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Reference: Registration No. 64-R-0001, USDA Annual Report of Research Facility

FY 2020 APHIS Form 7023 Column E Explanation:

- 16 rhesus macaques (*Macaca mulatta*) and 8 African Green Monkeys (*Chlorocebus aethiops*) on SARS-CoV-2 vaccination, challenge, and therapeutic efficacy studies experienced unrelieved pain and/or distress subsequent to virus challenge. The SR IACUC authorized the withholding of analgesics and anti-inflammatories based on the justification provided by the Study Director who stated that the animals which experienced SARS-CoV-2 related illnesses could not be treated with analgesics, as this would mask the clinical indicators of disease indicative of infection, could inadvertently enhance disease progression, and interfere with the viral pathogenesis, thus compromising the scientific integrity of the work. Narcotic analgesics were shown to interfere with the mechanism(s) responsible for interferon production (Geher, W.F. et al., J. Toxicol Environ Health 2:577-582, 1977; Hugh, C.Y. et al., Proc Soc Exp Biol Med 142:106-111, 1973). Moreover, opioids can suppress Natural Killer (NK) cell activity (Berlin, B., et al. Brain Behav Immun 3:129-137, 1989). Also analgesics including buprenorphine can cause histamine release (Marone, G., et al. Int Arch Allergy Immunol 124:249-252, 2001; Stellato, C., Ann NY Acad Sci 406:32-47, 1995). Histamine is a well-known inflammatory mediator and plays a central role in the pathogenesis of allergic and inflammatory diseases by modulating vascular and airway response. To this point, the use of analgesics and antihistamines could hinder the immunological response and pathogenesis to SARS-CoV-2 negating the purposes of this research.
- 1 cynomolgus macaque (*Macaca fascicularis*) on a monkeypox challenge study experienced unrelieved pain and/or distress subsequent to virus challenge. The SR IACUC authorized the withholding of analgesics and anti-inflammatories based on the justification provided by the Study Director who indicated that treatment would interfere with the course of infection and the development of signs of disease and that the development of disease is requisite to this model in order to test the efficacy of antiviral drugs and potential vaccines against a lethal dose challenge of orthopox virus infection.