prepared and suspended in saline for injection. The clots, which are labeled with non-radioactive gold microspheres (to allow for tracking of clot deposition in brain), are then injected through the carotid catheter into the brain to induce a stroke, either representing a lacunar small vessel stroke or a large vessel stroke.

   The Principal Investigator (P.I.), reported to the Institutional Animal Care & Use Committee (IACUC) that, although this procedure is done in conscious rabbits, it is his opinion that strokes are not painful since the brain does not have nociceptive receptors, and ischemic strokes are not associated with pain in humans, and in animals that have previously undergone the procedure, there is no indication by observation of any pain with the embolization.

   Nevertheless, the IACUC requested additional information about the rabbits' responses to the embolization procedure. The P.I. noted that the typical initial response of a rabbit to the stroke is vocalization in some rabbits; nystagmus occurs in many rabbits; and occasionally rabbits will kick in the restrainer, briefly. The P.I. noted that he does not think that the vocalization is a result of the rabbit being in pain or distress, but rather a new sensation of a clot being lodged in a vessel in the brain.

   The IACUC required the P.I. to perform a pilot study to compare the results of the embolization procedure performed in isoflurane anesthetized rabbits versus unanesthetized rabbits. In addition, IACUC members have observed the procedures.

5. Attach or include an explanation with the reasons(s) for why anesthetics, analgesics and tranquilizers could not be used. (For Federally mandated testing, see item 6 below.)

   A presentation to the IACUC by the P.I. included several references that noted that translational stroke research in "animal models" should simulate as closely as possible "human stroke," which is frequently caused by permanent vascular obstruction by a blood clot (i.e., an embolic stroke). Stroke victims are rarely anesthetized at the time of their embolic stroke. An animal model that limits the use of any anesthetic closely simulates human stroke will lead to successful identification of drugs or therapies to treat human stroke. To accurately model human stroke, the use of anesthetics should be limited. Anesthetics can interfere with the pathophysiological mechanisms and stroke cascade. Research indicates that anesthetics will obscure or interact (negative, additive or synergistic) with the drug being investigated in any particular study.

   Based upon the Pilot study to compare the results of the embolization procedure performed in isoflurane anesthetized rabbits versus unanesthetized rabbits, it was determined that the protocol would require the use of many more rabbits to achieve statistical significance, if the rabbits are anesthetized for the embolization.

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:
   Not Applicable

7. We have no objections to the release of our Annual Report Attachments as received and do not intend to seek judicial review to bar release of our facility's Annual Report of Research Facility Column E Explanation(s) and/or Exception(s) for the 2016 USDA Report [FOIA Exemption 4, 5 U.S.C. 552(b)(4)].