

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: **52-R-0124**
2. Number of animals used in this study: **3**
3. Species (common name) of animals used in the study: **Rhesus macaques**
4. Explain the procedure producing pain and/or distress.

We hypothesize that opioid dependence and withdrawal are critical in the addictive properties of opioid drugs such as heroin and prescription opioids, and consequently, intermittent opioid withdrawal is critical to the proposed scientific experiments. Dependence is produced by chronically treating animals with an opioid or allowing animals to self-administer opioids and withdrawal is produced by briefly terminating opioid treatment or self-administration access conditions. We recognize that opioid withdrawal may be stressful, and we propose to minimize the impact of this potential stressor in the following ways. First, one goal of the studies is to determine the minimal degree of dependence/withdrawal necessary to produce the scientific endpoint. Second, we limit the frequency of opioid withdrawal to ≤ 2 times per week. Third, we will visually monitor animals three times during the withdrawal period to observe and document overt signs of opioid withdrawal using a custom opioid withdrawal check sheet designed for these studies. Importantly, this check sheet provides explicit instructions for clinical intervention in the event that severe withdrawal signs are observed.

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 the test results. (For federally mandated testing, see Item 6 below).

The distress produced by this procedure is the scientific end-point being measured. The use of anesthetics, sedatives, and analgesics would interfere with scientific dependent measure, as these compound classes would obscure our evaluation of the opioid withdrawal signs. In fact, one

goal of our studies is to test compounds for their ability to reduce overt withdrawal signs and withdrawal-associated changes in behavior.

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)

Not Applicable