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: **5**

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

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

   Withdrawal from novel opiate formulations (novel drug or known opiate combined with adjunctive therapy) in order to assess the propensity to produce physical dependence.

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 use of anesthetics, sedatives or analgesics would all interfere with evaluation of the withdrawal signs that characterize physical dependence.

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)

   The results from our testing may be used by the FDA.

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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.

   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.

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

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Description of Exceptions to Applicable Regulations

- The IACUC has approved one exception (13 rhesus macaques affected) that pertains to cage size for non-human primates. It has allowed a cage height of 30" to 31.5" (cages taper from front to back) for rhesus macaques up to 15 kg in weight. The "Guide" recommends a cage height of 32" for Group four animals. The design of the cage compensates for the height difference by providing 9 square feet of floor space for one animal rather than the 6 square feet recommended. Multiple veterinary staff report that in their opinion there is no impact on the animals' physiological or psychological well-being.

- The IACUC has approved a Non-Human Primate (NHP) protocol for an exception (23 NHPs affected) to the standard 2-week cage wash interval. Cage washing can disrupt chronic experiments for two reasons. First, NHPs have to be disconnected from drug infusion equipment while they are transferred from one cage to another. This will interrupt delivery of treatment medications. Second, NHPs are anesthetized with the anesthetic ketamine to enable their transfer from one cage to another. Ketamine is an antagonist at NMDA (*N*-methyl-D-aspartate) type glutamate receptors, and this drug can disrupt learning or interact with treatment drugs. To prevent cage-wash related disruption of chronic treatment studies, the PI requested permission to wash cages at intervals consistent with their studies (i.e. during recovery periods) and at intervals up to 1 month. An added complication is that NHPs are housed in racks holding two cages each. Accordingly, cage washing is least disruptive when it can be accomplished at a time when both NHPs on a rack are in a recovery period. When the cage wash interval exceeds a two-week interval, the PI staff will take steps to assure as clean a cage as possible.