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RABBITS **Explanation of Category E:**

Title	Explanation of the Procedure	Scientific Justification	Regulations Requiring this Procedure	Total
Pilot efficacy and impact on titers of (b) (4) in (b) potency test	This was a study to assess impact on titer if an NSAID (b) (4) was provided to alleviate pain from (b) (b) (4) vaccination. One animal had continuous lameness throughout the study despite treatment.	This is not a Category E protocol and pain was not expected on this test.	CVB notice 12-12 advocates to pursue 3Rs iniatives to address pain and distress for codified tests.	1
Quality Control Umbrella for Serology Testing in Rabbits of Serial Release and In-Process Antigens	One animal for XXXvirus potency resulted in forelimb lameness after vaccination and was deemed painful. Since treatment could confound study outcome, the rabbit was not treated, however it continued to eat and maintain body weight.	This is not a Category E protocol and pain was not expected for this test.	The XX test is in compliance with the (b) (4)	1
Quality Control Umbrella for Serology Testing in Rabbits of Serial Release and In-Process Antigens for (b) (4) (b) (4)	Rabbits receive a large volume of vaccination IM in one or both rear limbs, and have been deemed painful due to reluctance to move, or lameness.	This is a codified test requiring further investigation on any intervention to assure it does not have an impact on TEST outcome. Internal evaluation for pain medication is ongoing, however the test is intended to eventually move to an *in-vitro assay.*	USDA (APHIS) (b) (4) and Outlines of Production (b) (4)	291
				293

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HAMSTERS **Explanation of Category E:**

Title	Explanation of the Procedure	Scientific Justification	Regulations Requiring this Procedure	
Evaluation of Virulence Status of Isolates of (b) (4) in Hamsters	These two tests were to evaluate the virulence and optimal challenge dose for the XXX isolates of (b) (4) serovar	All these tests state that moribund animals exhibiting clinical signs consistent with the disease and were unable to rise or move will be humanely euthanized and considered as deaths. However, despite the additional daily observations, these reported had rapid progression of disease and were found dead, therefore are categorized as E.	NA	**25**
(b) (4) Challenge Dose Titration in Hamsters			NA	
(b) (4) Potency testing for Reference vaccine qualification through subcutaneous inoculation.	These animals in this study are required for evaluating the potency of a Reference vaccine via subcutaneous route in compliance with the CVB letter, (b) (4)		CVB letter, (b) (4)	**25**
(b) (4) Passage Process in Hamsters	This passage process is necessary to maintain virulence of (b) (4) organisms for challenge preparation for use in the below potency test.		USDA (APHIS CVB): (b) (4)	**1851**
(b) (4) Hamster Potency Tests	This tests are required by APHIS - Center for Veterinary Biologics (CVB) for the release of vaccine serials. These are tests are prescribed in Title 9 of the Code of Federal Regulations.			**5662**
				7563

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CATS **Explanation of Category E**

Title	Explanation of the Procedure	Scientific Justification	Regulations Requiring this Procedure	Total
Qualification of Elanco Animal Health's Feline XXXX Reference Vaccine for XXXXX	Four (4) control cats had significant oral ulcerations, in which two also had large swellings and skin ulcerations externally on the muzzle, which these were deemed locally painful for the animals, thus Category E.	Interpretation of the results of this study depends on clinical signs of disease. Medications will be withheld for only as long as scientifically necessary as not to impact outcome.	This Reference Requalification study was submitted for review by CVB, with response (from Dr. (b) (4) [redacted] specifically stated "please consider using more than 10 vaccinates and controls in order to increase the precision of the test and reduce the possibility of an invalid study." That study was then submitted using 30 cats and was approved for use by CVB .	4
				4

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Dogs **Explanation of Category E**

Title	Explanation of the Procedure	Scientific Justification	Regulations Requiring this Procedure	Total
Canine XXXX Virus Alterative Route Challenge Model Development in Dogs	Symptoms exhibited in these dogs, such as diarrhea and inappetence, are considered distressful for the animals based on the duration seen, therefore are categorized as E.	Intent of this study was to humanely euthanize when animals progressed to the expected neurological signs, however this study did not exhibit those signs therefore other clinical signs observed were recorded to build a case definition for XXXX disease.	NA	25
Proof of Principle Study to Evaluate the Immunogenicity of XXXX Vaccine in Dogs with XXX Challenge	One dog on this study was found dead and another with uveitis and inappentence which is deemed painful/distressful.	Proof of Principle Study	NA	2
Proof of Principle Study to Evaluate the Immunogenicity of Three Different XXX vaccines of XXXX with XXX Challenge in Dogs	These dogs were symptomatic of (b) (4) disease and despite additional welfare daily checks, dogs died before intervention.	Proof of Principle Study	NA	11
Proof of Principle Study to Evaluate the Immunogenicity of Three Different XXX vaccines of XXXX with XXX Challenge in Dogs	A control animal with ongoing symptoms of XXXX (disease) including photophobia and corneal edema which is deemed painful, however ended with normal observation on last day of study.	Proof of Principle Study	NA	1
				39

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GUINEA PIGS **Explanation of Category E :**

Title	Explanation of the Procedure	Scientific Justification	Regulations Requiring this Procedure	
Guinea Pig Potency with (b) (4)	Per 9CFR - This test involves a vaccination and challenge phase which requires control animals to be challenged at D14-15 with 100 LD_{50} of the (b) (4)	The validity of this test requires death in the control animals.	USDA (APHIS-CVB): (b) (4)	**6**
Guinea Pig Safety Using Intramuscular Administration	This test requires a large volume (1 ml) of vaccine administered by the IM route into each rear limb, resulting in pain for the animals.	The use of analgesics may mask an adverse reaction that could affect the outcome of the test.	Outlines of Production and (b) (4) test specifications	**26**
				32