TERF
Thoroughbred Education Research Foundation

Grant Application

Today's Date June 15, 2025	Name of 501 (c)(3) Organization The Trustees of the University of Pennsylvania		
Federal Tax-Exempt ID# 23-1352685			
Year Established 1740	Amount Requested $ **20,370**		
Name of Executive Director	Elizabeth Peloso - Office of the Vice Provost For Research		
Mailing Address	3541 Walnut St Franklin Bldg. 5th Floor		
City Philadelphia	State PA	ZIP 19104-6205	
Email Address PENNAORS@lists.upenn.edu	Work Phone # 215-898-7293		
Organization's Website https://researchservices.upenn.edu			

Copy and paste the link to your organization's most recent filed IRS Financial Statements (#990):

IRS Financial Statements (#990) link: https://www.finance.upenn.edu/financial-reports/

Note: all other supporting documents, along with your completed application, email to: office@terfusa.org

Farm/Facility Name Department of Clinical Studies, New Bolton Center, School of Veterinary Medicine

City	State	ZIP
Kennett Square	PA	19348

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City	Kennett Square	State	ZIP
		PA	19348

Contact Name and Title	Bernd Driessen, DVM, PhD, Dipl. ACVAA, Dipl. ECVPT, Professor of Anesthesiology, Head of the Section of Anesthesia

Work Telephone	484-849-1308	Email Address	driessen@upenn.edu

Provide a response to each question below:

1. Brief mission statement and describe the distinguishing features of your organization that supports the mission of TERF and the relevance to this proposal.

The University of Pennsylvania's New Bolton Center at the School of Veterinary Medicine is an internationally renowned institution providing high-quality care for equine patients of all genres, ranging from ponies and pleasure horses to elite equine athletes. The hospital carries one of the largest caseloads of any large animal teaching hospital and offers advanced diagnostic and surgical services delivered by highly trained, board-certified veterinary specialists.

The faculty of the anesthesia service has a long-standing record in developing new techniques of pain management and studying the pharmacological profile of novel anesthetic and analgesic drugs. Over the past 5 decades, a strong collaboration has emerged between the anesthesia group and the Pennsylvania Equine Toxicology and Research Laboratory (PETRL), which is affiliated with the University of Pennsylvania and performs equine drug testing for racetracks in the Commonwealth. Under the leadership of the former head of the Section of Anesthesia at New Bolton Center, Dr. Larry Soma, PETRL emerged as the leading laboratory performing equine drug testing for the Commonwealth racetracks and beyond. The laboratory continues to develop novel methods for screening, confirming, and quantifying the presence of therapeutic and illegal drugs in equine plasma or urine samples. The collaboration with the analytical chemistry specialists at PETRL is an essential component for the proposed study.

2. Briefly outline 3-5 goals for the requested funds and how these goals support your mission.

i. Determine in horses the pharmacokinetic properties including uptake into the blood (oral bioavailability), time to peak blood concentration, plasma half-life, metabolic pathways, and elimination from the body of suzetrigine (SUZ, Journavx®), the first selective sodium channel blocker (= local anesthetic) most recently approved by the Food and Drug Administration (FDA) for oral treatment of moderate to severe acute pain in human patients.

ii. Determine the analgesic (antinociceptive) efficacy and potential adverse effects of SUZ administration in horses.

iii. Develop an effective analgesic dosing regimen based on the pharmacokinetic data obtained and SUZ's pharmacological actions and duration of effect.

3. Provide a detailed description of the proposed project, how it is related to the mission of TERF and how it will impact the health and welfare of the horse. *(Note: research applications should be understandable to a non-scientific audience and include sufficient detail and rigor for the scientific reviewers).*

Title: Pharmacokinetics of suzetrigine and antinociceptive effects after single dosing in horses – a pilot study.

A. Outline of problem and justification for the project

In horses, there is a high unmet need for safe and effective pain medications that lack the risk of serious adverse effects and that can be administered orally (PO). The drugs currently commonly administered for systemic pain treatment in horses belong to four different pharmacological classes: non-steroidal anti-inflammatory drugs (NSAIDs; Banamine®, Butazolidin®), opioids, α_2-agonists (e.g., Rompun®, Detomidor®), and local anesthetics (Driessen and Zarucco 2013; Sanchez and Robertson 2014; Guedes 2017). Except NSAIDs, none of the other analgesics are available for oral administration. In addition, those drugs are associated with substantial side effects involving the central nervous, gastro-intestinal, and/or the cardio-vascular system, therefore limiting their suitability for long-term pain treatment (Driessen and Zarucco 2013; Sanchez and Robertson 2014; Guedes 2017). Treatment with NSAIDs is also frequently associated with adverse effects, manifesting as gastro-intestinal ulceration and/or renal failure, thus limiting their use in equine patients (Driessen and Zarucco 2013; Guedes 2017). Horses with severe and persistent inflammatory diseases often display increased pain sensitivity (hyperalgesia) and may develop neuropathic pain (frequently described as burning, shooting, or tingling sensations) over time and are then treated with additional therapeutics such as gabapentin and pregabalin or systemic ketamine, however, with mixed efficacy (Driessen and Zarucco 2013).
Suzetrigine (SUZ, Journavx® – Vertex Pharmaceuticals, Boston, MA, USA) is the first selective sodium channel blocker recently FDA-approved for systemic treatment of moderate to severe acute pain in humans (Osteen et al. 2025). Commonly used local anesthetics that non-selectively block sodium channels in peripheral nerve fibers must be injected into the vicinity of peripheral nerves to elicit their local anesthetic effect. However, if absorbed into circulation or even administered intravenously, they may cause central nervous and cardiac toxicity. In contrast, SUZ is a potent and selective blocker of only the voltage-gated sodium channel subtype 1.8 (NaV1.8). This channel is predominantly located in peripheral small-medium diameter, nociceptive afferent C and A_δ nerve fibers that participate in pain signaling from the periphery to the brain, making it a particularly desirable therapeutic target for suppression of pain (Caterall 2012; Ramachandra et al. 2013; Osteen et al. 2025). The channel is also expressed in non-nociceptors, including large diameter A_β sensory nerve fibers that under physiological conditions transmit proprioceptive and touch/vibration signals (Ramachandra et al. 2013), but are also thought to be critically involved in the development of neuropathic pain (Devor 2009). Since the NaV1.8 channel is present only in the peripheral nervous system of mammalian species, SUZ lacks any appreciable central nervous or cardiotoxic activity (Osteen et al. 2025). In addition, SUZ is administered orally (Osteen et al. 2025).

In surgical patients with moderate to severe pain, an initial oral SUZ dose of 100 mg followed by 50 mg twice daily produces significant pain relief when compared with placebo, without any major side effects (Jones et al. 2023; Osteen et al. 2025; Hu et al. 2025). Likewise, SUZ administered for up to 14 days to surgical and non-surgical patients with moderate to severe acute pain produces clinical analgesia (Osteen et al. 2025). Only mild adverse reactions have been noted upon repetitive administration, including itching, muscle spasms, elevated blood creatine phosphokinase levels, and rash (Hu et al. 2025).

Given the clinical efficacy of SUZ in human patients and the favorable side effect profile, its use as part of a multi-modal analgesia regimen in the equine patient may offer important advantages, particularly in horses undergoing surgical procedures that are associated with moderate to severe

pain that lasts for up to 72 hours. The drug may also further facilitate surgical interventions in the non-anesthetized and only sedated horse, thereby preventing the risk of complications associated with anesthesia in horses, which occur with higher frequency compared to small animal species.

According to a current literature search in all databases, there is no published report on the pharmacokinetic (PK) and pharmacodynamic (PD) properties and the metabolites of SUZ in the horse. Furthermore, determining in a pilot study the PK profile of this drug is important for developing in the future proper therapeutic dosing regimens for use in horses and minimizing conflicts with medication rules in the racing horse industry.

B. Specific Aims/Hypotheses

Hypotheses:

1. In the otherwise non-medicated conscious and overnight fasted horse, SUZ, when administered intravenously (IV) and orally (PO) at a dose of 2 mg/kg, will have a similar PK profile as described in monkeys (Jones et al. 2023), and will produce plasma concentrations known to be associated with an effective blockade of NaV1.8 channels and hence pain relief.

2. In the otherwise non-medicated conscious and overnight-fasted horse, SUZ, when administered IV and PO at a dose of 2 mg/kg, will exhibit antinociceptive effects towards thermal stimuli.

Specific aims:

1. To determine the PK parameters of SUZ (including maximum drug concentrations in blood plasma, distribution and elimination half-lives, volume of distribution, clearance, and oral bioavailability) following IV and PO administration of a 2 mg/kg body weight dose using a randomized three-way cross-over study design including a placebo group with a washout period of 2 weeks after each treatment. Concentrations of the drug and its metabolites in plasma and urine will be measured by using a liquid chromatography-mass spectrometry (LC-MS) technique adapted from that previously described by Zhang et al. (2024), and standard compartmental and non-compartmental analyses will be applied to model drug kinetics.

2. To measure the thermal nociceptive thresholds (pharmacodynamic (PD) data) before and repeatedly following SUZ administration by the IV and PO routes of administration or placebo (saline) administration. Pharmacometrics (i.e., PK/PD modeling) will correlate the PK data with the simultaneously recorded PD (pain relief) data.

3. To compare the experimentally obtained data for SUZ with published information in humans, primates, and other experimental animals regarding the pharmacokinetic and pharmacodynamic profile of SUZ in the horse.

C. Experimental Approach

1. Materials and methods

Research facilities to be used

Research barn at New Bolton Center and PA Equine Toxicology & Research Laboratory (PETRL).

Study design

A randomized placebo-controlled blinded 3-way cross-over study.

Animals

Three healthy Thoroughbred horses of moderate age range and with a median body weight of 500 kg will be enrolled. The horses will be fasted overnight before drug dosing but maintain free access to water. Hay will then be reintroduced 1 hour after the IV or oral dose is administered. Free access to water is permitted throughout the study.

Animal instrumentation and data recording

On the day before experimentation, in all horses a 3 × 3 cm site over the left and right withers (Location A), cranial (Location B) and caudal (Location C) abdominal areas, the area over the tuber coxae (Location D) and over left and right pelvic limb dorsal pastern regions (Location E) will be clipped and shaved (see Figure 1 below) in preparation for placement of sensors of the wireless thermal threshold (TT) testing system.

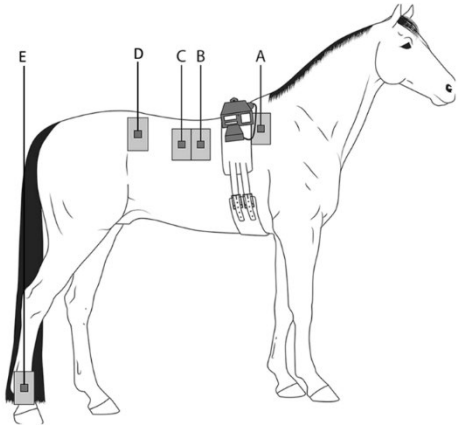

Figure 1. Sites of thermal (pain) threshold testing.

On the morning of the study, both jugular veins will be catheterized using aseptic technique for drug administration and blood collection, respectively. A urinary catheter will be inserted into the bladder and attached to a collection bag to allow continuous urine sampling.

Thermal threshold testing

After IV and urinary catheter placement, each horse will be fitted with a wireless TT testing device ([Wireless Thermal Threshold Testing System [WTT 1]; Topcat Metrology Ltd, UK), which will be attached to the back of the horse with a belt and Velcro straps. Thermal probes will be placed over the pre-prepared sites. Contact with the skin over the withers will be maintained using air bladders pressurized to approximately 80 mmHg. After equilibrating to skin temperature, the heating rate will be set at 0.6 °C/second for stimulation and the cut-out temperature will be set at 55 °C as described by Poller et al. (2013). Detection of thermal sensation will be recorded when the horse lifts the limb, looks at the limb, by skin twitching (cutaneous trunci muscle reflexive movement), or movement of head and neck toward the stimulated side. The temperature at the time of response to stimuli will be recorded as thermal sensation threshold (TST) for each sensor location A-E. If no response is noted and the cut-out temperature is reached, a temperature of 56 °C will be recorded for data analysis (Poller et al. 2013).

Experimental protocol and measured parameters

Each horse will be tested after IV SUZ, after PO SUZ, and after IV placebo (saline; IV SAL) administration in randomized order. Drug and placebo preparation and administration as well as blood collection during IV SUZ or placebo infusion will be performed by a person unrelated to the study investigators, who remain blind until the quantitative analysis of SUZ in the plasma and urine samples has been completed.
All experiments will begin at 8:00 AM EST to minimize variation imposed by circadian rhythm changes, which have been identified in horses. Thermal nociceptive testing for each location will be performed at 120 (t = -120 min), 90 (t = -90 min), and 60 (t = -60 min) before drug administration.
At t = 0 min, 2 mg/kg body weight of SUZ will be administered intravenously or via nasogastric tube or a placebo (saline, SAL) will be administered. The SUZ solution (50 mg/mL) for IV administration will be subject to internal quality control using the analytical technique described below. The 2 mg/kg dose will be diluted in 500 mL saline (0.9% NaCl) and SUZ or placebo in controls infused over 30 min at 16.7 mL /min to avoid severe or unpredicted responses to drug administration. The orally administered solution will be prepared by suspending crushed SUZ tablets in 10 mL of water and 5 mL of molasses in a 60-mL dose syringe. This suspension will be delivered directly into the stomach via a nasogastric tube and followed by water to ensure complete medication administration.
In all animals, nociceptive threshold (TST) data will be recorded at t = 30 min and 1-, 2-, 4-, 6-, 8-, 10-, 12-, and 24-hours post drug or placebo administration.
In the IV SUZ and IV SAL groups, venous blood samples will be collected at times 0 and 2-, 4-, 6-, 10-, 15-, and 30-minutes during the infusion of SUZ or placebo, and 2-, 4-, 6-, 10-, 15-, 30-, 45-minutes and 1-, 2-, 4-, 6-, 8-, 10-, 12-, 16-, 20-, 24-, 36- and 48-hours post-infusion. In the PO group, blood samples will be collected at times 0-, 2-, 4-, 6-, 10-, 15-, 30-, 45-minutes and 1-, 2-, 4-, 6-, 8-, 10-, 12-, 16-, 20-, 24-, 36- and 48-hours after PO dosing. Samples will be transferred into tubes containing heparin sodium as an anticoagulant. Blood samples will be centrifuged (2,500 g for 15 min) to obtain plasma. Aliquots of 2 mL plasma will be immediately frozen at -80 °C and later stored at -80 °C until analyzed. Each aliquot of plasma will be used once to eliminate any effect of freeze-thaw cycles on the concentration of SUZ in the sample.

Total volume of urine collected at t = 0, 1-, 2-, 3-, 4-, 6-, 8-, 12-, 16-, 20-, 24-, 36-, and 48-hours following IV SUZ and SAL infusion, respectively or after PO SUZ administration will be measured. Aliquots of 2 mL of urine will be immediately frozen at -80 °C and later stored at -80 °C until analyzed. Each aliquot is used once to eliminate any effect of freeze-thaw cycles on the concentration of SUZ.
There will be a 2-week washout period between IV SUZ, PO SUZ, and IV SAL administrations.
All plasma and urine samples will be analyzed for SUZ and metabolites using an LC-MS technique to be established at the PA Equine Toxicology & Research Laboratory based on a previously described technique (Zhang et al. 2024).

2. Pharmacokinetic (PK) data analysis

Both linear compartmental and non-compartmental analyses (NCA) will be conducted to estimate PK parameters of SUZ and metabolites in plasma and urine using the current WinSAAM modeling software (University of Pennsylvania, Kennett Square, PA). Only SUZ plasma concentrations greater than the respective lower limit of quantification (LLOQ) for the assay will be included in the PK analysis.

3. Statistical analysis

Data analysis will be performed by Dr. Darko Stefanovski who is a statistician at the University of Pennsylvania's School of Veterinary Medicine. All statistical analyses will be conducted with Stata 18MP, Stata Corp., College Station TX, with two-sided tests of hypotheses and a p-value < 0.05 as the criterion for statistical significance unless otherwise specified. Descriptive analyses will include the computation of means (with 95% confidence intervals [95%CI]), standard deviations, medians, interquartile ranges (IQR) of continuous variables, and tabulation of categorical variables. Normal distribution tests (Shapiro-Wilk test) will be performed to determine the extent of skewness of continuous data. Frequency counts and percentages will be used to summarize categorical variables.
Spearman rank correlation will be used to assess the association between PK kinetic parameters and outcomes of interest. As part of inference statistical analysis for specific aim 3, an interactive t-test will be used to compare previously published values of various PK parameters of SUZ in humans and other species and the estimates generated in horses.

D. Expected Results

We recently treated a horse with clinically apparent headshaking, a disease believed to be caused by trigeminal neuropathy and eliciting chronic (neuropathic) pain, multiple times with SUZ at a dose of 2 mg/kg PO. Within a few hours of administration, the animal's pain behaviors stopped and returned each time when drug treatment was discontinued. Therefore, we believe that SUZ in this oral dose produces noteworthy analgesia. However, only a systematic investigation will validate this assumption and provide data to allow the development of a proper dosing regimen for clinical practice. If successful, this pilot study may open a new avenue toward a more comprehensive investigation in horses and hence lead to better pain management in the equine with reduced adverse effects.

4. Provide a timeline detailing the expected progress of the project and specific milestones.

i. Months 1 - 3: Establishing and validating an LC-MS analytical technique at the PETRL for detection and quantification of SUZ in plasma and urine samples.
ii. Month 4: Recruitment/acquisition of horses for the study.
iii. Month 5: Study preparation, purchase of disposables, SUZ, and other consumables.
iv. Months 6-9: Performing experiments, data collection, sample processing at the PETRL.
v. Months 9-10: Data analysis including statistical analysis
vi. Months 11-12: Summary of results and main findings, writing of study report/publication.

5. Provide a detailed budget for the projected use of the funds. *(Note: no funds will be provided for administrative overhead or capital spending; TERF reserves the right to modify funding based on foundation requirements)*. Attach budget to submitted proposal as needed.

Boarding costs:	
- 42 $ per horse per day	
- 3 horses in 3 trails with 3 boarding days/horse/trial = 27 days	
- 27 days x 42 $ =	1,134 $
Subtotal	1,134 $
Drugs:	
- Suzetrigine oral (2 mg/kg = 20 x 50-mg tbl./horse x 3 x 16 $/tbl.)	960 $
- Saline 500 mL x 6 for SUZ IV and placebo IV groups	30 $
- Saline 1L x 9 for heparinized flush solution	38 $

- 27 vials heparin (1000 IU/mL) heparinized flush solution		54 $
Subtotal		1,082 $
Disposables:		
- 18 IV catheters, 3 " extension lines and caps (codes 600164, 600509,602239)		316 $
- 18 urinary catheters (Code 9289) & extension (code 3288)		353 $
- 18 urine collecting bags		105 $
- 6 infusion sets		42 $
- 336 heparin sodium tubes		336 $
- 672 plasma/urine sample freezer tubes		202 $
Subtotal		1,354 $
Chemical analysis:		
Plasma samples		
- Total number of plasma samples per horse in group SUZ IV:	26	
- Total number of plasma samples per horse in group SUZ PO:	20	
- Total number of plasma samples per horse in group SUZ PLACEBO:	26	
- Total number of urine samples per horse in group SUZ IV:	13	
- Total number of urine samples per horse in group SUZ PO:	13	
- Total number of urine samples per horse in group SUZ PLACEBO:	13	
Total number of plasma samples per horse for the study: 72		
Total number of urine samples per horse for the study: 39		
SUZ solution sample for internal quality control: 1		
Total number of samples for all 3 horses in the experiment:	336	
Chemical analysis per sample		50 $
Subtotal		16,800 $

The LC-MS method for the analysis of all plasma and urine samples will be developed and validated by the Pennsylvania Equine Toxicology & Research Laboratory (PETRL) with funding from the Commonwealth of Pennsylvania.

Total	**20,370 $**

6. Provide a list of all other sources of funding and the amount(s) received.

Funding for establishing an LC-MS analytical technique at the PETRL laboratory for detection and quantification of SUZ in plasma and urine samples and immediate sample processing is provided by the Commonwealth of Pennsylvania and its annual appropriation to PETRL. If the manufacturer of suzetrigine (Vertex Pharmaceuticals, Boston, MA, USA) will not provide the drug as an injectable solution, 3 g of suzetrigine will be purchased from AmBeed Chemicals (Buffalo Grove, IL, USA) and prepared as an injectable solution (50 mg/mL) by a compounding pharmacy in Pennsylvania.

7. Briefly summarize your charity's past public education research efforts.

Not applicable.

8. If you received funding from TERF previously, describe how these funds were used and outcomes achieved. Include any relevant publicity your charity received relating to the funding. (I.e.: media coverage, such as news articles, scientific publications, provide links to copies, as appropriate).

Not applicable.

9. List other organizations or major contributors that have provided funding to your organization in the last calendar/fiscal year. For research grants, provide a list of all current funding relating to your current proposal.

   Not applicable.

10. Name a responsible person with whom TERF may communicate regarding specific questions and who will be responsible for follow-up information regarding the project.

    Dr. Bernd Driessen

11. Provide appropriate references to support the proposed research.

Driessen B, Zarucco L (2013) Treatment of acute and chronic pain in horses. In: Pain Management in Veterinary Practice. Eds Egger C, Love LC, Doherty TJ, Wiley-Blackwell, Ames, IA.; pp. 323ff. (DOI:10.1002/9781118999196)

Sanchez LC, Robertson SA Pain control in horses: What do we really know? EVJ 2014; 4:517-523 (https://doi.org/10.1111/evj.12265)

Guedes A. Pain Management in Horses. Vet Clin North Am Equine Pract 2017, 33:181-211. (doi: 10.1016/j.cveq.2016.11.006)

Osteen JD, Immani S, Tapley TL, Indersmitten T, Hurst NW, Healey T, Aertgeerts K, Negulescu PA, Lechner SM. Pharmacology and mechanism of action of suzetrigine, a potent and selective NaV1.8 pain signal inhibitor for the treatment of moderate to severe pain. Pain Ther 2025, 14:655-674 (doi: 10.1007/s40122-024-00697-0)

Catterall WA. Voltage-gated sodium channels at 60: structure, function and pathophysiology. J Physiol. 2012, 590(11):2577-2589

Ramachandra R, McGrew SY, Baxter JC, Howard JR, Elmslie KS. NaV1.8 channels are expressed in large, as well as small, diameter sensory neurons. Channels 2013, 7(1):34-37

Devor M. Ectopic discharge in Aβ afferents as a source of neuropathic pain. Exp Brain Res 2009, 196:115-128 (https://doi.org/10.1007/s00221-009-1724-6)

Hu S, Lyu D, Gao J. Suzetrigine: The first Nav1.8 inhibitor approved for the treatment of moderate to severe acute pain. Drug Discoveries & Therapeutics 2025; Advance Publication (DOI: 10.5582/ddt.2025.01010)

Jones J, Correll DJ, Lechner SM, Jazic I, Miao X, Shaw D, Simard C, Osteen JD, Hare B, Beaton A, Bertoch T, Buvanendran A, Habib AS, Pizzi LJ, Pollak RA, Weiner SG, Bozic C, Negulescu P, White PF. Selective inhibition of NaV1.8 with VX-548 for acute pain. N Engl J Med 2023, 389(5):393-405 (doi: 10.1056/NEJMoa2209870)

Zhang H, Chen Y, Huang J, Sun W. A simple and sensitive ultra-high performance liquid chromatography tandem mass spectrometry method for the quantitative analysis of VX-548 in monkey plasma: Method validation and application to pharmacokinetic study. Biomed Chromatography 2024, 38:e5907 (doi: 10.1002/bmc.5907)

Poller C, Hopster K, Rohn K, Kästner SB. Evaluation of contact heat thermal threshold testing for standardized assessment of cutaneous nociception in horses - comparison of different locations and environmental conditions. BMC Vet Res. 2013, 9(1):4 (doi:10.1186/1746-6148-9-4)

12.List the names and titles of your organization's executive staff and Board of Director's names and affiliations. (If needed use #14 Additional Items and Notes)

Name Director Names & Affiliations----> please follow this link for a detailed list of UPenn Trustees: https://upenn.app.box.com/s/mksbtjp9wkkkdwtoyzzoed1b0bdyxoj9		
City Philadelphia	State PA	ZIP 19104-6303
Work Telephone 215-898-7005	Home Telephone	

13.List names and, briefly, the duties of volunteers and paid employees in your organization. Also, provide salaries paid to directors and employees if applicable. (If needed use #14 Additional Items and Notes)

Name Not applicable to the University of Pennsylvania.	Salary $
Duties	

14. Additional Information and Notes:

***Applicants should refer to the instructions for additional information required for grants to support education or summits/meetings.**

Please print completed document, scan it, and email along with supporting documents to: office@terfusa.org.

UNIVERSITY of PENNSYLVANIA

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e-mail: driessen@upenn.edu

Re: IACUC Approval

June 15, 2025

To whom is may concern:

The proposed research project has been approved. Please see below the copy of the e-mail message I received on May 13, 2025 that serves as the official notification of the IACUC office. The IACUC protocol is currently approved until 05/12/2028.

Sincerely,

From: aries_help@lists.upenn.edu <aries_help@lists.upenn.edu>
Sent: Tuesday, May 13, 2025 1:15 PM
To: Driessen, Bernd <driessen@vet.upenn.edu>; Parman, Traci <tparman@vet.upenn.edu>; Hopster, Klaus <khopster@vet.upenn.edu>
Cc: Office of Animal Welfare ARIES <Provost-OAW_ARIES@pobox.upenn.edu>
Subject: ARIES: Approval (protocol #: 807720)

THIS EMAIL SERVES AS THE OFFICIAL NOTIFICATION FROM THE UNIVERSITY OF PENNSYLVANIA'S OFFICE OF ANIMAL WELFARE (OAW) OF INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) APPROVAL FOR THE SUBMISSION NOTED BELOW.

Please keep a copy of this email for your records as signed letters are no longer generated for protocol approvals.

The Form A below was reviewed and APPROVED by the University of Pennsylvania's IACUC and you are authorized to begin animal work on this protocol:

Protocol #: 807720
Confirmation #: aahaaga
Principal Investigators: BERND DRIESSEN and KLAUS HOPSTER
Protocol Title: Pharmacokinetics and Dynamics of suzetrigine in horses Approval Date: 05/12/2025 3-Year Expiration Date: 05/12/2028

The protocol is approved until the "3-Year Expiration Date" shown above. If you need to continue the project after that date, you will need to submit a 3-Year Renewal in the Animal Research Information and Electronic Submissions (ARIES) system. This requires a full de novo review of the protocol, which must be approved BEFORE 05/12/2028 to keep the protocol active. Therefore, per IACUC policy (https://iacuc.upenn.edu/iacuc-documents/policies/renewals-expiring-protocols), you should SUBMIT YOUR 3-YEAR RENEWAL NO LATER THAN 90 DAYS PRIOR TO THE EXPIRATION DATE to ensure there is time for reapproval.

The principal investigator should contact ULAR to verify animal housing availability and to coordinate activities for any special animal study needs (including special housing) or equipment requirements if this was not done during the planning phases of the protocol. IACUC protocol approval DOES NOT guarantee the availability of required resources for animal work.

Additionally, if this protocol includes funding from the Department of Defense (DoD) or the Department of Veterans Affairs (VA), the approval of animal use protocols and any subsequent changes made to them through amendments must be reported to the granting agency providing this funding. Therefore, you should report the approval of your protocol to the appropriate DoD division or to the VA.

Please take note of the following information:

- Personnel Training: It is the responsibility of the Principal Investigator to ensure that all persons have completed all necessary training prior to participating in the research described in this protocol. Outstanding training can be seen on the 'Training' tab of the protocol.