Institutional Animal Care and Use Committee (IACUC)
Office of Research Integrity and Assurance
Arizona State University

[redacted]

Animal Protocol Review

ASU Protocol Number: 21-1867R
Protocol Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics
Principal Investigator: [redacted]
Date of Action: 8/26/2021

The animal protocol review was considered by the Committee and the following decisions were made:

The protocol was approved.

NOTE: If you have not already done so, documentation of Level III Training (i.e., procedure-specific training) will need to be provided to the IACUC office before participants can perform procedures without supervision. For more information on Level III requirements see https://researchintegrity.asu.edu/animals/training, or contact Research Support Services within DACT at [redacted]

Additional requirements:

☐ This protocol requires that Research Support Services group within DACT provide supervision for the first time a procedure is conducted. Contac[redacted]to schedule.

☐ This protocol indicates that there are surgical procedures. A surgical checklist may be required to be submitted to Research Support Services within DAC[redacted]rior to starting surgeries.

☒ **Other requirements: IBC approval is required before work with biohazardous agents may begin**

Total # of Animals: 18
Species: NHPs **Pain Category:** D

Protocol Approval Period: 8/26/2021 – 8/25/2024

Sponsor: National Institute of Health
ASU Proposal/Award #: [redacted]
Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics

Signature: [redacted] Date: 8/31/2021
IACUC Chair or Designee

Cc: IACUC Office
IACUC Chair

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IACUC Use Only	**IACUC Protocol #:** 21-1867R
Date: 6/30/2021	☒ IBC ☐ RSC ☐ Chem

ANIMAL USE PROTOCOL
ARIZONA STATE UNIVERSITY INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE
(Revised April 2021)

Read "Instructions for Submitting the ASU Animal Use Protocol" before completing. **Upon approval, this protocol will become a public record so follow instructions carefully.**

PROJECT/PROGRAM TITLE: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics

SPECIES REQUESTED: Cynomolgus macaque (*Macaca fascicularis*)

I. PERSONNEL INFORMATION

A. A single member of the university faculty and/or Principal Investigator (PI) is considered the responsible individual.

NAME: [redacted] TITLE: Director

AFFILIATION: [redacted] Office Phone # [redacted]

Cell Phone #: [redacted] E-Mail: [redacted]

B. Additional contact, if any, for IACUC business

NAME: [redacted] TITLE: Primate Lab Supervisor

AFFILIATION: [redacted] Office Phone # [redacted]

Cell Phone #: [redacted] E-Mail: [redacted]

C. Protocol Type

☐ Non-funded research

☐ Internal Funding

Account Number:

☒ External Funding (Grant/Contract)

Granting Agency: NIH Deadline:

Co-Investigator(s) [redacted]

Proposal Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics

ASU Proposal or Award # [redacted]

If, ASU proposal or award number is not provided, attach a copy of the complete proposal or grant document.

☐ Teaching - Course Number and Title:

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D. Protocol Status:

☒ New

☐ Renewal—Previous Protocol #:

☐ Revision—Previous Protocol #:

E. Do you plan to use Department of Animal Care & Technologies (DACT) personnel and resources? If yes, describe the support needed? (If this use is new or an expansion of previous use, contact the DACT well in advance of need). Yes, surgical anesthesia and post-op monitoring as well as standard husbandry and clinical care.

II. PROJECT DESCRIPTION AND PROGRAM REQUIREMENTS

The Institutional Animal Care and Use Committee (IACUC) is composed of both active animal users and lay persons. Regardless of background, each member has a vote, so it is particularly important that the language of the application be understood by all. This applies to all sections of the application, but it is especially important that the goals and justifications of the proposed research be spelled out in the clearest possible terms. NOTE: Upon approval, this protocol will become a public record, so do not disclose proprietary information.

A. Provide a brief (300 words or less) synopsis in **NON-SCIENTIFIC TERMS** of proposed research.

Our goal is to develop a rapid, affordable, and accessible diagnostic tool to detect α-synuclein (α-syn) protein in the retina of nonhuman primate (NHP) models of two related diseases, Parkinson's disease (PD) and Multiple system atrophy (MSA), and to use this to differentiate between the two diseases.

B. PLANNED USE OF ANIMALS. Begin with a clear **statement of purpose** and briefly provide **background** information and **references** to previous work (especially if this is a renewal protocol). Include a clear description of the **experimental design** for all animal experiments planned and explain **why** the experiments must be performed. It is critical that for each procedure you provide a detailed sequence of events that effectively describes what happens to the animals from acquisition to euthanasia (if applicable). As the focus of the IACUC protocol is on animal use, do not simply cut and paste research objective statements from grant proposals. Flow charts, diagrams or tables are strongly recommended for complicated experimental designs. State how the research is expected to benefit the human community, the animal community, and/or society as a whole. **Details regarding surgical procedures, drug treatments, and field techniques are not necessary, as they will be addressed later in the form.**

Background: Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's disease (AD) and a major cause of disability in individuals over 65 years of age. PD belongs to a spectrum of diseases termed the "synucleinopathies", defined by the progressive aggregation of misfolded α-synuclein (α-syn) protein in the brain, and includes other disorders such as Multiple system atrophy (MSA) and Lewy body dementia (LBD). Currently, there are no objective tests that can be used to definitively diagnose PD. In addition, differential diagnosis of synucleinopathies is very challenging and relies heavily on a physician's clinical evaluation. A critical goal in the field is to reliably identify synucleinopathies at early stages of the disease before symptoms begin, to allow the best chance for disease modifying or preventative treatments to be effective. Our aim is to establish the 3D visualization of α-syn in the retina of NHP models of PD and MSA usin g and structural ele ments within the retina. Our collab orators have developed a retinal contrast agent, dubbed [redacted] which has demonstrated the ab lity to [redacted] has undergone dosing, safety, and toxicity studies in rats and rabbits and has demonstrated efficacy and abse nce of toxicity at the planned dose (15 mg/kg) [redacted] The contrast agent has also demonstrated the a bility to [redacted]. Our group has previou sly develo ped and characterized NHP models for both PD [redacted] and MSA [redacted] t at will be used to test this retinal contrast agent. Several studies have demonstrated that α-syn deposits accumu late in the retina of PD patients and animal models in a distinctive

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pattern from amyloid beta deposition in AD [redacted] Differential diagnosis between neurodegenerative diseases is made possible by differences in both the pattern of amyloid deposition and also by differences in emission profiles of retinal contrast agents when bound to different amyloids. Accordingly, a retinal diagnostic based on detection of α-syn deposits may aid in the differential diagnosis of PD and MSA.

Experimental Design: 18 cynomolgus macaques (M/F, 3-15 years old) will be acquired from commercial vendors. All animals will first have baseline serum, plasma, and cerebrospinal fluid (CSF) collected. All animals will undergo Preop MRI for surgical targeting. For the PD model, six animals will receive unilateral injections of α-syn preformed fibrils (PFFs) into the putamen (2 mg/mL, 4 sites, 40, 40, 25, 15 µL rostrocaudally per site [redacted] For the MSA model, six animals will receive unilateral injections of AAV-Oligo-α-syn vector into the putamen (3.7E12 vg/mL, 4 sites, 40, 40, 25, 15 µL rostrocaudally per site [redacted]. The remaining six animals will receive unilateral injections of AAV-Oligo-GFP) into the putamen as a control (3.7E12 vg/mL, 4 sites, 40, 40, 25, 15 µL rostrocaudally per site). One month post-op all animals will undergo in vivo fundus fluorescence (FF) and optical coherence tomography (OCT) retinal imaging pre and post (2, 5, 15, 30, 60-minutes, and 24 hours) injection with [redacted] (15 mg/kg, IV). Imaging pre and post injection with [redacted] will be repeated at three months post-op. Serum, plasma, and CSF will be collected at baseline and once per month post-op for disease confirmation via real-time quaking-induced conversion (RT-QuIC) [redacted] Three to four months post-op all animals will be euthanized and their brains and eyes collected for histological analysis.

Procedures:

Blood and CSF Collection (typically once per month for up to 5 months, including baseline): Animals will be anesthetized with ketamine (3-10 mg/kg, IM) and either dexmedetomidine (0.03 mg/kg, IM) or midazolam (0.05-0.5 mg/kg). Blood samples (≤10 mL) will be obtained from the femoral vein and separated for serum and plasma collection. CSF samples (≤0.5 mL) will be obtained via lumbar or cisternal puncture. CSF collection is performed as a sterile procedure. The lumbar or cervical area of the animal will be shaved and scrubbed alternating with povidone iodine and alcohol three times to prepare the collection site. A sterile drape will be placed over the collection site and sterile surgical gloves will be worn for the collection. For lumbar collection, a 22G spinal needle will be advanced into the spinal subarachnoid space until CSF begins to flow spontaneously. For cisternal collection, a 22G spinal needle attached to a 3-6 mL syringe will be advanced into the cisterna magna and CSF will be withdrawn. Sedation is expected to last 30 minutes. In the event that a CSF/blood collection attempt does not yield an adequate sample (i.e.: no sample, inadequate volume [<0.2 mL CSF or <1.0 mL serum/plasma], or blood contamination), the CSF/blood collection may be repeated up to one additional time within a 7-day period. Due to the small CSF collection volume and the analgesic effects of dexmedetomidine/midazolam, post-procedural monitoring for pain or distress is not expected to be necessary. By the time the animals recover from anesthesia (~1 hr) their total CSF volume will have equilibrated and we have never seen signs of headaches or other adverse effects following CSF collection in previous studies.

MRI Scanning (one or two times): Stereotaxic intracranial injections are performed under intraoperative MRI guidance. Preop MRIs will be performed on a [redacted] MRI scanner at th[redacted] After transportation t[redacted] animals will be anesthetized with ketamine (3-10 mg/kg, IM) and either dexmedetomidine (0.03 mg/kg, IM) or midazolam (0.05-0.5 mg/kg) and maintained with gas anesthesia (e.g., isoflurane, sevoflurane) or booster injections of ketamine (1.5 mg/kg, IM) and dexmedetomidine (0.015 mg/kg, IM) if necessary. Animals will be intubated to maintain a stable airway. Cetacaine spray (200 mg, topical) may be applied to the throat to assist with intubation. Animals will be placed in an MRI compatible stereotaxic frame and MRI-opaque fiducial markers will be placed around the skull for neuronavigation registration. T1 and/or T2-weighted images will be obtained. Following scanning, the locations of the fiducial markers will be permanently marked with a tattoo dot on the skin using a commercial tattoo marker [redacted] with sterile needle and ink. The MRI scan time is approximately 20 minutes, sedation is expected to last [redacted] hour. Following the procedure, dexmedetomidine/midazolam may be reversed with atipamezole (0.15-0.3 mg/kg, IM) or flumazenil (0.025 mg/kg, IV), respectively. As MRI registration is essential for accurate surgical guidance, if in the opinion of the surgeon the MR images prove inadequate (due to animal movement, fiducial placement, or other confounding factors), up to one repeat MRI may be performed.

Retinal Imaging (twice, one month and three months post-op): Animals will be sedated with ketamine (10 mg/kg, IM) or ketamine (3-10 mg/kg, IM) and either dexmedetomidine (0.03 mg/kg, IM) or midazolam (0.05-0.5 mg/kg) and maintained with ketamine (5 mg/kg, IM) or ketamine (1.5 mg/kg, IM) and dexmedetomidine (0.015 mg/kg, IM) boosters as needed. FF and OCT images will be obtained with a [redacted] device

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[redacted] with a modified chinrest to accommodate the facial contour of NHPs. Imaging will be performed pre and post (2, 5, 15, 30, 60-minutes, and 24 hours) injection with [redacted]. A catheter will be placed in the cephalic or saphenous vein, and [redacted] (15 mg/kg, IV) will be administered via bolus injection. Sedation is expected to last 1.5 hours. Following the procedure (60-minute and 24-hour timepoints), dexmedetomidine/midazolam may be reversed with atipamezole (0.15-0.3 mg/kg, IM) or flumazenil (0.025 mg/kg, IV), respectively.

Euthanasia (once): The animal will be anesthetized with ketamine (10 mg/kg, IM), xylazine (2 mg/kg, IM) or midazolam (0.05-0.5 mg/kg), and either hydromorphone (0.2 mg/kg, IM) or morphine (1 mg/kg, IM), followed by gas anesthesia (e.g., isoflurane, sevoflurane) or additional drug delivered IV [ketamine (≤20 mg/kg, IV), xylazine (≤4 mg/kg, IV), and either hydromorphone (≤0.4 mg/kg, IV) or morphine (≤2 mg/kg, IV)], if needed to achieve a surgical plane of anesthesia. Once a surgical plane of anesthesia is achieved as verified by lack of response to toe/finger pinch, palpebral reflex, and corneal reflex, the thoracic cavity will be opened, heparin (5,000 IU, IC) will be injected into the left ventricle of the heart and the animal will be euthanized via transcardial perfusion of 0.9% saline (1-2 L) followed by 4% buffered formaldehyde (1-2 L). If perfusion cannot be performed for any reason, animals will be anesthetized with ketamine (10 mg/kg, IM) followed by pentobarbital euthanasia solution (86-120 mg/kg, IV).

C. RATIONALE FOR INVOLVING ANIMALS AND THE APPROPRIATENESS OF THE **SPECIES AND NUMBER** USED. Keeping in mind the principles of the "3 R's" (Refinement, Reduction, and Replacement), answer the following:

1. Why must live vertebrates be used in this study?
   Our laboratory's experiments are aimed to help human patients with neurodegenerative diseases. Preclinical research requires a model that can inform about the applicability of diagnostic tools as well as the potential complications of its utilization. To the best of our knowledge, in vitro and computer models are still not able to give us enough information for clinical projection in complex neurodegenerative diseases such as PD and MSA.

2. Why are you using the requested species rather than other species?
   Cynomolgus macaques were chosen because these models of PD and MSA were developed in this species. The brains and eyes of NHP are similar in many respects to humans, enhancing the applicability of the data obtained to human diseases. While similar rodent models of PD and MSA have been established, the NHP models better mimic what is seen in the human brain. Additionally, the visual systems of rodents are less complex than that of NHP and humans.

3. What is the rationale supporting the numbers of animals proposed? Typically, a power analysis should be performed to support the proposed sample sizes. A table depicting the number of animals to be used is required.
   The protocol includes an N of 18 animals, which includes three groups of 6. There are currently no available in vivo retinal α-syn imaging data for our NHP models upon which to estimate an effect size therefore a group size of n=6 was chosen based on the investigator's prior experience with similar study designs and the expected diversity of presentation of α-syn deposits in NHP models.. The numbers chosen per group are based upon previous experience and standards

Group	Disease Model	Putamenal injectate	N=
1	PD	α-syn PFFs	6
2	MSA	AAV-Oligo-α-syn	6
3	Control	AAV-Oligo-GFP	6

4. What refinements, if any, have been made to reduce the number of animals used and the potential detrimental effects on the study animals?
   We feel the number of animals requested is the minimum necessary to achieve the aims of this study. We expect the effect to be binary with the control and PD groups providing no signal but signal will be present in the MSA group. Based upon previous experience we believe an n=6/group will be sufficient to discern these differences per group. Furthermore, we have taken every precaution to avoid pain and discomfort in our animals. The stereotaxic injections proposed will be conducted under general anesthesia with proper perioperative pain management and postoperative monitoring and care.

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III. EMERGENCY CONTACT

A. Who should be contacted in case of an animal emergency? **Note: This information will be redacted if this protocol is requested as a public document.**

Name:
Office Phone #
Home Phone
Cell Phone #: [redacted]

IV. DUPLICATION AND ALTERNATIVES PLEASE READ ALL INSTRUCTIONS.

The Animal Welfare Act requires that you document your justifications with data from **two** or more sources. **One source** must **be a set of searches of a relevant database: name the database searched, the keyword and keyword combinations searched, the date the search was performed, and the date range searched. The second source can be a set of searches of a second relevant database, or consultation with a laboratory animal science veterinarian, or courses/meetings/consultations with qualified personnel.** Sufficient documentation, such as the consultant's name and qualifications and the date and content of the consult, should be provided to the IACUC to demonstrate the expert's knowledge of the availability of alternatives in the specific field of study. Examples of appropriate databases to search include PUBMED, Web of Science, or Animal Welfare Information Center (AWIC – recommended for USDA-covered species https://www.nal.usda.gov/awic/databases).

A. Provide the following details for the most recent literature search used to explore for duplicative research. (The literature search documents that the research will not unnecessarily duplicate previous research). **Teaching protocols do not need to conduct this search.**

Date that search was conducted (*Must be within 60 days of the IACUC review date*): 06/16/2021
Database(s) used: ALTBIB, PUBMED
Publication years covered by the search: 1980 - present
Keyword combinations used: synuclein, retina, nonhuman primate
synuclein, retina, parkinson's disease
synuclein, retina, multiple system atrophy

B. Provide the following details for the most recent literature search used to explore for **alternatives to animal use** and **alternatives to painful procedures.** Alternatives should be considered for any aspect of the protocol that may cause more than momentary or slight pain or distress to the animal. Alternatives to be considered include those that would: 1) refine the procedure to minimize discomfort that the animal(s) may experience; 2) reduce the number of animals used overall; or 3) replace animals with non-animal alternatives (e.g., computer models or tissue culture). **All protocols (research and teaching) MUST conduct this search.**

Date that search was conducted (*Must be within 60 days of the IACUC review date*): 06/07/2021
Database(s) used: ALTBIB, PUBMED
Publication years covered by the search: 2000 - present
Keyword combinations used: multiple system atrophy, animal model
parkinson's disease, animal model
nonhuman primate, intracranial injection alternative

C. **Results of literature search for alternatives**: Comment on the application(s) of any identified alternatives (found with your search terms, including how these alternatives may be or may not be incorporated to modify a procedure to either lessen or eliminate potential pain and distress. **All protocols must complete this section and must describe how the literature search results relate to painful procedures and alternatives to animal use.** You must include sufficient information for the IACUC to determine that a reasonable, good faith effort was made to determine the availability of alternatives. If the search identified any alternative methods (ones that could be used to accomplish the goals of the animal use proposal), you must clearly explain and justify why this alternative cannot be used.

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For instance, if your search terms retrieved eight publications, summarize how many of those described alternatives to painful procedures and the use of animals.
No studies have been published demonstrating the ability to image α-syn deposits in vivo in NHP or human retinas. While similar rodent models of PD and MSA have been established, the NHP models better mimic what is seen in the human brain. Additionally, the visual systems of rodents are less complex than that of NHP and humans. No alternatives to intracranial injection were found for delivering PFFs or vector to the putamen.

D. Describe any other procedures (e.g., participation in meetings, review of journals) that are used to explore and evaluate alternatives: The PI, lab manager, graduate students, and other lab staff regularly attend national meetings and discuss recent updates in technology and methodology for these experiments with colleagues. Additionally, they remain up to date with the scientific literature on new and alternative procedures.

E. Does this research replicate previous work? **(Your answer will be based in part on the literature search above.)**

☒ No. Proceed to section **VI.**

☐ Yes. Explain why the replication is necessary:

☐ Not applicable. This is a teaching protocol.

V. CATEGORY OF PAIN OR DISTRESS

For non-USDA covered species, answer question A only. For USDA covered species, answer question B only. USDA covered species are all mammals EXCEPT laboratory mice and rats bred for research. All other rodents, including wild mice and rats, are covered.

A. Do the procedures in this protocol have the potential to involve more than slight or momentary pain or distress that will **NOT** be relieved with anesthetics, analgesics, tranquilizer drugs, or other method for relieving pain or distress (e.g., negative conditioning, unrelieved post-surgical pain, death without euthanasia)? ☐ No ☐ Yes

If yes, describe and justify:

B. Using the table below, list all USDA covered species to be used in the proposed study and indicate the number of animals to be used under each USDA pain category. For an animal undergoing multiple procedures, include the animal under the highest level of pain/distress expected for that animal.

USDA Covered Species	Number per USDA Category*				Total number of animals requested
	B	C	D	E	
Cynomolgus macaque			18		18

*USDA PAIN CATEGORIES: (see http://researchintegrity.asu.edu/animals/forms for a more complete description of the below categories)

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Classification B: Includes animals that are used solely for breeding or are being acclimatized or held for use in teaching, testing, experiments, research, or surgery but have not yet been used for such purposes.

Classification C: Includes the use of animals in procedures involving no, momentary, or slight pain or distress (e.g., non-invasive parenteral drug delivery, peripheral blood collection, euthanasia, short-term manual or chemical restraint, toe clipping).

Classification D: Includes the use of animals used in procedures that could cause pain or distress but appropriate anesthetics, analgesics, and/or tranquilizing drugs or other methods for relieving pain or distress are used (e.g., surgery, perfusion, administration of irritating chemicals, humane endpoint euthanasia).

Classification E: Includes the use of animals in procedures that have the potential to involve pain or distress that will **not** be relieved with anesthetics, analgesics, tranquilizer drugs, or other method for relieving pain or distress (e.g., negative conditioning, unrelieved post-surgical pain, death without euthanasia).

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VI. ASSURANCE:

The information contained herein is accurate to the best of my knowledge. I have carefully compared the proposed work with the current state of knowledge in this field by reviewing the literature and it is my professional opinion that the proposed work meets high standards of scientific merit. If the study involves pain and distress to the animal, whether or not it is relieved by anesthetics or analgesics, I have (1) reviewed the literature related to this work and have found no significant studies which could make this protocol unnecessarily duplicative, and (2) considered alternatives to animal use and found none available, as described above. Procedures involving animals will be carried out humanely and all procedures will be performed by or under the direction of trained or experienced persons. Any revisions to animal care and use in this project will be promptly forwarded to the Institutional Animal Care and Use Committee for review. Revised protocols will not be used until Committee clearance is received. The use of alternatives to animal models has been considered and found to be unacceptable at this time.

The principal investigator, by signing below, and the IACUC recognize that other medications may be given to the animals for veterinary care purposes. This includes the humane euthanasia of animals in uncontrollable pain or distress as determined by the Attending Veterinarian or the Clinical Veterinarian acting for the Attending Veterinarian. However, the veterinarians will make all efforts to contact and discuss the case with the Principal Investigator or designee prior to making a unilateral decision.

[redacted] 6/30/21

Principal Investigator –Print Date

[redacted] 07/24/21

Principal Investigator Signature Date

NOTE: Principal investigators must submit a current curriculum vitae or biosketch that reflects their most recent pertinent experience.

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PERSONNEL CHART

ASU requires that all personnel engaged in animal research or teaching be qualified through training or experience in order to conduct the work humanely. The IACUC requires the following training:

- **Level I Basic** – Required of ALL participants (must be renewed every 4 years)
- **Level II Species-Specific** – Required for each participant that will have direct contact with that species (must be renewed every 4 years)
- **Level III Hands-on Training** – Required to perform specific procedures independently. Training can be received from DACT staff or PIs can have a member of their lab approved by DACT to be a Certified Trainer who can then train others. Simply being Level III certified does not allow the training of others. A Level III Certification form must be submitted to the IACUC office by the person providing the training within 5 days of the training.

You can access the training modules at https://asu.co1.qualtrics.com/jfe/form/SV_b2b2XRXRRs1309f. See the IACUC web site (https://researchintegrity.asu.edu/animals/training) for more information on training and Level III forms.

*** Procedures other than husbandry, handling, or behavioral testing MUST be performed under supervision unless the person is Level III certified to conduct the procedure independently. Personnel are not Level III certified until the IACUC has reviewed and approved the Level III training documentation. The PI is responsible for ensuring that personnel who are not Level III certified are supervised at all times.**

Name	Title	ASURITE name	Role in Protocol: What activities will each person perform on live animals ONLY while under direct supervision?	Role in Protocol: What activities will each person be allowed to perform independently (including appropriate Level 3 certification*) at the time of protocol submission?	Species with which individual will have direct contact ("none," "all", or list species)	FOR IACUC USE ONLY: Training Confirmation
[redacted]	PI	[redacted]	None	Intracranial surgery, blood/CSF collection, MRI, administration of any medications, and necropsy.	All	7/2021 OHSP

For each individual, describe the individual's years of experience with all listed species and procedures they will be conducting under this protocol. For procedures for which they are not yet trained, but will likely be trained to do during the activity period of this protocol, provide a description of who will provide such training:
[redacted] has 37 years' experience conducting research with nonhuman primates and is experienced with all procedures in this protocol.

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DETAILED USE OF ANIMALS

This section must be completed for each species used.

(additional Detailed Use of Animals forms can be found at https://researchintegrity.asu.edu/animals/forms)

Common Name: Cynomolgus macaque

Scientific Name: *Macaca fascicularis*

I. ANIMAL INFORMATION

A. Is this a threatened or endangered species?
- ☒ No. Proceed to section I. B.
- ☐ Yes. Describe why this work must be done on this species and why the project will not have a significant negative impact on the species:

B. Maximum # of animals to be used over the 3-year life of the protocol: 18

C. Sex: M/F Age or Weight Range: 3-15 years

D. Source (e.g., commercial, in-house breeding, captured from wild): Commercial

E. List all labs and/or rooms **outside of the ASU centralized vivaria** where you intend to keep or use live animals in connection with the animal use covered under this protocol. This list is for IACUC information to assure each location is inspected semi-annually. **Listing rooms here does not assure approval of this space for use.**

Building	Room #	Max Length of Stay	Method of Transport	Purpose
[redacted]		4 hours	NHP cage inside DACT truck	MR Imaging

F. If you use DEA-controlled substances, list the location where they are stored (building and room number). If you acquire controlled substances from DACT for same day use, state this. The IACUC is required to inspect all controlled substance storage locations semi-annually. Controlled substances will be stored in Dr [redacted] office, [redacted]

II. MAJOR CATEGORIES OF USE

A. Will animals be immunized solely for the production and harvesting of antibodies to be used in vitro rather than as a vaccine study?
- ☒ No. Proceed to section II. B.
- ☐ Yes. Complete the following table.

Injection:

Volume of injectate	Adjuvant	Route	Min. Frequency	Max. # of injections

Collection: If terminal, check here ☐ otherwise complete the following.

Route	Max. Volume	Min. Frequency	Max. # of collections

B. Will tissues, blood, or other body fluids be harvested (other than for antibody production)?
- ☐ No. Proceed to section II. C.
- ☒ Yes. Will tissues, blood, or other body fluids be collected post-mortem only?
  - ☐ Yes. Proceed to section II.C.
  - ☒ No. Complete Appendix 1: Antemortem Specimen Collection.

C. Will animals be food restricted (calorically or specific constituents) other than for surgical procedures?
- ☒ No. Proceed to section II. D.

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☐ Yes. [note: restriction paradigms exceeding a single 24-hr period must follow the ASU IACUC Standard Institutional Guideline for Food and Water Restriction available at https://researchintegrity.asu.edu/index.php/animals/procedures-library-and-guidelines

1. What are the restriction parameters? Provide scientific justification and include the length of restriction.

2. How will you monitor for negative effects of food restriction (include information on how you will account for animal growth)?

D. Will animals be water restricted?
☒ No. Proceed to section II. E.
☐ Yes. [note: restriction paradigms exceeding a single 24-hr period must follow the ASU IACUC Standard Institutional Guideline for Food and Water Restriction available at https://researchintegrity.asu.edu/index.php/animals/procedures-library-and-guidelines

1. What are the restriction parameters? Provide scientific justification and include the length of restriction.

2. How will you monitor for negative effects of water restriction (include information on how you will account for animal growth)?

E. Will animals be exposed to trauma, injury, burning, freezing, electric shock, UV radiation, magnetic fields, lasers, loud noise, or other physical agents that might cause distress?
☐ No. Proceed to section II. F.
☒ Yes. List and justify each exposure.
Provide scientific justification: Magnetic Resonance Imaging (MRI): Due to the variability in NHP neuroanatomy, MR imaging is the best way to accurately target surgical injections within the brain. MRI scans involve strong magnetic fields, and precautions are made to ensure that no incompatible metals are present in the room during the scan. Noise levels inside an MRI machine typically vary from 65 to 95 dB, and intermittent spikes of ~110 dB may be produced. MRI scans are performed under anesthesia, and ear protection using ear plugs or gauze/cotton will be placed in the animal's ears to prevent damage and mitigate distress.

F. Will animals be exposed to environmental stress (e.g., non-natural temperature exposure, prolonged physical restraint, forced exercise)?
☒ No. Proceed to section II. G.
☐ Yes. List and scientifically justify each exposure.

G. Will animals undergo surgery?
☐ No. Proceed to section II. H.
☒ Yes. Complete Appendix 2: Surgical Procedures.

H. Will any animals have a device (e.g., thermocouple, cannula, electrode) that extends chronically through the skin?
☒ No. Proceed to section II. I.
☐ Yes. Describe wound management measures to minimize chances of infection around the device where it penetrates the skin:

I. Will individuals of a social species (e.g., most rodents) need to be housed singly at any time?
☐ No. Proceed to section II. J.
☒ Yes.

1. What would be the maximum duration that an individual would be singly housed? Provide scientific justification for singly housing for this duration:

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Animals will be pair housed when possible and do not need to be singly housed for research-related needs. However, because of the relatively small number of animals involved, suitable pairing partners may not be available. If necessary, single housing will be determined in conjunction with the veterinary staff and will continue until a suitable pairing partner becomes available or the experiment concludes.

2. Singly housed animals should receive additional enrichment. Describe what enrichment will be provided or scientifically justify why additional enrichment cannot be provided:
Animals will be housed in a room with other conspecifics and have access to visual, olfactory, and vocal/auditory contact. All animals are also provided a variety of enrichment items including manipulanda and destructibles; these may be increased in number or variety for singly housed animals as determined by the veterinary staff on a case-by-case basis.

J. Will animals need any other special husbandry considerations, including but not limited to altering standard cage type, cage change frequencies, housing temperature, or lack of enrichment?
☒ No. Proceed to section II. K.
☐ Yes. Describe special procedures and provide scientific justification:

K. Will animals be transported off campus (e.g., to/from the field, or between institutions) in a vehicle other than one owned by the DACT?
☒ No. Proceed to section II. L.
☐ Yes. Describe details (e.g., vehicle to be used, destinations, and driven by whom), read the IACUC *SIG - Off-campus Transport of Animals by Laboratory Personnel*, and complete and submit with this protocol the *Assurance to Abide by the Requirements for Transporting Live Animals*:

L. Will any work be conducted in the field (this includes field experiments or the capture of animals to be used in laboratory experiments)?
☒ No. Proceed to section II. M.
☐ Yes. Complete Appendix 3: Field Research.

M. Will any animals need to be individually identified?
☐ No. Proceed to section III.
☒ Yes. Describe the marking technique to be used, why that technique was chosen, how it will be performed, and on what age range of animals?
Animals will be tattooed with an identification number on their chest or inner thigh. Animals either have the tattoo upon arrival or are tattooed while under sedation by DACT staff during quarantine. Touch ups may be done while sedated/anesthetized (e.g., for TB testing), and the hair in the region is shaved as needed to maintain visibility of the tattoo. This identification method is the most widely used means of permanently marking macaques.

III. CHEMICALS AND OTHER POTENTIAL HAZARDS

(If you answer yes to any of the following questions, this information may be forwarded to another oversight unit to aid you in assuring safe practices. Approval by these units or additional training may be required prior to using any of these materials)

A. Will drugs or chemicals be used with animals?
☐ No. Proceed to section III. B.
☒ Yes. For each drug or chemical, list the agent, dose, route, purpose, and grade in the table below:

Agent	Dose	Route	Purpose	Frequency	Pharmaceutical grade (Y/N)?	Is this a DEA controlled substance (Y/N)?
[redacted]	15 mg/kg	IV	Test article	Twice	N	N
Atipamezole	0.15-0.3 mg/kg	IM	Dexmedetomidine reversal	As needed	Y	N

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Atropine	0.02-0.05 mg/kg	IM	Reduce respiratory secretions and prevent bradycardia	As needed	Y	N
Betadine	N/A	Topical	Topical disinfectant	As needed	Y	N
Bupivacaine	1-2 mg/kg	SC	Analgesia	Once during closure	Y	N
Buprenorphine Sustained release	0.2 mg/kg	SC	Analgesia	Once post-op	Y	Y
Cefazolin	20-25 mg/kg	IV or IM	Antibiotic	Every 2-4 hours intra-op, as needed	Y	N
Cephalexin	20-30 mg/kg	PO	Antibiotic	Twice daily, as needed	Y	N
Cetacaine Spray (Benzocaine 14%, Butamben 2%, Tetracaine 2%)	200 mg	Topical	Anesthesia	As needed for intubation	Y	N
Chlorhexidine	N/A	Topical	Topical disinfectant	As needed	Y	N
Dexmedetomidine	0.015-0.05 mg/kg	IM	Anesthesia	As needed	Y	N
4% Formaldehyde	1-2 L	IC	Perfusion	Once	N	N
Flumazenil	0.025 mg/kg	IV	Benzodiazepine reversal	As needed	Y	N
Gelfoam	Cut to size	Topical	Hemostasis/Seal surgical holes	As needed	Y	N
Heparin	5,000 IU	IC	Anticoagulant for perfusion	Once	Y	N
Hydromorphone	0.05-0.4 mg/kg	SC, IM, IV	Analgesia	As needed	Y	Y
Isoflurane	0.5-5%	Inhalation	Anesthesia	As needed	Y	N
Isopropyl alcohol	70%	Topical	Topical disinfectant	As needed	Y	N
Ketamine	1.5-20 mg/kg	IM, IV	Anesthesia	As needed	Y	Y
Meloxicam	0.1-0.2 mg/kg	PO, SC	Analgesia	Once daily, as needed	Y	N
Meloxicam Sustained release (10 mg/mL)	0.6 mg/kg	SC	Analgesia	Once post-op	Y	N
Midazolam	0.05-0.5 mg/kg	IM, IV	Sedative, anticonvulsant	As needed	Y	Y
Morphine	1-2 mg/kg	IV	Analgesia	As needed	Y	Y
Ophthalmic ointment	Dab	Topical	Prevent corneal desiccation	As needed	Y	N
Pentobarbital-containing euthanasia solution	86-120 mg/kg	IV	Euthanasia	Once	Y	Y
Propofol	2-5 mg/kg Bolus	IV	Anesthesia	As needed	Y	N

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	0.2-0.6 mg/kg/min CRI			Continuous, as needed		
Saline or Lactated Ringer's Solution	5-15 mg/kg/hr	IV	Fluid replacement	Constant-rate infusion	Y	N
Saline	1-2 L	IC	Perfusion	Once	Y	N
Sevoflurane	1-8%	Inhalation	Anesthesia	As needed	Y	N
Sufentanil	0.25-2 µg/kg/hr	IV	Analgesia	Constant-rate infusion	Y	Y
Xylazine	2-4 mg/kg	IM, IV	Anesthesia	As needed	Y	N

1. For each drug or chemical that is not pharmaceutical grade, indicate whether no pharmaceutical grade equivalent exists or provide scientific justification for using the non-pharmaceutical grade product.
Fo[redacted] no pharmaceutical grade equivalent exists. Formaldehyde is not available in a pharmaceutical grade, and is only used once in a terminal procedure.

B. Does this project involve transgenic, knockout, or knock-in animals?
☒ No. Proceed to section III. C.
☐ Yes. List the strains, any special care needs, and any expected clinical signs that are associated with the strain. Transgenic animals need to be covered by an IBC disclosure.

C. Does this project involve the use of biohazardous agents in animals (microorganisms, microbial toxins, recombinant DNA)?
☐ No. Proceed to section III. D.
☒ Yes. List the agent, as well as concentration, dose, and route if applicable.

Agent	Concentration	Dose	Route	ADMIN. USE ONLY	
				ABSL	IBC # if Req'd
α-syn PFFs	2 mg/mL	120 µL	Intracranial unilateral injection into putamen	2	
AAV-Oligo-α-syn	3.7E12 vg/mL	120 µL	Intracranial unilateral injection into putamen	2	
AAV-Oligo-GFP	3.7E12 vg/mL	120 µL	Intracranial unilateral injection into putamen	2	

D. Does this project involve irradiation or the use of radiological material in animals?
☒ No. Proceed to section III. E.
☐ Yes. List the agent, dose, route, and purpose in the table below:

Agent	Dose	Route	Purpose

1. Provide the date of **Radiation Safety Committee** approval:

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E. Describe any health hazards to **researchers** and include a description on how the risk is mitigated or managed:
Risk of bites, scratches, or Herpes B (Herpes B virus is not being used in animals but can be transmitted to personnel if there is an NHP bite/exposure). Risks are mitigated with the use of additional PPE as required by University policies (such as, but not limited to, Tyvek sleeves and double gloves), NHP primate certification, annual B Virus training (including Bite/Scratch policy), proof of 2 MMR vaccines or a measles titer, annual TB screening, and ear protection during MRI scans.

F. Describe any health hazards to **animals** and include a description on how the risk is mitigated or managed:
Zoonosis such as TB, measles, and flu are agents of concern that may spread from humans to monkeys. Before working with an NHP, all researchers are required to show proof of 2 MMR vaccines or a measles titer and annual TB screening. All people interacting with the monkeys are also required to wear a surgical mask to prevent the spread of these infections.

IV. DETRIMENTAL SEQUELAE

A. Will animals possibly experience clinical signs intentionally or as a possible side effect of the study?
☐ No. Proceed to section V.
☒ Yes. Complete the following.

Possible Clinical Effect	Probability of Occurrence	Treatment
Animals injected with AAV-Oligo-αSyn may exhibit MSA symptoms	Previous animals injected with this vector did not exhibit any clinical symptoms at up to 6 months post-op [redacted] and we expect any clinical symptoms to be mild and not affect the animals' ability to locomote or eat.	Consult with veterinary staff if clinical signs develop
Animals injected with α-syn PFFs may exhibit PD symptoms	Previous animals injected with PFFs did not exhibit any clinical symptoms at up to 15 months post-op [redacted] and we expect any clinical symptoms to be mild and not affect the animals' ability to locomote or eat.	Consult with veterinary staff if clinical signs develop

V. END POINT CRITERIA

A. What clinical signs will be used as a basis for removal of an animal from the study?
Weight loss in excess of 20% of ideal weight (as determined by veterinary staff based on body weight and body condition score) that does not resolve after two weeks of supportive treatment (as determined and provided in conjunction with the DACT veterinary team).

VI. EUTHANASIA

A. List the primary method of euthanasia:
Transcardial perfusion under anesthesia. If not perfusing, pentobarbital-containing euthanasia solution.

B. If using a chemical or gas, complete the chart below:

Various combinations of the following drugs may be used in coordination with euthanasia via injection of a euthanasia solution or perfusion.

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Agent	Dose	Route	Is this a DEA controlled substance (Y/N)?	Secondary method used to confirm euthanasia
Pentobarbital-containing euthanasia solution	86-120 mg/kg	IV	Y	Removal of brain
Ketamine	10-20 mg/kg	IM, IV	Y	Used in conjunction with perfusion
Xylazine	2-4 mg/kg	IM, IV	N	Used in conjunction with perfusion
Midazolam	0.05-0.5 mg/kg	IM	Y	Used in conjunction with perfusion
Atropine	0.02-0.05 mg/kg	IM	N	Used in conjunction with perfusion
Morphine	1-2 mg/kg	IM, IV	Y	Used in conjunction with perfusion
Hydromorphone	0.2-0.4 mg/kg	IM, IV	Y	Used in conjunction with perfusion
Heparin	5,000 IU	IC	N	Used in conjunction with perfusion
Isoflurane	3-5%	Inhalation	N	Used in conjunction with perfusion
Sevoflurane	5-8%	Inhalation	N	Used in conjunction with perfusion
0.9% saline	1-2 L	IC	N	Used in conjunction with perfusion
4% formaldehyde	1-2 L	IC	N	Used in conjunction with perfusion

C. If euthanasia is being done by a physical means (e.g., decapitation, cervical dislocation) without anesthesia, provide scientific justification:
N/A

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APPENDIX 1: ANTEMORTEM SPECIMEN COLLECTION

I. BLOOD COLLECTION

A. Will blood be collected?

☐ No. Proceed to section II.

☒ Yes. Complete the following.

Site	Volume (ml)	% BW	Max. # of collections	Min. Interval
femoral vein	≤10 mL	≤0.5%	5 planned, 8 max including potential redraws	Typically 1 month; Rarely within 7 days (see below)

B. Will anesthetics, sedatives, or other drugs be used during blood collection?

☐ No. Proceed to section I. C.

☒ Yes. Complete the following.

Drug	Dose	Route	Purpose
Ketamine	3-10 mg/kg	IM	Anesthesia
Dexmedetomidine	0.03 mg/kg	IM	Anesthesia
Midazolam	0.05-0.5 mg/kg	IM	Anesthesia
Atropine	0.02-0.05 mg/kg	IM	Reduce respiratory secretions

C. Describe the methods used to draw the blood including physical restraint, if any.

Animals will be anesthetized with ketamine and either dexmedetomidine or midazolam. Blood samples will be obtained from the femoral vein and separated for serum and plasma collection. Sedation is expected to last 30 minutes.

D. Provide scientific justification for blood collection and justification for the frequency of it.

Plasma and serum will be stored for future analysis of disease biomarkers. Collections spaced approximately a month apart will allow for adequate bodily replacement. In the event that a blood collection attempt does not yield an adequate sample (i.e.: no sample, inadequate volume [<1.0 mL serum/plasma]), the blood collection may be repeated up to one additional time within a 7-day period. In the event of a repeat collection, total volume collected will not exceed 10 mL in a 7-day period, well below accepted blood draw volume levels and frequency limits for animals of this size (2 - 10 kg).

II. OTHER TISSUE/BODY FLUID COLLECTION

A. Will other tissues or body fluids be collected prior to death?

☐ No. Appendix 1 is completed.

☒ Yes. Complete the following. Surgical procedures should be described more fully in Appendix 2.

Tissue/Fluid	Site and Method	Amt	# of collections	Min Interval
CSF	lumbar or cisternal puncture	≤0.5 mL	5 planned, 8 max including potential redraws	Typically 1 month; Rarely within 7 days (see below)

B. Will anesthetics, sedatives, or other drugs be used during tissue/body fluid collection?

☐ No. Proceed to section II. C.

☒ Yes. Complete the following.

Drug	Dose	Route	Purpose
Ketamine	3-10 mg/kg	IM	Anesthesia
Dexmedetomidine	0.03 mg/kg	IM	Anesthesia
Midazolam	0.05-0.5 mg/kg	IM	Anesthesia
Atropine	0.02-0.05 mg/kg	IM	Reduce respiratory secretions

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Betadine/Isopropyl alcohol	N/A	Topical	Topical disinfectant

C. Describe the methods used to collect the samples, including physical restraint, if any.
Animals will be anesthetized with ketamine and either dexmedetomidine or midazolam. CSF collection is performed as a sterile procedure. The lumbar or cervical area of the animal will be shaved and scrubbed alternating with povidone iodine and alcohol three times to prepare the collection site. A sterile drape will be placed over the collection site and sterile surgical gloves will be worn for the collection. For lumbar collection, a 22G spinal needle will be advanced into the spinal subarachnoid space until CSF begins to flow spontaneously. For cisternal collection, a 22G spinal needle attached to a 3-6 mL syringe will be advanced into the cisterna magna and CSF will be withdrawn. Sedation is expected to last 30 minutes.

D. Provide scientific justification for the sample collection(s) and justification for the frequency of it.
CSF will be used for disease confirmation via RT-QuIC. Collections spaced approximately a month apart will allow for adequate bodily replacement. In the event that a CSF collection attempt does not yield an adequate sample (i.e.: no sample, inadequate volume [<0.2 mL], or blood contamination), the CSF collection may be repeated up to one additional time within a 7-day period.

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APPENDIX 2: SURGICAL PROCEDURES

I. GENERAL INFORMATION

A. Species
Cynomolgus macaque

B. Surgical Procedure(s)
Intracranial injection

C. Room/location of surgery
[redacted]

II. PRE-SURGICAL CARE

A. Will the animals undergo pre-surgical fasting?
☐ No. Proceed to section III.
☒ Yes. Provide the details:
The day before a scheduled surgical procedure, animals are offered their full diet allotment in the early afternoon, and any remaining diet is removed at the end of the workday. The animal is then fasted overnight until the scheduled surgery the following morning in order to mitigate the risk of emesis and aspiration during the procedure.

III. SURGICAL PROCEDURE:

☒ Survival ☐ Nonsurvival

***Note:** A surgical checklist is recommended for each survival surgery, and possibly non-survival surgeries. These checklists should be submitted to DACT's Research Support Services [redacted] for review before implementing procedures.

A. Describe each surgical procedure (e.g., approach, tissue manipulation, closure):
Intracranial Injections
Animals will be placed in stereotaxic frames. Surgical targeting will be accomplished using a [redacted] surgical neuronavigation system, which will allow in-op visualization of the surgical instruments within and around the brain. The MRI images will be uploaded to the [redacted] system and coordinates for target areas will be marked. Under sterile conditions, an 8 cm incision will be made along the midsagittal plane of the scalp. Entry points will be identified using the [redacted] system. Two entry holes (10 mm x 10 mm, per hemisphere) will be drilled through the skull dorsal to the target coordinates. For the PD model, six animals will receive unilateral injections of α-syn preformed fibrils (PFFs) into the putamen (2 mg/mL, 4 sites, 40, 40, 25, 15 µL rostrocaudally per site). For the MSA model, six animals will receive unilateral injections of AAV-Oligo-α-syn vector into the putamen (3.7E12 vg/mL, 4 sites, 40, 40, 25, 15 µL rostrocaudally per site). The remaining six animals will receive unilateral injections of AAV-Oligo-GFP) into the putamen as a control (3.7E12 vg/mL, 4 sites, 40, 40, 25, 15 µL rostrocaudally per site). Infusion will be performed with an infusion pump attached to a stereotaxic micromanipulator [redacted] syringes will be lowered to the targets, and the contents infused at a rate of 1 µL/min. After the injection is complete, the needle/syringe will be left in place for an additional 2 minutes to allow infusate to diffuse from the needle tip and prevent backflow prior to retracting the syringe. The entry holes will be filled with Gelfoam and the skin will be sutured in anatomical layers with absorbable suture.

B. Anesthetic regimen:

Various combinations of the following drugs may be used in the induction and maintenance of anesthesia for surgery.

Drug & concentration (e.g., mg/ml)	Dose (e.g., mg/kg) & maximum volume to be given	Route	Is this a DEA controlled substance (Y/N)?
Ketamine (100 mg/mL)	10-15 mg/kg, 1 mL	IM	Y

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Midazolam (5 mg/mL)	0.05-0.5 mg/kg	IM	Y
Dexmedetomidine	0.015-0.05 mg/kg	IM	N
Atropine (0.54 mg/mL)	0.02-0.05 mg/kg	IM	N
Isoflurane	0.5-5%	Inhalation	N
Sevoflurane	1-8%	Inhalation	N
Propofol (10 mg/mL)	2-5 mg/kg, 5 mL (Bolus) 0.2-0.6 mg/kg/min (CRI)	IV	N
Cetacaine Spray (Benzocaine 14%, Butamben 2%, Tetracaine 2%)	200 mg	Topical	N

Please refer to the IACUC approved document "**Macaque Anesthesia/Analgesia/Antibiotics Regimens**"

Note: Use of gas anesthetics requires completion of the EH&S-based Anesthetic Gas Safety training prior to use and refreshed annually.

1. Describe measures used to indicate a surgical plane of anesthesia to keep animals from getting too light or too deep:
   Anesthesia depth will be monitored approximately every 10 minutes through jaw tone, palpebral reflex, and vitals measurements (e.g., ECG, heart rate, ventilatory rate, oxygen saturation, blood pressure, temperature, end tidal gases).

C. Additional pharmacological agents used during surgery (include analgesics, supportive medications, and research drugs):

Drug and concentration	Dose & max volume	Route	Purpose	Frequency	Is this a DEA controlled substance (Y/N)?
Betadine/Chlorhexidine/ Isopropyl alcohol	N/A	Topical	Topical Disinfectant	Once, as needed	N
Bupivacaine (5 mg/mL)	1-2 mg/kg, 2 mL	SC	Analgesia	Once during closure	N
Cefazolin (330 mg/mL)	20-25 mg/kg, 0.76 mL	IV	Antibiotic	Every 2-4 hours, intraoperatively	N
Gelfoam	Cut to size	Topical	Hemostasis/Seal surgical holes	Once, as needed	N
Hydromorphone (2 mg/mL)	0.05-0.2 mg/kg	SC, IM, IV	Analgesia	Once, as needed	Y
Ophthalmic ointment	Dab	Topical	Prevent corneal desiccation	Once, as needed	N
Saline or Lactated Ringer's Solution	5-15 mg/kg/hr, 300 mL	IV	Fluid replacement	Constant-rate infusion	N
Sufentanil (0.5 µg/mL)	0.25-2 µg/kg/hr, 120 mL	IV	Analgesia	Constant-rate infusion	Y

D. Describe the steps taken to maintain an aseptic surgery:
Trained individuals will perform standard sterile prep of the scalp. The site will be scrubbed alternating with povidone iodine/chlorhexidine and alcohol three times. Sterile drapes, gowns, gloves, and instruments will be used.

E. What is the maximum duration of each surgery?
3 hours

F. Will any animals recover from surgery?
☐ No. This involves terminal, or non-survival, procedures; Appendix 2 is complete.
☒ Yes. Complete Section IV.

IV. POST-SURGICAL CARE

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A. Is there a potential for post-operative pain or distress?
☐ No. Proceed to section C.
☒ Yes.

B. Will analgesics be used?
(For analgesic options, refer to the IACUC Standard Institutional Guideline on analgesia (https://researchintegrity.asu.edu/animals/procedures-library-and-guidelines) or contact a DACT veterinarian.
☐ No. Provide a scientific justification:

☒ Yes. Complete the following.

Drug & concentration	Dose & max. volume	Route	Frequency	Is this a DEA controlled substance (Y/N)?
Buprenorphine Sustained release (1-3 mg/mL)	0.2 mg/kg	SC	Once post-op	Y
Meloxicam Sustained release (10 mg/mL)	0.6 mg/kg	SC	Once post-op	N
Melo icam (5 mg/mL injection; 1 5 mg/mL oral)	0 1 0 2 mg/kg	SC, PO	SID a needed/ variable duration based on procedure	N

Please refer to the IACUC approved document "Macaque Anesthesia/Analgesia/Antibiotic Regimens"

Who will administer these drugs?
Veterinary staff or other trained individuals.

C. Post-operative routine care:

i. What other drugs will be administered, if any (e.g., antibiotics, fluids)?

Drug & concentration	Dose & max. volume	Route	Purpose	Frequency	Is this a DEA controlled substance (Y/N)?
Cefazolin (330 mg/mL)	20-25 mg/kg	IM	Antibiotic	BID as needed/ variable duration based on procedure	N
Cephalexin (50 mg/mL)	20-30 mg/kg	PO	Antibiotic	BID as needed/ variable duration based on procedure	N

Please refer to the IACUC approved document "Macaque Anesthesia/Analgesia/Antibiotic Regimens" (Choice of antibiotic and route of administration dictated by patient compliance. We try oral administration first, but default to injectable if NHP is not compliant)

ii. What other post-operative support and monitoring will be provided, how often, for how long, and by whom?
Pain assessment scoring (see attached form) is performed twice daily for at least three days following major surgical procedures and continues until the pain score is 0 as determined by the veterinarians or trained research staff. Monitoring is provided by both trained DACT and PI personnel. Should any animal experience adverse effects post-surgery (including signs of cerebral infection, cranial incision complications, or neurologic deficits) as determined by the veterinary staff, they will be evaluated and treated as appropriate by the veterinary staff.

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D. Is post-operative intensive care required?
☒ No. Proceed to section E.
☐ Yes.
What special care is required?

Who will provide special care and what are their qualifications?

For how long will special care be needed?

E. Will animals undergo multiple survival surgical procedures?
☒ No. Appendix 2 is complete.
☐ Yes. Describe which surgeries, the sequence (specifying time between surgeries), and frequency. Provide scientific justification:

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IACUC Protocol Trackable Components Checklist

Protocol #: 21-1867R If for amendment, amendment #:

PI: [redacted]

Species: Macaque Highest Category of Pain: D

Completed by: [redacted] Date completed: 7/2/21

☐ No trackable components in this document

Exceptions to the Guide:

☐ Food/Fluid Regulation
- Species:
- What Restricted:
- Parameters:

☐ Prolonged Restraint
- Species:
- Details:

☒ Husbandry Deviation from the Guide
- Species: Macaque
- Deviation: Single housing if suitable pairing partners are not available.

☐ Other:

Other Trackable Components:

☒ Survival Surgerie(s)
- Species: Macaque
- Surgerie(s): Intracranial injection
- Multiple Major?: ☐ Yes ☒ No

☒ Hazardous Agents
- Biological (list agent and hazard level):
- Chemical (note category – toxicant, toxin, irritant, carcinogen, etc.): 4% Formaldehyde
- Physical (note type - radiation, UV light, lasers, noise, magnetic fields, etc.): MRI (magnetic fields and up to ~110 dB noise)

☐ Non-Centralized Animal Housing
- Location:
- Maximum duration:

☐ Decapitation

☐ USDA-covered Species exempt from USDA reporting

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From: [redacted]
To:
Subject: FW: Chair Agenda
Date: Tuesday, August 31, 2021 1:34:00 PM
Attachments: image001.png

If you have any questions, please contact IACUC@asu.edu.

Thank you,

[redacted] MLS | IACUC Coordinator, Office of Research Integrity & Assurance
Arizona State University | Knowledge Enterprise | Operations
[redacted] | f 480-965-7772
[redacted] http://researchintegrity.asu.edu
How am I doing? Email my [redacted] or send a Sun Award
[redacted] (ASU Users Only)

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From [redacted]
Sent: Thursday, August 26, 2021 2:25 PM
To: Karen Kible [redacted]
Subject: RE: Chair Agenda

Dr [redacted] received his OHSP clearance on 8/9/21, EH didn't notify us, but I just got it. So if there are no other issues with his protocols today, they can be approved.

If you have any questions, please contact IACUC@asu.edu.

Thank you,

[redacted] MLS | IACUC Coordinator, Office of Research Integrity & Assurance
Arizona State University | Knowledge Enterprise | Operations
[redacted] 480-965-7772
[redacted] | http:// rity.asu.edu
How am I doing? Email my [redacted] or send a Sun Award
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From: Karen Kibler [redacted]

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

From: IACUC@asu.edu
To: [redacted]
Subject: FW: [redacted] 21-1867R Vet Cleared_ses2_SJM-mtg-mod-DR
Date: Wednesday, July 28, 2021 12:02:16 PM
Attachments: [redacted]

From: Karen Kibler [redacted]
Sent: Wednesday, July 28, 2021 5:59:14 PM (UTC+00:00) Monrovia, Reykjavik
To: [redacted]
Cc: iacuc@asu.edu <iacuc@asu.edu>; Dale DeNardo [redacted]
Subject: RE: [redacted] 21-1867R Vet Cleared_ses2_SJM-mtg-mod-DR

Thanks, everyone. I've attached the final version with the changes accepted. The official approval will be emailed by iacuc@asu.edu.

Karen

From: [redacted]
Sent: Monday, July 26, 2021 9:16 PM
To: Karen Kibler [redacted]
Cc: iacuc@asu.edu; Dale DeNardo [redacted]
Subject: Re: [redacted] 21 1867R Vet Cleared_ses2_SJM mtg mod DR

Thanks. These changes address my concerns.

Best,
[redacted]

~*~

[redacted] | she/her
Associate Professor
[redacted]
Ira A. Fulton Schools of Engineering
Arizona State University
Tempe, AZ 85287
PH: [redacted]

**Note: My working hours may not be your working hours. Please do not feel obligated to respond outside of your normal working schedule.*

From: Karen Kibler [redacted]
Sent: Monday, July 26, 2021 04:08 PM
To: [redacted]
Cc: [redacted] iacuc@asu.edu <iacuc@asu.edu>; Dale DeNardo [redacted]
Subject: RE: [redacted] 21 1867R Vet Cleared_ses2_SJM mtg mod DR

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

Hello [redacted]

Dale has suggested an alternative to the addition of listing "face shield" as part of the PPE, so I've revised that section.

Karen

From: Karen Kibler
Sent: Monday, July 26, 2021 8:50 AM
To [redacted]
Cc [redacted] iacuc@asu.edu
Subject: [redacted]21 1867R Vet Cleared_ses2_SJM mtg mod DR

Hello [redacted]

I've attached a version with all the resolved changes accepted. The outstanding issue is on page 4, sections II.3 and II.4. Please add wording to indicate that the numbers are based on prior experience and standards.

Also, check the wording I added on page 15 regarding face shields [redacted] point is well taken, that there is nothing wrong with wearing safety glasses in addition to the face shield.

Thanks,
Karen

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

Institutional Animal Care and Use Committee (IACUC)
Office of Research Integrity and Assurance
Arizona State University
[redacted]

Animal Protocol Review

ASU Protocol Number: 21-1867R RFC 1
Protocol Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics
Principal Investigator: [redacted]
Date of Action: 12/6/2021

The animal protocol review was considered by the Committee and the following decisions were made:

The request for changes was administratively approved to add [redacted] and [redacted] as additional personnel to the protocol.

NOTE: If you have not already done so, documentation of Level III Training (i.e., procedure-specific training) will need to be provided to the IACUC office before participants can perform procedures without supervision. For more information on Level III requirements see https://researchintegrity.asu.edu/animals/training, or contact Research Support Services within DACT a[redacted]

Additional requirements:

☐ This protocol requires that Research Support Services group within DACT provide supervision for the first time a procedure is conducted. Contact [redacted] to schedule.
☐ This protocol indicates that there are surgical procedures. A surgical checklist may be required to be submitted to Research Support Services within DACT [redacted] prior to starting surgeries.
☒ Other requirements: [redacted] must be added to IBC disclosure before working with biohazardous materials.

Total # of Animals: 18
Species: NHP **Pain Category:** D

Protocol Approval Period: 8/26/2021 – 8/25/2024

Sponsor: National Institutes of Health
ASU Proposal/Award #: [redacted]
Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics

Signature: [redacted] **Date:** 12/17/2021
IACUC Chair or Designee

Cc: IACUC Office, IACUC Chair

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

PERSONNEL MODIFICATION FORM
IACUC and IBC

This form can be used to add or remove participants from both an IACUC protocol and an IBC disclosure. Please submit only one form to Research.Integrity@asu.edu and it will be processed by both committees.

Principal Investigator Name: [redacted]		Phone [redacted]	
Dept [redacted]		Email: [redacted]	

Participant #1	Add to: ☐ IBC # ☒ IACUC #21-1867R, 22-1872R, 22-1873R, 22-1880R, 22-1886R, 22-1887R Delete from: ☐ IBC # ☐ IACUC #	FOR ORIA USE ONLY Training Verification
Name: [redacted]	ASURITE [redacted] Email: [redacted]	
Project Responsibilities in IBC:		
Experience/Training in These Responsibilities:		
What procedures are they responsible for on the IACUC protocol (please note which procedures are being done independently and which are done under supervision: Intracranial surgery, intracarotid surgery, intracisternal injection, MRI, PET scan, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified).		11/2021 OHSP
Species: Macaques, Mice **Experience and training with species and procedures:** 17 years' experience in primate research. 14 years' experience in rodent research. Experienced with intracranial surgery, intracarotid surgery, MRI, PET scan, blood/CSF collection, behavioral tests, administration of medications, and necropsy. Will be trained in intracisternal injection by Dr [redacted]		

Participant #2	Add to: ☐ IBC # ☒ IACUC #21-1867R, 22-1872R, 22-1873R, 22-1880R, 22-1886R, 22-1887R Delete from: ☐ IBC # ☐ IACUC #	FOR ORIA USE ONLY Training Verification
Name: [redacted]	ASURITE [redacted] Email: [redacted]	
Project Responsibilities in IBC:		
Experience/Training in These Responsibilities:		
What procedures are they responsible for on the IACUC protocol (please note which procedures are being done independently and which are done under supervision: Intracranial surgery, intracarotid surgery, intracisternal injection, MRI, PET scan, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified).		11/2021 OHSP
Species: Macaques, Mice **Experience and training with species and procedures:** 2 years' experience in primate research. 3 years' experience in rodent research. Experienced with intracranial surgery, MRI, PET scan, blood/CSF collection, behavioral tests, administration of medications, and necropsy. Will be trained in intracarotid surgery by [redacted] and [redacted] will be trained in PET scan by [redacted] will be trained in intracisternal injection by Dr [redacted]		

Assurance

As Principal Investigator, I assure that personnel will receive appropriate training prior to working with animals or biological materials as applicable.

Principal Investigator Signature: [redacted] Date: 12/2/2021

Revised 11/20/12

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

FOR ORIA USE ONLY	☐ IBC Approved	☒ IACUC Approved 12/6/2021

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

Institutional Animal Care and Use Committee (IACUC)
Office of Research Integrity and Assurance
Arizona State University

[redacted]

Animal Protocol Review

ASU Protocol Number: 21-1867R RFC 2
Protocol Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics
Principal Investigator: [redacted]
Date of Action: 12/10/2021

The animal protocol review was considered by the Committee and the following decisions were made:

The request for changes was administratively approved to add [redacted] as additional personnel to the protocol.

NOTE: If you have not already done so, documentation of Level III Training (i.e., procedure-specific training) will need to be provided to the IACUC office before participants can perform procedures without supervision. For more information on Level III requirements see https://researchintegrity.asu.edu/animals/training, or contact Research Support Services within DACT a[redacted]

Additional requirements:

☐ This protocol requires that Research Support Services group within DACT provide supervision for the first time a procedure is conducted. Contac[redacted] to schedule.

☐ This protocol indicates that there are surgical procedures. A surgical checklist may be required to be submitted to Research Support Services within DACT [redacted], prior to starting surgeries.

☒ **Other requirements [redacted] must be added to IBC disclosure before working with biohazardous materials.**

Total # of Animals: 18
Species: NHP **Pain Category:** D

Protocol Approval Period: 8/26/2021 – 8/25/2024

Sponsor: National Institutes of Health
ASU Proposal/Award #: [redacted]
Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics

Signature: [redacted] Date: 12/17/2021
IACUC Chair or Designee
Cc: IACUC Office, IACUC Chair

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

PERSONNEL MODIFICATION FORM
IACUC and IBC

This form can be used to add or remove participants from both an IACUC protocol and an IBC disclosure. Please submit only one form to Research.Integrity@asu.edu and it will be processed by both committees.

Principal Investigator Name: [redacted]	Phone: [redacted]
Dept: [redacted]	Email: [redacted]

Participant #3	Add to: ☐ IBC # ☒ IACUC #21-1867R, 22-1872R, 22-1873R, 22-1880R, 22-1886R, 22-1887R Delete from: ☐ IBC # ☐ IACUC #	FOR ORIA USE ONLY Training Verification
Name [redacted]	ASURITE [redacted] Email: [redacted]	
Project Responsibilities in IBC:		
Experience/Training in These Responsibilities:		
What procedures are they responsible for on the IACUC protocol (please note which procedures are being done independently and which are done under supervision: Intracranial surgery, intracarotid surgery, intracisternal injection, MRI, PET scan, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified).		11/2021 Basics & NHP 12/2021 Rodent OHSP
Species: Macaques, Mice **Experience and training with species and procedures:** 2 years' experience in primate research. 4 years' experience in rodent research. Experienced with intracranial surgery, MRI, blood/CSF collection, behavioral tests, administration of medications, and necropsy. Will be trained in intracarotid surgery by [redacted] and [redacted], will be trained in PET scan by [redacted] will be trained in intracisternal injection by Dr. [redacted]		

Assurance

As Principal Investigator, I assure that personnel will receive appropriate training prior to working with animals or biological materials as applicable.

Principal Investigator Signature: [redacted] Date: 12/2/2021

FOR ORIA USE ONLY	☐ IBC Approved	☒ IACUC Approved 12/10/2021

Revised 11/20/12

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

Institutional Animal Care and Use Committee (IACUC)
Office of Research Integrity and Assurance
Arizona State University

[redacted]

Animal Protocol Review

ASU Protocol Number: 21-1867R RFC 3
Protocol Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics
Principal Investigator: [redacted]
Date of Action: 4/21/2022

The animal protocol review was considered by the Committee and the following decisions were made:

The request for changes was approved by Designated Review to add the option for an additional craniotomy during intracranial injection surgeries.

NOTE: If you have not already done so, documentation of Level III Training (i.e., procedure-specific training) will need to be provided to the IACUC office before participants can perform procedures without supervision. For more information on Level III requirements see https://researchintegrity.asu.edu/animals/training, or contact Research Support Services within DACT a[redacted]

Additional requirements:

- ☐ This protocol requires that Research Support Services group within DACT provide supervision for the first time a procedure is conducted. Contac[redacted] to schedule.
- ☐ This protocol indicates that there are surgical procedures. A surgical checklist may be required to be submitted to Research Support Services within DACT[redacted] prior to starting surgeries.
- ☐ Other requirements:

Total # of Animals: 18
Species: NHP **Pain Category:** D

Protocol Approval Period: 8/26/2021 – 8/25/2024

Sponsor: National Institutes of Health
ASU Proposal/Award #: [redacted]
Title: Differential diagnosis of Parkinson's and multiple system atrophy in nonhuman primate models using a novel a-synuclein retinal contrast agent and AI assisted analytics

Signature: [redacted] **Date:** 4/22/2022
IACUC Chair or Designee
Cc: IACUC Office; IACUC Chair

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

ARIZONA STATE UNIVERSITY

Institutional Animal Care and Use Committee

REQUEST FOR CHANGES TO AN APPROVED PROTOCOL

Protocol No. 21-1867R, 22-1873R, 22-1880R, 22-1886R, 22-1887R, 22-1918R
Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics
Reprogramming astrocytes to functional dopaminergic neurons in non-human primate brain
Co-Pathologies Drive Neuroinflammation and Progression in PD
Genetic Silencing of Striatal CaV1.3 Calcium Channels as a Potent Antidyskinetic Therapy for PD
AAV Trehalose in an NHP model of Alzheimer's DiseaseAAV-GBA Therapy in an NHP model of PD

Principal Investigator: [redacted] Email Address [redacted]
If not PI, whom should [redacted] contact for questions related to this amendmen [redacted] mail Address:

☒ Funded ☐ Unfund

Requested Change (check all that apply):

☐ New procedures to be performed complete Part A, and Appendix 1 and/or 2 as applicable, and sign assurance.
☐ New species and or an increase in the number of animals to be used complete Part A and sign assurance.
☐ New location of housing or procedures complete Part A and sign assurance.
☐ New personnel – complete Part B and sign assurance.
☒ Other (includes changes in dosages, funding, etc.) complete Part A and sign assurance.

A. Description of Requested Changes

For new procedures or additional animals that are USDA-covered species (all mammals EXCEPT mice and rats bred for research), list the **Category of Pain:**

For new procedures or additional animals that are not USDA-covered species, will there be the potential to involve more than slight or momentary pain or distress that will NOT be relieved with anesthetics, analgesics, tranquilizer drugs, or other methods for relieving pain or distress (e.g., negative conditioning, unrelieved post-surgical pain, death without euthanasia)? ☐ No ☐ Yes

If yes, describe and justify:

If you are adding a procedure that could create pain or distress, you need to include a **literature search** for alternatives.
If you are adding a new survival surgery, submit a surgical checklist.
If you are requesting an increase in animal numbers, provide justification with supportive statistics.
If you are adding additional funding sources, provide the grant agency, grant title and ASU proposal or award number.

Describe the changes you are requesting. We would like to add the option to make one additional craniotomy to visualize the superior sagittal sinus during intracranial injection surgeries under this protocol. Intraoperative navigation with the [redacted] is generally highly accurate following initial skin registration (i.e., correlation of the MRI scan with the animal's actual position in the stereotaxic frame using fiducial marker locations or tracing the skin surface with a tracked instrument). However, it is occasionally necessary for the surgeon to confirm navigational accuracy after the skin has been retracted with an anatomical landmark that is clearly visible on MRI. The superior sagittal sinus is ideal for this purpose and, prior to the adoption of intraoperative navigation with the [redacted] visualizing the sinus was the primary method of establishing a mediolateral zero point for stereotaxic MRI coordinates in all surgical cases, as described by [redacted] In cases where visualizing the sinus is deemed necessary, the surgeon will make a small craniotomy (up to 10 x 3 mm) along the mediolateral axis. It is usually not necessary for the craniotomy to fully penetrate the skull and the surgeon will stop once the sinus is visible through the bone. In the very rare occasions when the sinus is inadvertently penetrated, digital pressure with surgical gel foam is sufficient to control bleeding. The craniotomy will be filled with gel foam prior to wound closure, which will be as previously described.

References:

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

[redacted]

B. Addition of Personnel

All personnel who work with animals are required to have animal care training within the last four years. ASU IACUC training modules can be completed at https://asu.co1.qualtrics.com/jfe/form/SV_b2b2XRXRRs1309f. Personnel are required to have Level III training certification on file with the IACUC office in order to perform procedures independently (without supervision). Training can be received from DACT staff or PIs can have a member of their lab approved by DACT to be a Certified Trainer who can then train others. Simply being Level III certified does not allow the training of others. See the IACUC web site (https://researchintegrity.asu.edu/animals/training) for more information on training and Level III forms.

*** Procedures other than husbandry, handling, or behavioral testing MUST be performed under supervision unless the person is Level III certified to conduct the procedure independently. Personnel are not Level III certified until the IACUC has reviewed and approved the Level III training documentation. The PI is responsible for ensuring that personnel who are not Level III certified are supervised at all times.**

Name	Title	ASURITE name	What activities will each person perform on live animals ONLY while under direct supervision?	What activities will each person be allowed to perform independently (including appropriate Level 3 certification*) at the time of protocol submission?	Species with which individual will have direct contact ("all" or list species) *	IACUC USE ONLY Training (mm/yy)

For each individual, describe the individual's training and years of experience with all listed species and procedures they will be conducting under this protocol. For procedures for which they are not yet trained, but will likely be trained to do during the activity period of this protocol, provide a description of who will provide such training:

Assurance

As Principal Investigator of this protocol, I assure that all procedures will be conducted as described in this request for changes and that personnel will receive appropriate additional training prior to conducting any new procedures that are not listed above.

SIGNED:

[redacted] _____ 4/6/2022

Principal Investigator Date

For IACUC use only:

☐ Administratively approved - Approving administrator: Date of approval:

☐ Administratively handled by VCV - Veterinarian providing verification: Date of verification:

Sources used for verification:

☒ Approved by Designated Review – Designated reviewer: [redacted] Date of approval: 4/21/2022

☐ Approved by Full Committee Review – Primary reviewer: Date of approval:

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

From: [redacted]
To: [redacted]
Cc: [redacted] IACUC@asu.edu
Subject: RE: Action Required: Designated Review for [redacted] Multiprotocol RFC
Date: Tuesday, April 19, 2022 4:18:09 PM
Attachments: image002.png

Thanks [redacted] approve the modified amendment as the designated reviewer.

Good luck on the research [redacted]

From: [redacted]
Sent: Tuesday, April 19, 2022 2:51 PM
To [redacted]
Cc: [redacted] IACUC@asu.edu <IACUCasu.edu@mainex1.asu.edu>
Subject: RE: Action Required: Designated Review for [redacted] Multiprotocol RFC

Great, please see the attached revisions.

[redacted]
Laboratory Manager
[redacted]
Arizona State University
p: [redacted]
email: [redacted]

From [redacted]
Sent: Tuesday, April 19, 2022 2:34 PM
To [redacted]
Cc: [redacted] ACUC@asu.edu <IA[redacted]>
Subject: RE: Action Required: Designated Review for [redacted] Multiprotocol RFC

Hi [redacted] - Yes this outlines and justifies the process. This is very helpful. Please add a sentence with the reference to the amendment. Thanks!

From: [redacted]
Sent: Tuesday, April 19, 2022 2:14 PM
To: [redacted]
Cc: [redacted] IACUC@asu.edu <IACUCasu.edu@mainex1.asu.edu>
Subject: RE: Action Required: Designated Review for [redacted] Multiprotocol RFC

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

Hi [redacted] the attached paper describes the stereotaxic surgery without the [redacted] neuronavigation, including the exposure of the sagittal sinus for mediolateral zero. Is that what you are looking for?

[redacted]
Laboratory Manager
[redacted]
Arizona State University
p[redacted]
email: [redacted]

From: [redacted]
Sent: Tuesday, April 19, 2022 10:21 AM
To: [redacted]
Subject: FW: Action Required: Designated Review for [redacted] Multiprotocol RFC

See below

[redacted]
Professor of Life Sciences
College of Liberal Arts and Sciences

Arizona State University
[redacted]
Tempe Arizona 85287

[redacted]

From [redacted]
Date: Tuesday, April 19, 2022 at 10:15 AM
To [redacted]
Cc [redacted] "iacuc@asu.edu" <iacuc@asu.edu>
Subject: RE: Action Required: Designated Review for [redacted] Multiprotocol RFC

H[redacted]

I am the designated reviewer for your amendment. I have no concerns, but can you please add some references to justify your discussion. Thank you!

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

Best,
[redacted]

[redacted]
Professor of Nutrition
Arizona State University [redacted]
[redacted] | chs.asu.edu

College of Health Solutions
Arizona State University

From [redacted]
Sent: Tuesday, April 19, 2022 9:47 AM
To [redacted] Dale DeNardo [redacted] Karen Kible [redacted]
Cc: IACUC@asu.edu
Subject: Action Required: Designated Review for [redacted] Multiprotocol RFC
Importance: High

Designated Reviewer: [redacted]
Principal Investigator:
Peer Reviewer:
Protocol Number: **Multiprotocol RFC**

A request for an amendment to the referenced protocols has been submitted. The request for amendment is attached and the various related protoc s are available at the SharePoint site. The Designated Review process allows IACUC members, by voting, to permit the Designated Reviewer to approve or disapprove an amendment request.

Select "**YES**" if you approve the use of the designated review process for this amendment.

Select "**NO**" if you disapprove the use of designated review process regarding this amendment request. The amendment will then be reviewed at the next monthly IACUC meeting.

Select "**Abstain**" if you would like to abstain from the vote for any reason.

Select "**Recuse**" if you have a conflict of interest.

Please indicate your approval or disapproval of the request for designated review by using the YES or NO

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

[redacted]

To: [redacted] iacuc@asu.edu
Subject: RE: Action Required: Designated Review fo[redacted] Multiprotocol RFC

From [redacted]
Sent: Tuesday, April 19, 2022 10:47 AM
To: [redacted]; Dale DeNardo [redacted] Karen Kibler [redacted]
Cc: IACUC@asu.edu
Subject: Action Required: Designated Review for [redacted] Multiprotocol RFC
Importance: High

Designated Reviewer: [redacted]
Principal Investigator:
Peer Reviewer:
Protocol Number: Multiprotocol RFC

Tracking:	Recipient	Response
	[redacted]	Yes: 4/19/2022 3:25 PM
		Yes: 4/19/2022 4:18 PM
		Yes: 4/19/2022 11:56 AM
	Dale DeNardo	Yes: 4/19/2022 11:02 AM
	[redacted]	
	Karen Kibler	Yes: 4/19/2022 10:49 AM
	[redacted]	Yes: 4/19/2022 12:20 PM
		Yes: 4/19/2022 4:08 PM
		Yes: 4/19/2022 12:53 PM
		Yes: 4/19/2022 11:51 AM

A request for an amendment to the referenced protocols has been submitted. The request for amendment is attached and the various related protocols are available at the SharePoint site. The Designated Review process allows IACUC members, by voting, to permit the Designated Reviewer to approve or disapprove an amendment request.

Select "**YES**" if you approve the use of the designated review process for this amendment.

Select "**NO**" if you disapprove the use of designated review process regarding this amendment request. The amendment will then be reviewed at the next monthly IACUC meeting.

Select "**Abstain**" if you would like to abstain from the vote for any reason.

Select "**Recuse**" if you have a conflict of interest.

Please indicate your approval or disapproval of the request for designated review by using the YES or NO button in the toolbar at the top of this message. The use of "YES or NO" buttons allows you to submit comments along with your choice. **You may also send your comments to me directly or to the primary reviewer without using the selection buttons. Please copy me on all correspondence and email related to this request.**

Sincerely,

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

PRR22-11_0391

IACUC Protocol Trackable Components Checklist

Protocol #: 21-1867R If for amendment, amendment #: 3

PI [redacted]

Species: Macaque Highest Category of Pain: D

Completed by [redacted] Date completed: 4/13/2022

☐ No trackable components in this document

Exceptions to the Guide:

☐ Food/Fluid Regulation
- Species:
- What Restricted:
- Parameters:

☐ Prolonged Restraint
- Species:
- Details:

☒ Husbandry Deviation from the Guide
- Species: Macaque
- Deviation: Single housing if suitable pairing partners are not available.

☐ Other:

Other Trackable Components:

☒ Survival Surgerie(s)
- Species: Macaque
- Surgerie(s): Intracranial injection
- Multiple Major?: ☐ Yes ☒ No

☒ Hazardous Agents
- Biological (list agent and hazard level):
- Chemical (note category – toxicant, toxin, irritant, carcinogen, etc.): 4% Formaldehyde
- Physical (note type - radiation, UV light, lasers, noise, magnetic fields, etc.): MRI (magnetic fields and up to ~110 dB noise)

☐ Non-Centralized Animal Housing
- Location:
- Maximum duration:

☐ Decapitation

☐ USDA-covered Species exempt from USDA reporting

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

Institutional Animal Care and Use Committee (IACUC)
Office of Research Integrity and Assurance
Arizona State University
[redacted]

Animal Protocol Review

ASU Protocol Number: 21-1867R RFC 4
Protocol Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics
Principal Investigator: [redacted]
Date of Action: 6/29/2022

The animal protocol review was considered by the Committee and the following decisions were made:

The request for changes was approved by Designated Review to add 8 rats (new species), additional procedures, and [redacted] to the protocol.

NOTE: If you have not already done so, documentation of Level III Training (i.e., procedure-specific training) will need to be provided to the IACUC office before participants can perform procedures without supervision. For more information on Level III requirements see https://researchintegrity.asu.edu/animals/training, or contact Research Support Services within DACT at [redacted]

Additional requirements:

☐ This protocol requires that Research Support Services group within DACT provide supervision for the first time a procedure is conducted. Contact [redacted] to schedule.
☐ This protocol indicates that there are surgical procedures. A surgical checklist may be required to be submitted to Research Support Services within DACT [redacted], prior to starting surgeries.
☐ Other requirements:

Total # of Animals: 26
Species: NHP — **Pain Category:** D - 18
Species: Rats — **Unalleviated Pain/Distress:** No

Protocol Approval Period: 8/26/2021 – 8/25/2024

Sponsor: National Institutes of Health
ASU Proposal/Award #: [redacted]
Title: Differential diagnosis of Parkinson's and multiple system atrophy in nonhuman primate models using a novel a-synuclein retinal contrast agent and AI assisted analytics

Signature [redacted] Date: 6/30/2022
IACUC Chair or Designee
Cc: IACUC Office; IACUC Chair

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

ARIZONA STATE UNIVERSITY

Institutional Animal Care and Use Committee

REQUEST FOR CHANGES TO AN APPROVED PROTOCOL

Protocol No. 21-1867R RFC 4
Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics

Principal Investigator: [redacted] Email Address: [redacted]
If not PI, whom should be contact for questions related to this amendment: [redacted] Email Address: [redacted]

☒ Funded ☐ Unfunded

Requested Change (check all that apply):

☒ New procedures to be performed – complete Part A, and Appendix 1 and/or 2 as applicable, and sign assurance.
☒ New species and or an increase in the number of animals to be used – complete Part A and sign assurance.
☐ New location of housing or procedures – complete Part A and sign assurance.
☒ New personnel – complete Part B and sign assurance.
☐ Other (includes changes in dosages, funding, etc.) – complete Part A and sign assurance.

A. Description of Requested Changes

For new procedures or additional animals that are USDA-covered species (all mammals EXCEPT mice and rats bred for research), list the **Category of Pain:**

For new procedures or additional animals that are not USDA-covered species, will there be the potential to involve more than slight or momentary pain or distress that will NOT be relieved with anesthetics, analgesics, tranquilizer drugs, or other methods for relieving pain or distress (e.g., negative conditioning, unrelieved post-surgical pain, death without euthanasia)? ☒ No ☐ Yes

If yes, describe and justify:

If you are adding a procedure that could create pain or distress, you need to include a **literature search** for alternatives.
If you are adding a new survival surgery, submit a surgical checklist.
If you are requesting an increase in animal numbers, provide justification with supportive statistics.
If you are adding additional funding sources, provide the grant agency, grant title and ASU proposal or award number.

Describe the changes you are requesting. Nonhuman primates in research are a valuable and limited resource, therefore as an additional quality control step, we would like to test the specificity and safety of the AAV-Oligo-α-syn and AAV-Oligo-GFP vectors prior to using them in NHPs. Each vector will be tested in four Sprague Dawley rats via Bilateral intracranial injection into the striatum (2 µL per hemisphere; see DUA and Appendix 2 below). One month following injection, all animals will be sacrificed via cardiac perfusion. Their brains will be removed, passed through graded sucrose, and sectioned and stained for histology. The number of animals chosen is based on our experience with similar experiments in the past, the decision is not statistically compared across groups. We feel fewer rats would not provide sufficient evidence and assurance to make an informed decision whether to proceed with the vector in monkeys.

Provide the following details for the most recent literature search used to explore for **alternatives to animal use** and **alternatives to painful procedures.** Alternatives should be considered for any aspect of the protocol that may cause more than momentary or slight pain or distress to the animal. Alternatives to be considered include those that would: 1) refine the procedure to minimize discomfort that the animal(s) may experience; 2) reduce the number of animals used overall; or 3) replace animals with non-animal alternatives (e.g., computer models or tissue culture). **All protocols (research and teaching) MUST conduct this search.**

Date that search was conducted (*Must be within 60 days of the IACUC review date*): 6/7/22
Database(s) used: ALTBIB, PUBMED
Publication years covered by the search: 1980 - present
Keyword combinations used: intracranial injection alternative, rat

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Results of literature search for alternatives: Comment on the application(s) of any identified alternatives (found with your search terms, including how these alternatives may be or may not be incorporated to modify a procedure to either lessen or eliminate potential pain and distress. **All protocols must complete this section and must describe how the literature search results relate to painful procedures and alternatives to animal use.** You must include sufficient information for the IACUC to determine that a reasonable, good faith effort was made to determine the availability of alternatives. If the search identified any alternative methods (ones that could be used to accomplish the goals of the animal use proposal), you must clearly explain and justify why this alternative cannot be used.

For instance, if your search terms retrieved eight publications, summarize how many of those described alternatives to painful procedures and the use of animals.
No non-animal models were found that would allow us to test the specificity and safety of these vectors. No alternatives to intracranial injection were found for delivering vector to the target areas in the brain.

Describe any other procedures (e.g., participation in meetings, review of journals) that are used to explore and evaluate alternatives: The PI, lab manager, graduate students, and other lab staff regularly attend national meetings and discuss recent updates in technology and methodology for these experiments with colleagues. Additionally, they remain up to date with the scientific literature on new and alternative procedures.

B. Addition of Personnel

All personnel who work with animals are required to have animal care training within the last four years. ASU IACUC training modules can be completed at https://asu.co1.qualtrics.com/jfe/form/SV_b2b2XRXRRs1309f. Personnel are required to have Level III training certification on file with the IACUC office in order to perform procedures independently (without supervision). Training can be received from DACT staff or PIs can have a member of their lab approved by DACT to be a Certified Trainer who can then train others. Simply being Level III certified does not allow the training of others. See the IACUC web site (https://researchintegrity.asu.edu/animals/training) for more information on training and Level III forms.

*** Procedures other than husbandry, handling, or behavioral testing MUST be performed under supervision unless the person is Level III certified to conduct the procedure independently. Personnel are not Level III certified until the IACUC has reviewed and approved the Level III training documentation. The PI is responsible for ensuring that personnel who are not Level III certified are supervised at all times.**

Name	Title	ASURITE name	What activities will each person perform on live animals ONLY while under direct supervision?	What activities will each person be allowed to perform independently (induding appropriate Level 3 certification*) at the time of protocol submission?	Species with which individual will have direct contact ("all" or list species) *	IACUC USE ONLY Training (mm/yy)
[redacted]	Graduate Student	[redacted]	Intracranial surgery, administration of medications, and necropsy		Rat	11/2021 Basics 12/2021 Rodent OHSP

For each individual, describe the individual's training and years of experience with all listed species and procedures they will be conducting under this protocol. For procedures for which they are not yet trained, but will likely be trained to do during the activity period of this protocol, provide a description of who will provide such training:
[redacted] years' experience in rodent research. Experienced with all procedures in this protocol.

Assurance

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As Principal Investigator of this protocol, I assure that all procedures will be conducted as described in this request for changes and that personnel will receive appropriate additional training prior to conducting any new procedures that are not listed above.

[redacted]

Principal Investigator

6/7/2022
Date

For IACUC use only:

☐ Administratively approved - Approving administrator: Date of approval:

☐ Administratively handled by VCV - Veterinarian providing verification: Date of verification:
Sources used for verification:

☒ Approved by Designated Review – Designated reviewer: Karen K bler Date of approval: 6/29/2022

☐ Approved by Full Committee Review – Primary reviewer: Date of approval:

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DETAILED USE OF ANIMALS
This section must be completed for each species used.

(additional Detailed Use of Animals forms can be found at https://researchintegrity.asu.edu/animals/forms)

Common Name: Rat

Scientific Name: *Rattus norvegicus*

I. ANIMAL INFORMATION

A. Is this a threatened or endangered species?
- ☒ No. Proceed to section I. B.
- ☐ Yes. Describe why this work must be done on this species and why the project will not have a significant negative impact on the species:

B. Maximum # of animals to be used over the 3-year life of the protocol: 8

C. Sex: M/F Age or Weight Range: 3 months

D. Source (e.g., commercial, in-house breeding, captured from wild): commercial

E. List all labs and/or rooms **outside of the ASU centralized vivaria** where you intend to keep or use live animals in connection with the animal use covered under this protocol. This list is for IACUC information to assure each location is inspected semi-annually. **Listing rooms here does not assure approval of this space for use.**

Building	Room #	Max Length of Stay	Method of Transport	Purpose

F. If you use DEA-controlled substances, list the location where they are stored (building and room number). If you acquire controlled substances from DACT for same day use, state this. The IACUC is required to inspect all controlled substance storage locations semi-annually. Controlled substances will be stored in D[redacted] office [redacted]

II. MAJOR CATEGORIES OF USE

A. Will animals be immunized solely for the production and harvesting of antibodies to be used in vitro rather than as a vaccine study?
- ☒ No. Proceed to section II. B.
- ☐ Yes. Complete the following table.

Injection:

Volume of injectate	Adjuvant	Route	Min. Frequency	Max. # of injections

Collection: If terminal, check here ☐ otherwise complete the following.

Route	Max. Volume	Min. Frequency	Max. # of collections

B. Will tissues, blood, or other body fluids be harvested (other than for antibody production)?
- ☐ No. Proceed to section II. C.
- ☒ Yes. Will tissues, blood, or other body fluids be collected post-mortem only?
  - ☒ Yes. Proceed to section II.C.
  - ☐ No. Complete Appendix 1: Antemortem Specimen Collection.

C. Will animals be food restricted (calorically or specific constituents) other than for surgical procedures?
- ☒ No. Proceed to section II. D.

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☐ Yes. [note: restriction paradigms exceeding a single 24-hr period must follow the ASU IACUC Standard Institutional Guideline for Food and Water Restriction available at https://researchintegrity.asu.edu/index.php/animals/procedures-library-and-guidelines

1. What are the restriction parameters? Provide scientific justification and include the length of restriction.

2. How will you monitor for negative effects of food restriction (include information on how you will account for animal growth)?

D. Will animals be water restricted?
☒ No. Proceed to section II. E.
☐ Yes. [note: restriction paradigms exceeding a single 24-hr period must follow the ASU IACUC Standard Institutional Guideline for Food and Water Restriction available at https://researchintegrity.asu.edu/index.php/animals/procedures-library-and-guidelines

1. What are the restriction parameters? Provide scientific justification and include the length of restriction.

2. How will you monitor for negative effects of water restriction (include information on how you will account for animal growth)?

E. Will animals be exposed to trauma, injury, burning, freezing, electric shock, UV radiation, magnetic fields, lasers, loud noise, or other physical agents that might cause distress?
☒ No. Proceed to section II. F.
☐ Yes. List and justify each exposure.
Provide scientific justification:

F. Will animals be exposed to environmental stress (e.g., non-natural temperature exposure, prolonged physical restraint, forced exercise)?
☒ No. Proceed to section II. G.
☐ Yes. List and scientifically justify each exposure.

G. Will animals undergo surgery?
☐ No. Proceed to section II. H.
☒ Yes. Complete Appendix 2: Surgical Procedures.

H. Will any animals have a device (e.g., thermocouple, cannula, electrode) that extends chronically through the skin?
☒ No. Proceed to section II. I.
☐ Yes. Describe wound management measures to minimize chances of infection around the device where it penetrates the skin:

I. Will individuals of a social species (e.g., most rodents) need to be housed singly at any time?
☐ No. Proceed to section II. J.
☒ Yes.

1. What would be the maximum duration that an individual would be singly housed? Provide scientific justification for singly housing for this duration:
Animals will be pair or group housed when possible and do not need to be singly housed for research-related needs. However, some animals may need to be singly housed under certain circumstances (e.g., fighting, unexpected death, early end point euthanasia of cagemate). The

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necessity for single housing will be determined in conjunction with the veterinary staff and will continue until a suitable pairing partner becomes available or the experiment concludes.

2. Singly housed animals should receive additional enrichment. Describe what enrichment will be provided or scientifically justify why additional enrichment cannot be provided:
Animals will be housed in a room with other conspecifics and have access to visual, olfactory, and vocal/auditory contact. Single housed animals will also be provided access to alternative enrichment option(s) per DACT policies.

J. Will animals need any other special husbandry considerations, including but not limited to altering standard cage type, cage change frequencies, housing temperature, or lack of enrichment?
☒ No. Proceed to section II. K.
☐ Yes. Describe special procedures and provide scientific justification:

K. Will animals be transported off campus (e.g., to/from the field, or between institutions) in a vehicle other than one owned by the DACT?
☒ No. Proceed to section II. L.
☐ Yes. Describe details (e.g., vehicle to be used, destinations, and driven by whom), read the IACUC *SIG - Off-campus Transport of Animals by Laboratory Personnel*, and complete and submit with this protocol the *Assurance to Abide by the Requirements for Transporting Live Animals*:

L. Will any work be conducted in the field (this includes field experiments or the capture of animals to be used in laboratory experiments)?
☒ No. Proceed to section II. M.
☐ Yes. Complete Appendix 3: Field Research.

M. Will any animals need to be individually identified?
☐ No. Proceed to section III.
☒ Yes. Describe the marking technique to be used, why that technique was chosen, how it will be performed, and on what age range of animals?
Animals will be identified with a commercial ear tag [redacted] applied on 3-month-old animals after receipt. If the ear tag is lost, a second tag may be placed in the opposite ear. If the second tag is lost, no further tags will be applied to the animal. This identification method is commonly used in rodents and considered minimally painful.

III. CHEMICALS AND OTHER POTENTIAL HAZARDS

(If you answer yes to any of the following questions, this information may be forwarded to another oversight unit to aid you in assuring safe practices. Approval by these units or additional training may be required prior to using any of these materials)

A. Will drugs or chemicals be used with animals?
☐ No. Proceed to section III. B.
☒ Yes. For each drug or chemical, list the agent, dose, route, purpose, and grade in the table below:

Agent	Dose	Route	Purpose	Frequency	Pharmaceutical grade (Y/N)?	Is this a DEA controlled substance (Y/N)?
Ketamine	25-90 mg/kg	IP	Anesthesia	As needed	Y	Y
Xylazine	5 mg/kg	IP	Anesthesia	As needed	Y	N
Atipamezole	1 mg/kg	IP	Xylazine reversal	As needed	Y	N
Meloxicam	1-2 mg/kg	SC	Analgesia	Once pre-op and then once daily for up	Y	N

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				to 5 days, as needed		
Buprenorphine	0.02-0.1 mg/kg	SC	Analgesia	Once daily for up to 3 days, as needed	Y	Y
Saline	1 mL/100g	SC	Fluid Replacement	As needed	Y	N
Lidocaine	1 spray pump	Topical	Analgesia	Once	Y	N
Ophthalmic ointment	Dab	Topical	Prevent corneal desiccation	Once	Y	N
Triple antibiotic ointment	Dab	Topical	Antibiotic	Once	Y	N
Povidone iodine	10%	Topical	Topical Disinfectant	Once	Y	N
Chlorhexidine	2%	Topical	Topical disinfectant	Once	Y	N
Isopropyl alcohol	70%	70%	Topical	Topical disinfectant	Y	N
Saline	200 mL	IC	Perfusion	Once	Y	N
4% Formaldehyde	200 mL	IC	Perfusion	Once	N	N

1. For each drug or chemical that is not pharmaceutical grade, indicate whether no pharmaceutical grade equivalent exists or provide scientific justification for using the non-pharmaceutical grade product.
   Formaldehyde is not available in a pharmaceutical grade and is only used once in a terminal procedure.

B. Does this project involve transgenic, knockout, or knock-in animals?
☒ No. Proceed to section III. C.
☐ Yes. List the strains, any special care needs, and any expected clinical signs that are associated with the strain. Transgenic animals need to be covered by an IBC disclosure.

C. Does this project involve the use of biohazardous agents in animals (microorganisms, microbial toxins, recombinant DNA)?
☐ No. Proceed to section III. D.
☒ Yes. List the agent, as well as concentration, dose, and route if applicable.

Agent	Concentration	Dose	Route	ADMIN. USE ONLY	
				ABSL	IBC # if Req'd
AAV-Oligo-α-syn	3.7E12 vg/mL	4µL	Bilateral Intracranial Injection into striatum		SPROTO2021-70
AAV-Oligo--GFP	3.7E12 vg/mL	4µL	Bilateral Intracranial Injection into striatum		SPROTO2021-70

D. Does this project involve irradiation or the use of radiological material in animals?
☒ No. Proceed to section III. E.

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☐ Yes. List the agent, dose, route, and purpose in the table below:

Agent	Dose	Route	Purpose

1. Provide the date of **Radiation Safety Committee** approval:

E. Describe any health hazards to **researchers** and include a description on how the risk is mitigated or managed:
Risk of bites, scratches, allergies. Risks are mitigated with the use of PPE as required by university policies and through rodent training/certification.

F. Describe any health hazards to **animals** and include a description on how the risk is mitigated or managed:
Rarely, rats may experience post-operative complications from intracranial injections that may include acute mortality or manifestation of neurological clinical signs. Risks are mitigated by close monitoring under anesthesia and post-operatively, as well as by consulting with veterinary staff if clinical signs develop.

IV. DETRIMENTAL SEQUELAE

A. Will animals possibly experience clinical signs intentionally or as a possible side effect of the study?
☐ No. Proceed to section V.
☒ Yes. Complete the following.

Possible Clinical Effect	Probability of Occurrence	Treatment
Intracranial injections may exhibit temporary post-op clinical signs related to the procedure.	Post-op clinical signs occur infrequently following injection and typically resolve after a few days. We expect any clinical signs to be mild and not affect the animals' ability to locomote or eat.	Consult with veterinary staff if clinical signs develop

V. END POINT CRITERIA

A. What clinical signs will be used as a basis for removal of an animal from the study?
Any animal that shows general signs of poor health (e.g., hunched posture, lethargy) will be weighed. Animals with weight loss in excess of 20% of pre-surgery weight will be provided supportive care as determined and provided in conjunction with the DACT veterinary team and weighed every other day. If weight does not return to ≥80% of pre-surgery weight after two weeks of supportive treatment or if weight loss is in excess of 25% of pre-surgery weight at any time, the animal will be euthanized.

Additionally, if an animal becomes laterally recumbent or has difficulty locomoting or feeding itself, it will be euthanized or provided supportive care as determined by the DACT Veterinary Team (i.e., veterinary discretion).

VI. EUTHANASIA

A. List the primary method of euthanasia:
Transcardial perfusion under anesthesia. Perfusion will be performed in accordance with the Whole Animal Perfusion SIG. If not perfusing, carbon dioxide followed by cervical dislocation in accordance with the Euthanasia SIG.

B. If using a chemical or gas, complete the chart below:

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Agent	Dose	Route	Is this a DEA controlled substance (Y/N)?	Secondary method used to confirm euthanasia
Ketamine	90 mg/kg	IP	Y	Used in conjunction with perfusion
Xylazine	5 mg/kg	IP	N	Used in conjunction with perfusion
Saline	200 mL	IC	N	Used in conjunction with perfusion
4% formaldehyde	200 mL	IC	N	Used in conjunction with perfusion
Carbon dioxide	100% chamber flow at 30-70% air change/minute	Inhalation	N	Cervical dislocation

C. If euthanasia is being done by a physical means (e.g., decapitation, cervical dislocation) without anesthesia, provide scientific justification:
N/A

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APPENDIX 2: SURGICAL PROCEDURES

I. GENERAL INFORMATION

A. Species
Rat

B. Surgical Procedure(s)
Intracranial Injection

C. Room/location of surgery
[redacted]

II. PRE-SURGICAL CARE

B. Will the animals undergo pre-surgical fasting?
☒ No. Proceed to section III.
☐ Yes. Provide the details:

III. SURGICAL PROCEDURE:

☒ Survival ☐ Nonsurvival

***Note:** A surgical checklist is recommended for each survival surgery, and possibly non-survival surgeries. These checklists should be submitted to DACT's Research Support Services [redacted] for review before implementing procedures.

A. Describe each surgical procedure (e.g., approach, tissue manipulation, closure):
Intracranial Injections (Survival)
All surgical surfaces will be sanitized with a quaternary ammonium solution. Surgical instruments will be autoclaved before surgery and will be cleaned and kept immersed in a hot bead sterilizer between surgical procedures. Animals will be anesthetized with ketamine/xylazine mix and placed on a heating pad. Animals will be administered meloxicam pre-op. A complete lack of toe-pinch response must be observed. Their heads and necks will be shaved and prepared with povidone iodine or chlorhexidine followed by alcohol wipe 3 times and placed in a [redacted] stereotaxic frame. An ophthalmic ointment will be placed in their eyes to prevent drying. The animal's body will be covered with a drape. An approximately 10 mm midline sagittal incision will be made. Immediately following midline incision, all animals will be given sterile lidocaine misted topically over the incision site. Two burr holes (1 mm diameter) will be created dorsal to the striatum in each hemisphere using an 18G needle. Animals will receive bilateral intracranial injections of AAV-Oligo-α-syn or AAV-Oligo-GFP vector, 2µL per hemisphere, into the striatum. All injections will be administered using a 10 µ[redacted]syringe with a 30G needle connected to an infusion pump at a rate of 0.2 µL/minute. The needle will be left in situ for an additional 5 minutes following injection to allow the vector to diffuse from the needle tip. The scalp will be closed using wound clips. All animals will be given atipamezole post-op to reverse the effects of xylazine and improve post-operative survival rate, and the wound will be covered with triple antibiotic ointment. Animals will be given sterile saline post-op for fluid maintenance. Surgery will last approximately 45 minutes per animal. Each animal will be returned to a clean cage, and the cage will be placed on a heating pad until the animal is recovered. If any animal exhibits signs of pain or distress after recovery from surgery, they may be administered meloxicam or buprenorphine once per day as needed for further analgesia. If an animal has not begun to ambulate 20 minutes post-op, it will be given an additional dose of saline. Animals will continue to be monitored every 10-15 mins until able to ambulate in accordance with the Post-operative Care SIG.

B. Anesthetic regimen:

Drug & concentration (e.g., mg/ml)	Dose (e.g., mg/kg) & maximum volume to be given	Route	Is this a DEA controlled substance (Y/N)?
Ketamine	90 mg/kg	IP	Y

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Xylazine	5 mg/kg	IP	N
Ketamine	25 mg/kg (booster to extend anesthesia as needed)	IP	Y

Note: Use of gas anesthetics requires completion of the EH&S-based Anesthetic Gas Safety training prior to use and refreshed annually.

1. Describe measures used to indicate a surgical plane of anesthesia to keep animals from getting too light or too deep:
   Anesthesia depth will be monitored approximately every 10 minutes through toe pinch.

C. Additional pharmacological agents used during surgery (include analgesics, supportive medications, and research drugs):

Drug and concentration	Dose & max volume	Route	Purpose	Frequency	Is this a DEA controlled substance (Y/N)?
Povidone iodine	10%	Topical	Topical disinfectant	Once	N
Isopropyl alcohol	70%	Topical	Topical disinfectant	Once	N
Chlorhexidine	2%	Topical	Topical disinfectant	Once	N
Atipamezole	1 mg/kg, 0.1 mL/100 g	IP	Xylazine reversal	Once	N
Meloxicam	1-2 mg/kg, 0.8 mL/100 g	SC	Analgesia	Once	N
Lidocaine	1 spray pump	Topical	Analgesia	Once	N
Ophthalmic ointment	Dab	Topical	Prevent corneal desiccation	Once	N

Describe the steps taken to maintain an aseptic surgery:
Trained individuals will perform standard sterile prep of the scalp. The site will be scrubbed alternating with povidone iodine/chlorhexidine and alcohol three times. Sterile instruments will be used and aseptic technique will be observed.

D. What is the maximum duration of each surgery?
45 minutes

E. Will any animals recover from surgery?
☐ No. This involves terminal, or non-survival, procedures; Appendix 2 is complete.
☒ Yes. Complete Section IV.

IV. POST-SURGICAL CARE

A. Is there a potential for post-operative pain or distress?
☐ No. Proceed to section C.
☒ Yes.

B. Will analgesics be used?
(For analgesic options, refer to the IACUC Standard Institutional Guideline on analgesia (https://researchintegrity.asu.edu/animals/procedures-library-and-guidelines) or contact a DACT veterinarian
☐ No. Provide a scientific justification:

☒ Yes. Complete the following.

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Drug & concentration	Dose & max. volume	Route	Frequency	Is this a DEA controlled substance (Y/N)?
Meloxicam (0.25 mg/mL)	1-2 mg/kg, 0.8 mL/100 g	SC	Once daily for up to 5 days, as needed	N
Buprenorphine	0.02-0.1 mg/kg	SC	Once daily for up to 3 days, as needed	Y

Who will administer these drugs?
Investigator staff or other trained individuals.

C. Post-operative routine care:

i. What other drugs will be administered, if any (e.g., antibiotics, fluids)?

Drug & concentration	Dose & max. volume	Route	Purpose	Frequency	Is this a DEA controlled substance (Y/N)?
Saline	1 mL/100 g	SC	Fluid replacement	As needed	N
Triple antibiotic ointment	Dab	Topical	Antibiotic	Once	N

ii. What other post-operative support and monitoring will be provided, how often, for how long, and by whom?
Animals will be observed daily for at least three days post-op. Monitoring is provided by both trained DACT and PI personnel. Should any animal experience adverse effects post-surgery (including signs of cerebral infection, cranial incision complications, or neurologic deficits) as determined by the veterinary staff, they will be evaluated and treated as determined by the veterinary staff.

D. Is post-operative intensive care required?
☒ No. Proceed to section E.
☐ Yes.
What special care is required?

Who will provide special care and what are their qualifications?

For how long will special care be needed?

E. Will animals undergo multiple survival surgical procedures?
☒ No. Appendix 2 is complete.
☐ Yes. Describe which surgeries, the sequence (specifying time between surgeries), and frequency.
Provide scientific justification:

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From: IACUC@asu.edu
To: [redacted]
Subject: FW: [redacted] RFC
Date: Wednesday, June 29, 2022 2:11:32 PM
Attachments: [redacted] 21-1867R RFC 4 vet-cleared-DR-cleared.docx

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From: Karen Kibler [redacted]
Sent: Wednesday, June 29, 2022 8:08:44 PM (UTC+00:00) Monrovia, Reykjavik
To: IACUC@asu.edu <iacuc@asu.edu>
Subject: [redacted] RFC

Hello, [redacted] and [redacted]

I think I forgot to send you this approved version last Friday.

Thanks,
Karen

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

[redacted]

To: [redacted]iacuc@asu.edu
Subject: RE: Action Required: Designated Review for [redacted]21 1867R RFC 4

From [redacted]
Sent: Friday, June 24, 2022 9:35 AM
To: [redacted] Dale DeNardo [redacted] Karen Kibler [redacted]
Cc: IACUC@asu.edu [redacted]
Subject: Action Required: Designated Review for [redacted]21-1867R RFC 4
Importance: High

Designated Reviewer: **Karen Kibler**
Principal Investigator: [redacted]
Peer Reviewer: **N/A**
Protocol Number: [redacted]**21-1867R RFC 4**

Tracking:	**Recipient**	**Response**
	[redacted] Dale DeNardo	Yes: 6/24/2022 9:51 AM
	[redacted] Karen Kibler	Yes: 6/24/2022 9:41 AM
	[redacted]	Yes: 6/24/2022 9:43 AM
	[redacted]	Yes: 6/25/2022 11:46 AM
	[redacted]	Yes: 6/24/2022 10:39 AM
	[redacted]	Yes: 6/26/2022 10:55 PM
	[redacted]	Yes: 6/24/2022 9:42 AM
	[redacted]	Yes: 6/24/2022 2:24 PM
	[redacted]	Yes: 6/24/2022 10:04 AM

A request for an amendment to the referenced protocols has been submitted. The request for amendment is attached and the various related protocols are available at the SharePoint site. The Designated Review process allows IACUC members, by voting, to permit the Designated Reviewer to approve or disapprove an amendment request.

Select "**YES**" if you approve the use of the designated review process for this amendment.

Select "**NO**" if you disapprove the use of designated review process regarding this amendment request. The amendment will then be reviewed at the next monthly IACUC meeting.

Select "**Abstain**" if you would like to abstain from the vote for any reason.

Select "**Recuse**" if you have a conflict of interest.

Please indicate your approval or disapproval of the request for designated review by using the YES or NO button in the toolbar at the top of this message. The use of "YES or NO" buttons allows you to submit comments along with your choice. **You may also send your comments to me directly or to the primary reviewer without using the selection buttons. Please copy me on all correspondence and email related to this request.**

Sincerely,

Obtained by Rise for Animals.
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PRR22-11_0407

IACUC Protocol Trackable Components Checklist

Protocol #: 21-1867R If for amendment, amendment #: 4

PI: [redacted]

Species: Macaque, Rats (RFC 4) Highest Category of Pain: Macaques – D

Rats - no unalleviated pain

Completed by: Dale DeNardo Date completed: 6/23/2022

☐ No trackable components in this document

Exceptions to the Guide:

☐ Food/Fluid Regulation
- Species:
- What Restricted:
- Parameters:

☐ Prolonged Restraint
- Species:
- Details:

☒ Husbandry Deviation from the Guide
- Species: Macaque; rats (RFC 4)
- Deviation: macaques single housing if suitable pairing partners are not available; rats singly housed under non-research related circumstances (e.g., fighting, unexpected death, early end point euthanasia of cagemate)

☐ Other:

Other Trackable Components:

☒ Survival Surgerie(s)
- Species: Macaque, rats (RFC 4)
- Surgerie(s): Intracranial injection
- Multiple Major?: ☐ Yes ☒ No

☒ Hazardous Agents
- Biological (list agent and hazard level): AAV
- Chemical (note category – toxicant, toxin, irritant, carcinogen, etc.): 4% Formaldehyde
- Physical (note type - radiation, UV light, lasers, noise, magnetic fields, etc.): MRI (magnetic fields and up to ~110 dB noise)

☐ Non-Centralized Animal Housing
- Location:
- Maximum duration:

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IACUC Protocol Trackable Components Checklist

☐ Decapitation

☐ USDA-covered Species exempt from USDA reporting

Obtained by Rise for Animals.
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Institutional Animal Care and Use Committee (IACUC)
Office of Research Integrity and Assurance
Arizona State University

[redacted]

Animal Protocol Review

ASU Protocol Number: 21-1867R RFC 5
Protocol Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics
Principal Investigator: [redacted]
Date of Action: 7/6/2022

The animal protocol review was considered by the Committee and the following decisions were made:

The request for changes was administratively approved to add [redacted] as additional personnel to the protocol.

NOTE: If you have not already done so, documentation of Level III Training (i.e., procedure-specific training) will need to be provided to the IACUC office before participants can perform procedures without supervision. For more information on Level III requirements see https://researchintegrity.asu.edu/animals/training, or contact Research Support Services within DACT at [redacted]

Additional requirements:

☐ This protocol requires that Research Support Services group within DACT provide supervision for the first time a procedure is conducted. Contact [redacted] to schedule.
☐ This protocol indicates that there are surgical procedures. A surgical checklist may be required to be submitted to Research Support Services within DACT [redacted], prior to starting surgeries.
☐ Other requirements:

Total # of Animals: 26
Species: NHP **Pain Category:** D - 18
Species: Rats **Unalleviated Pain/Distress:** No

Protocol Approval Period: 8/26/2021 – 8/25/2024

Sponsor: National Institutes of Health
ASU Proposal/Award #: [redacted]
Title: Differential diagnosis of Parkinson's and multiple system atrophy in nonhuman primate models using a novel a-synuclein retinal contrast agent and AI assisted analytics

Signature: [redacted] Date: 7/7/2022
IACUC Chair or Designee
Cc: IACUC Office; IACUC Chair

Obtained by Rise for Animals.
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PERSONNEL MODIFICATION FORM
IACUC and IBC

This form can be used to add or remove participants from both an IACUC protocol and an IBC disclosure. Please submit only one form to Research.Integrity@asu.edu and it will be processed by both committees.

Principal Investigator Name: [redacted]	Phone: [redacted]
Dept [redacted]	Email: [redacted]

Participant #1	**Add to:** ☒ **IBC #**SPROTO202100000070 ☒ **IACUC #** 21-1867R, 22-1872R, 22-1873R, 22-1880R, 22-1886R, 22-1887R, 22-1898R, 22-1901R, 22-1903R, 22-1918R **Delete from:** ☐ **IBC #** ☐ **IACUC #**	**FOR ORIA USE ONLY** **Training Verification**
Name: [redacted] **ASURITE:** [redacted] **Email:** [redacted]		
Project Responsibilities in IBC: Will handle AAV vir preformed fibrils, Human Lewy Body extracts, and mouse/rat/nonhuman primate blood/CSF/brain tissue.		Added in ERA
Experience/Training in These Responsibilities: 7 years' experience in rodent and macaque research with ASU DACT.		
What procedures are they responsible for on the IACUC protocol (please note which procedures are being done independently and which are done under supervision: Macaques: Intracranial surgery, intracarotid surgery, MRI, PET scan, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified). Rats: Intracranial surgery, blood/CSF collection, behavioral tests, administration of any medications, and necropsy (all under direct supervision until certified). Mice: Intracranial surgery, blood/CSF collection, behavioral tests, administration of any medications, and necropsy (all under direct supervision until certified).		5/2019 OHSP
Species: Macaques, Rats, Mice **Experience and training with species and procedures:** 7 years' experience in rodent and macaque research with ASU DACT.		

Assurance

As Principal Investigator, I assure that personnel will receive appropriate training prior to working with animals or biological materials as applicable.

Principal Investigator Signature: [redacted] Date: 7/1/22

FOR ORIA USE ONLY	☐ **IBC Approved**	☒ **IACUC Approved 7/6/2022**

Revised 11/20/12

Obtained by Rise for Animals.
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Institutional Animal Care and Use Committee (IACUC)
Office of Research Integrity and Assurance
Arizona State University

[redacted]

Animal Protocol Review

ASU Protocol Number: 21-1867R RFC 6
Protocol Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics
Principal Investigator: [redacted]
Date of Action: 7/13/2022

The animal protocol review was considered by the Committee and the following decisions were made:

The request for changes was approved by Designated Review to alter previously approved procedures.

NOTE: If you have not already done so, documentation of Level III Training (i.e., procedure-specific training) will need to be provided to the IACUC office before participants can perform procedures without supervision. For more information on Level III requirements see https://researchintegrity.asu.edu/animals/training, or contact Research Support Services within DACT a[redacted]

Additional requirements:

☐ This protocol requires that Research Support Services group within DACT provide supervision for the first time a procedure is conducted. Contac[redacted] to schedule.
☐ This protocol indicates that there are surgical procedures. A surgical checklist may be required to be submitted to Research Support Services within DACT [redacted], prior to starting surgeries.
☐ Other requirements:

Total # of Animals: 26
Species: NHP — **Pain Category:** D – 18
Species: Rats — **Unalleviated Pain/Distress:** No

Protocol Approval Period: 8/26/2021 – 8/25/2024

Sponsor: National Institutes of Health
ASU Proposal/Award #: [redacted]
Title: Differential diagnosis of Parkinson's and multiple system atrophy in nonhuman primate models using a novel a-synuclein retinal contrast agent and AI assisted analytics

Signature: [redacted] Date: 7/15/2022
IACUC Chair or Designee
Cc: IACUC Office; IACUC Chair

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

ARIZONA STATE UNIVERSITY

Institutional Animal Care and Use Committee

REQUEST FOR CHANGES TO AN APPROVED PROTOCOL

Protocol No. 21-1867R RFC 6
Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted anal ytics

Principal Investigator: [redacted] Email Address [redacted]
If not PI, whom should we contact for questions related to this amendment: [redacted] Email Address: [redacted]

☒ Funded ☐ Unfunded

Requested Change (check all that apply):

☐ New procedures to be performed – complete Part A, and Appendix 1 and/or 2 as applicable, and sign assurance.
☐ New species and or an increase in the number of animals to be used – complete Part A and sign assurance.
☐ New location of housing or procedures – complete Part A and sign assurance.
☐ New personnel – complete Part B and sign assurance.
☒ Other (includes changes in dosages, funding, etc.) – complete Part A and sign assurance.

A. Description of Requested Changes

For new procedures or additional animals that are USDA-covered species (all mammals EXCEPT mice and rats bred for research), list the **Category of Pain:**

For new procedures or additional animals that are not USDA-covered species, will there be the potential to involve more than slight or momentary pain or distress that will NOT be relieved with anesthetics, analgesics, tranquilizer drugs, or other methods for relieving pain or distress (e.g., negative conditioning, unrelieved post-surgical pain, death without euthanasia)? ☐ No ☐ Yes

If yes, describe and justify:

If you are adding a procedure that could create pain or distress, you need to include a **literature search** for alternatives.
If you are adding a new survival surgery, submit a surgical checklist.
If you are requesting an increase in animal numbers, provide justification with supportive statistics.
If you are adding additional funding sources, provide the grant agency, grant title and ASU proposal or award number.

Describe the changes you are requesting. After further discussions with the sponsor, it was decided to eliminate the Parkinson's disease model that was to receive alpha-synuclein PFF injections and focus solely on the MSA disease model at this time. This will reduce the total number of macaques needed to 12.

Group	Disease Model	Putamenal injectate	N=
1	MSA	AAV-Oligo-α-syn	6
2	Control	AAV-Oligo-GFP	6

Based on the sponsor's internal testing with the retinal contrast agent [redacted] it was determined that peak contrast was seen within 15 minutes of administration, so it was decided to eliminate the 60-minute and 24-hour post-injection timepoints and only image the retinas pre and 2-, 5-, 15-, and 30-minutes post-injection with [redacted] during each retinal imaging procedure.

As the length of time required for alpha-synuclein to make its way from the putamen to the retina has never been studied in nonhuman primates, it was decided to delay the first post-operative imaging procedure until 2 months following vector injection, and then to image the retinas once per month until we see evidence of alpha synuclein deposits in the retina. Once we see evidence of alpha synuclein deposits, we would like to increase the frequency of retinal imaging to every two weeks. It was also decided to delay sacrifice until 6 months post-op to increase the chance of seeing retinal synuclein deposits if the transport of alpha synuclein is slow. The total number of planned retinal imaging procedures will be at least 6, and up to 10 max, depending on how early we see evidence of alpha synuclein deposits. Blood and CSF collection will be performed pre- and once per month post-op as previously described, which will result in 7 planned (9 max including

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potential redraws) collections with the new timeframe. Blood and CSF will be collected during the same sedation event whenever possible.

Finally, since the putamen, the site of vector injections in our established MSA model has no direct connection to the optic pathway, we would like to add one injection of 10 µL of the same vector in each group into the ipsilateral lateral geniculate nucleus (LGN) in order to increase the chances of alpha-synuclein making its way to the retina. We will also reduce the number and volume of putamenal vector injections to 3 sites unilaterally, 25, 25, 15 µL rostrocaudally per site.

B. Addition of Personnel

All personnel who work with animals are required to have animal care training within the last four years. ASU IACUC training modules can be completed at https://asu.co1.qualtrics.com/ife/form/SV_b2b2XRXRRs1309f. Personnel are required to have Level III training certification on file with the IACUC office in order to perform procedures independently (without supervision). Training can be received from DACT staff or PIs can have a member of their lab approved by DACT to be a Certified Trainer who can then train others. Simply being Level III certified does not allow the training of others. See the IACUC web site (https://researchintegrity.asu.edu/animals/training) for more information on training and Level III forms.

*** Procedures other than husbandry, handling, or behavioral testing MUST be performed under supervision unless the person is Level III certified to conduct the procedure independently. Personnel are not Level III certified until the IACUC has reviewed and approved the Level III training documentation. The PI is responsible for ensuring that personnel who are not Level III certified are supervised at all times.**

Name	Title	ASURITE name	What activities will each person perform on live animals ONLY while under direct supervision?	What activities will each person be allowed to perform independently (including appropriate Level 3 certification*) at the time of protocol submission?	Species with which individual will have direct contact ("all" or list species) *	IACUC USE ONLY Training (mm/yy)

For each individual, describe the individual's training and years of experience with all listed species and procedures they will be conducting under this protocol. For procedures for which they are not yet trained, but will likely be trained to do during the activity period of this protocol, provide a description of who will provide such training:

Assurance

As Principal Investigator of this protocol, I assure that all procedures will be conducted as described in this request for changes and that personnel will receive appropriate additional training prior to conducting any new procedures that are not listed above.

SIGNED: [redacted]

Principal Investigator

Date

For IACUC use only:

- ☐ Administratively approved - Approving administrator: Date of approval:
- ☐ Administratively handled by VCV - Veterinarian providing verification: Date of verification:
  Sources used for verification:
- ☒ Approved by Designated Review – Designated reviewer: Karen K bler Date of approval: 7/13/2022
- ☐ Approved by Full Committee Review – Primary reviewer: Date of approval:

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Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

From: Karen Kibler
To: [redacted]
Cc: IACUC@asu.edu
Subject: RE: [redacted] 21-1867R RFC 6 - Ready for Assignment
Date: Monday, July 11, 2022 1:52:28 PM
Attachments: image001.png

Hi [redacted]

[redacted] answered my only concern, so if the process is approved, I approve the RFC as written.

Thanks,
Karen

From: [redacted]
Sent: Monday, July 11, 2022 11:32 AM
To: Karen Kibler; [redacted]
Cc: IACUC@asu.edu
Subject [redacted] 21 1867R RFC 6 Ready for Assignment

Hi Karen,

The attached RFC has cleared vet review. Who would you like to assign as the DR/PR?

Sincerely,

[redacted] | Compliance Coordinator, Office of Research Integrity & Assurance
Arizona State University | Knowledge Enterprise | Operations
[redacted] f 480-965-777
[redacted] | http://researchintegrity.asu.edu
H [redacted] or send a Sun Award
[redacted] ASU Users Only)

This message may contain information that is privileged, confidential and exempt from disclosure under applicable law. Please do not copy or forward this message without permission. If you are not the intended recipient, please delete all copies and notify me immediately by reply e-mail or by telephone [redacted] so we may correct our records

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[redacted]

To: IACUC@asu.edu
Subject: RE: Action Required: Designated Review for [redacted] 21 1867R RFC 6

From: [redacted]
Sent: Monday, July 11, 2022 7:57:24 PM (UTC+00:00) Monrovia, Reykjavik
To: [redacted] Dale DeNard Karen Kibler [redacted]
Cc: IACUC@asu.edu <iacuc@as[redacted]
Subject: Action Required: Designated Review for [redacted] 21-1867R RFC 6

Designated Reviewer: Karen Kibler
Principal Investigator: [redacted]
Peer Reviewer: N/A
Protocol Number: 21-1867R RFC 6

Tracking:	Recipient	Response
	[redacted]	Yes: 7/11/2022 3:35 PM
		Yes: 7/11/2022 5:48 PM
		Yes: 7/11/2022 4:22 PM
	Dale DeNardo	
	[redacted]	Yes: 7/12/2022 6:14 AM
	Karen Kibler	
	[redacted]	Yes: 7/11/2022 5:04 PM
		Yes: 7/11/2022 2:18 PM
		Yes: 7/11/2022 1:58 PM
		Yes: 7/11/2022 2:25 PM

A request for an amendment to the referenced protocols has been submitted. The request for amendment is attached and the various related protocols are available at the SharePoint site. The Designated Review process allows IACUC members, by voting, to permit the Designated Reviewer to approve or disapprove an amendment request.

Select "**YES**" if you approve the use of the designated review process for this amendment.

Select "**NO**" if you disapprove the use of designated review process regarding this amendment request. The amendment will then be reviewed at the next monthly IACUC meeting.

Select "**Abstain**" if you would like to abstain from the vote for any reason.

Select "**Recuse**" if you have a conflict of interest.

Please indicate your approval or disapproval of the request for designated review by using the YES or NO button in the toolbar at the top of this message. The use of "YES or NO" buttons allows you to submit comments along with your choice. **You may also send your comments to me directly or to the primary reviewer without using the selection buttons. Please copy me on all correspondence and email related to this request.**

Thank you,

[redacted] MLS | Compliance Coordinator, Office of Research Integrity & Assurance

Obtained by Rise for Animals.
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PRR22-11_0416

IACUC Protocol Trackable Components Checklist

Protocol #: 21-1867R If for amendment, amendment #: 6

PI [redacted]

Species: Macaque, Rats (RFC 4) Highest Category of Pain: Macaques D

Rats - no unalleviated pain

Completed by: [redacted] Date completed: 7/11/22

☐ No trackable components in this document

Exceptions to the Guide:

☐ Food/Fluid Regulation
- Species:
- What Restricted:
- Parameters:

☐ Prolonged Restraint
- Species:
- Details:

☒ Husbandry Deviation from the Guide
- Species: Macaque; rats (RFC 4)
- Deviation: macaques single housing if suitable pairing partners are not available; rats singly housed under non-research related circumstances (e.g., fighting, unexpected death, early end point euthanasia of cagemate)

☐ Other:

Other Trackable Components:

☒ Survival Surgerie(s)
- Species: Macaque, rats (RFC 4)
- Surgerie(s): Intracranial injection
- Multiple Major?: ☐ Yes ☒ No

☒ Hazardous Agents
- Biological (list agent and hazard level): AAV
- Chemical (note category toxicant, toxin, irritant, carcinogen, etc.): 4% Formaldehyde
- Physical (note type - radiation, UV light, lasers, noise, magnetic fields, etc.): MRI (magnetic fields and up to ~110 dB noise)

☐ Non-Centralized Animal Housing
- Location:
- Maximum duration:

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

IACUC Protocol Trackable Components Checklist

☐ Decapitation

☐ USDA-covered Species exempt from USDA reporting

Obtained by Rise for Animals.
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Institutional Animal Care and Use Committee (IACUC)
Office of Research Integrity and Assurance
Arizona State University

[redacted]

Animal Protocol Review

ASU Protocol Number: 21-1867R RFC 7
Protocol Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics
Principal Investigator: [redacted]
Date of Action: 8/2/2022

The animal protocol review was considered by the Committee and the following decisions were made:

The request for changes was administratively approved to ad[redacted] and [redacted]as additional personnel to the protocol.

NOTE: If you have not already done so, documentation of Level III Training (i.e., procedure-specific training) will need to be provided to the IACUC office before participants can perform procedures without supervision. For more information on Level III requirements see https://researchintegrity.asu.edu/animals/training, or contact Research Support Services within DACT at [redacted]

Additional requirements:

☐ This protocol requires that Research Support Services group within DACT provide supervision for the first time a procedure is conducted. Contac[redacted]to schedule.

☐ This protocol indicates that there are surgical procedures. A surgical checklist may be required to be submitted to Research Support Services within DACT [redacted]prior to starting surgeries.

☒ **Other requirements: IBC approval of new personnel is required before work with biohazardous materials may begin.**

Total # of Animals: 26
Species: NHP — **Pain Category: D – 18**
Species: Rats — **Unalleviated Pain/Distress: No**

Protocol Approval Period: 8/26/2021 – 8/25/2024
Sponsor: National Institutes of Health
ASU Proposal/Award #: [redacted]
Title: Differential diagnosis of Parkinson's and multiple system atrophy in nonhuman primate models using a novel a-synuclein retinal contrast agent and AI assisted analytics

Signature: [redacted] Date: 8/2/2022
IACUC Chair or Designee
Cc: IACUC Office; IACUC Chair

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PERSONNEL MODIFICATION FORM
IACUC and IBC

This form can be used to add or remove participants from both an IACUC protocol and an IBC disclosure. Please submit only one form to Research.Integrity@asu.edu and it will be processed by both committees.

Principal Investigator Name: [redacted]	Phone: [redacted]
Dept: [redacted]	Email: [redacted]

Participant #1	**Add to:** ☒ **IBC #**SPROTO202100000070 ☒ **IACUC #** 21-1867R, 22-1872R, 22-1873R, 22-1880R, 22-1886R, 22-1887R, 22-1898R, 22-1901R, 22-1903R, 22-1918R **Delete from:** ☐ **IBC #** ☐ **IACUC #**	**FOR ORIA USE ONLY** **Training Verification**
Name [redacted]	**ASURITE** [redacted]	**Email:** [redacted]
Project Responsibilities in IBC: Will handle AAV viral vectors, alpha-synuclein preformed fibrils, Human Lewy Body extracts, and mouse/rat/nonhuman primate blood/CSF/brain tissue.		
Experience/Training in These Responsibilities: No previous experience		
What procedures are they responsible for on the IACUC protocol (please note which procedures are being done independently and which are done under supervision: Macaques: Intracranial surgery, intracarotid surgery, MRI, PET scan, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified). Rats: Intracranial surgery, blood/CSF collection, behavioral tests, administration of any medications, and necropsy (all under direct supervision until certified). Mice: Intracranial surgery, blood/CSF collection, behavioral tests, administration of any medications, and necropsy (all under direct supervision until certified).		7/2022 OHSP
Species: Macaques, Rats, Mice **Experience and training with species and procedures:** No previous experience		
Participant #2	**Add to:** ☒ **IBC #**SPROTO202100000070 ☒ **IACUC #** 21-1867R, 22-1872R, 22-1873R, 22-1880R, 22-1886R, 22-1887R, 22-1898R, 22-1901R, 22-1903R, 22-1918R **Delete from:** ☐ **IBC #** ☐ **IACUC #**	**FOR ORIA USE ONLY** **Training Verification**
Name: [redacted]	**ASURITE:** [redacted]	**Email:** [redacted]
Project Responsibilities in IBC: Will handle AAV viral vectors, alpha-synuclein preformed fibrils, Human Lewy Body extracts, and mouse/rat/nonhuman primate blood/CSF/brain tissue.		
Experience/Training in These Responsibilities: No previous experience		
What procedures are they responsible for on the IACUC protocol (please note which procedures are being done independently and which are done under supervision: Macaques: Intracranial surgery, intracarotid surgery, MRI, PET scan, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified). Rats: Intracranial surgery, blood/CSF collection, behavioral tests, administration of any medications, and necropsy (all under direct supervision until certified). Mice: Intracranial surgery, blood/CSF collection, behavioral tests, administration of any medications, and necropsy (all under direct supervision until certified).		7/2022 OHSP
Species: Macaques, Rats, Mice **Experience and training with species and procedures:** No previous experience		

Assurance

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As Principal Investigator, I assure that personnel will receive appropriate training prior to working with animals or biological materials as applicable.

Principal Investigator Signature: [redacted] Date: 8/1/22

FOR ORIA USE ONLY	☐ IBC Approved	☒ IACUC Approved 8/2/2022

Revised 11/20/12

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

Institutional Animal Care and Use Committee (IACUC)
Office of Research Integrity and Assurance
Arizona State University

[redacted]

Animal Protocol Review

ASU Protocol Number: 21-1867R RFC 8
Protocol Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics
Principal Investigator: [redacted]
Date of Action: 8/11/2022

The animal protocol review was considered by the Committee and the following decisions were made:

The request for changes was approved by Designated Review to update the possible detrimental sequelae on the protocol.

NOTE: If you have not already done so, documentation of Level III Training (i.e., procedure-specific training) will need to be provided to the IACUC office before participants can perform procedures without supervision. For more information on Level III requirements see https://researchintegrity.asu.edu/animals/training, or contact Research Support Services within DACT at [redacted]

Additional requirements:

☐ This protocol requires that Research Support Services group within DACT provide supervision for the first time a procedure is conducted. Contact [redacted] to schedule.
☐ This protocol indicates that there are surgical procedures. A surgical checklist may be required to be submitted to Research Support Services within DACT [redacted] prior to starting surgeries.
☐ Other requirements:

Total # of Animals: 26
Species: NHP — **Pain Category:** D - 18
Species: Rats — **Unalleviated Pain/Distress:** No

Protocol Approval Period: 8/26/2021 – 8/25/2024

Sponsor: National Institutes of Health
ASU Proposal/Award #: [redacted]
Title: Differential diagnosis of Parkinson's and multiple system atrophy in nonhuman primate models using a novel a-synuclein retinal contrast agent and AI assisted analytics

Signature: [redacted] Date: 8/11/2022
IACUC Chair or Designee
Cc: IACUC Office; IACUC Chair

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

ARIZONA STATE UNIVERSITY

Institutional Animal Care and Use Committee

REQUEST FOR CHANGES TO AN APPROVED PROTOCOL

Protocol No. 21-1867R, 22-1872R, 22-1873R, 22-1880R, 22-1886R, 22-1887R, 22-1898R, 22-1901R, 22-1903R, 22-1918R

Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics
Kinase activation in multiple system atrophy
Reprogramming astrocytes to functional dopaminergic neurons in non-human primate brain
Co-Pathologies Drive Neuroinflammation and Progression in PD
Genetic Silencing of Striatal CaV1.3 Calcium Channels as a Potent Antidyskinetic Therapy for PD
AAV Trehalose in an NHP model of Alzheimer's Disease
BAG3 in Rodent Models of Neurodegenerative Disease
Bifunctional intrabody targeting intracellular alpha-synuclein
Primate Holding, Assessment, and Training
AAV-GBA Therapy in an NHP model of PD

Principal Investigator: [redacted] Email Address: [redacted]

If not PI, whom should we contact for questions related to this amendment: [redacted] Email Address: [redacted]

☒ Funded ☐ Unfunded

Requested Change (check all that apply):

☐ New procedures to be performed – complete Part A, and Appendix 1 and/or 2 as applicable, and sign assurance.
☐ New species and or an increase in the number of animals to be used – complete Part A and sign assurance.
☐ New location of housing or procedures – complete Part A and sign assurance.
☐ New personnel – complete Part B and sign assurance.
☒ Other (includes changes in dosages, funding, etc.) – complete Part A and sign assurance.

A. Description of Requested Changes

For new procedures or additional animals that are USDA-covered species (all mammals EXCEPT mice and rats bred for research), list the **Category of Pain:**

For new procedures or additional animals that are not USDA-covered species, will there be the potential to involve more than slight or momentary pain or distress that will NOT be relieved with anesthetics, analgesics, tranquilizer drugs, or other methods for relieving pain or distress (e.g., negative conditioning, unrelieved post-surgical pain, death without euthanasia)? ☐ No ☐ Yes

If yes, describe and justify:

If you are adding a procedure that could create pain or distress, you need to include a **literature search** for alternatives.
If you are adding a new survival surgery, submit a surgical checklist.
If you are requesting an increase in animal numbers, provide justification with supportive statistics.
If you are adding additional funding sources, provide the grant agency, grant title and ASU proposal or award number.

Describe the changes you are requesting. We would like to add additional possible detrimental sequelae.

Possible Clinical Effect	Probability of Occurrence	Treatment
Surgical and other procedures performed under anesthesia may rarely result in death or permanent disability due to hemorrhage, edema, thrombosis, infection, toxicity, or complications due to anesthesia.	Rare	Consult with veterinary staff if clinical signs develop. Euthanasia may be considered.

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

B. Addition of Personnel

All personnel who work with animals are required to have animal care training within the last four years. ASU IACUC training modules can be completed at https://asu.co1.qualtrics.com/jfe/form/SV_b2b2XRXRRs1309f. Personnel are required to have Level III training certification on file with the IACUC office in order to perform procedures independently (without supervision). Training can be received from DACT staff or PIs can have a member of their lab approved by DACT to be a Certified Trainer who can then train others. Simply being Level III certified does not allow the training of others. See the IACUC web site (https://researchintegrity.asu.edu/animals/training) for more information on training and Level III forms.

*** Procedures other than husbandry, handling, or behavioral testing MUST be performed under supervision unless the person is Level III certified to conduct the procedure independently. Personnel are not Level III certified until the IACUC has reviewed and approved the Level III training documentation. The PI is responsible for ensuring that personnel who are not Level III certified are supervised at all times.**

Name	Title	ASURITE name	What activities will each person perform on live animals ONLY while under direct supervision?	What activities will each person be allowed to perform independently (including appropriate Level 3 certification*) at the time of protocol submission?	Species with which individual will have direct contact ("all" or list species) *	IACUC USE ONLY Training (mm/yy)

For each individual, describe the individual's training and years of experience with all listed species and procedures they will be conducting under this protocol. For procedures for which they are not yet trained, but will likely be trained to do during the activity period of this protocol, provide a description of who will provide such training:

Assurance

As Principal Investigator of this protocol, I assure that all procedures will be conducted as described in this request for changes and that personnel will receive appropriate additional training prior to conducting any new procedures that are not listed above.

SIGNED: [redacted]

Principal Investigator

8/4/2022
Date

For IACUC use only:

- ☐ Administratively approved - Approving administrator: Date of approval:
- ☐ Administratively handled by VCV - Veterinarian providing verification: Date of verification:
  Sources used for verification:
- ☒ Approved by Designated Review – Designated reviewer: Karen K bler Date of approval: 8/11/2022
- ☐ Approved by Full Committee Review – Primary reviewer: Date of approval:

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

From: Karen Kibler
To: [redacted]
Cc: IACUC@asu.edu
Subject: Multiprotocol RFC
Date: Tuesday, August 9, 2022 10:46:50 AM
Attachments: [redacted]Multiprotocol RFC 8.5.2022 Final.docx

Hello, [redacted]

The attached version is DR approved.

Thanks,
Karen

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

[redacted]

To: [redacted] iacuc@asu.edu
Subject: RE: Action Required: Designated Review fo[redacted] Multiprotocol RFC 8.5.2022

From: [redacted]
Sent: Tuesday, August 9, 2022 9:47 AM
To: [redacted] Dale DeNardo [redacted] Karen Kibler [redacted]
Cc: IACUC@asu.edu
Subject: Action Required: Designated Review for[redacted] Multiprotocol RFC 8.5.2022
Importance: High

Designated Reviewer: Karen Kibler
Principal Investigator: [redacted]
Peer Reviewer: N/A
Protocol Number: [redacted] ultiprotocol RFC 8.5.2022

Tracking:	Recipient	Response
	[redacted]	Yes: 8/9/2022 10:15 AM
		Yes: 8/9/2022 10:10 AM
		Yes: 8/9/2022 10:31 AM
		Yes: 8/10/2022 7:56 AM
		Yes: 8/9/2022 10:15 AM
		Yes: 8/9/2022 11:17 AM
		Yes: 8/9/2022 3:29 PM
		Yes: 8/9/2022 10:13 AM
		Yes: 8/10/2022 5:06 PM

A request for an amendment to the referenced protocols has been submitted. The request for amendment is attached and the various related protocols are available at the SharePoint site. The Designated Review process allows IACUC members, by voting, to permit the Designated Reviewer to approve or disapprove an amendment request.

Select "**YES**" if you approve the use of the designated review process for this amendment.

Select "**NO**" if you disapprove the use of designated review process regarding this amendment request. The amendment will then be reviewed at the next monthly IACUC meeting.

Select "**Abstain**" if you would like to abstain from the vote for any reason.

Select "**Recuse**" if you have a conflict of interest.

Please indicate your approval or disapproval of the request for designated review by using the YES or NO button in the toolbar at the top of this message. The use of "YES or NO" buttons allows you to submit comments along with your choice. **You may also send your comments to me directly or to the primary reviewer without using the selection buttons. Please copy me on all correspondence and email related to this request.**

Sincerely,

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

PRR22-11_0426

IACUC Protocol Trackable Components Checklist

Protocol #: 21-1867R If for amendment, amendment #: 8

PI: [redacted]

Species: Macaque, Rats (RFC 4) Highest Category of Pain: Macaques – D

Rats - no unalleviated pain

Completed by: [redacted] Date completed: 8/8/22

☐ No trackable components in this document

Exceptions to the Guide:

☐ Food/Fluid Regulation
- Species:
- What Restricted:
- Parameters:

☐ Prolonged Restraint
- Species:
- Details:

☒ Husbandry Deviation from the Guide
- Species: Macaque; rats (RFC 4)
- Deviation: macaques single housing if suitable pairing partners are not available; rats singly housed under non-research related circumstances (e.g., fighting, unexpected death, early end point euthanasia of cagemate)

☐ Other:

Other Trackable Components:

☒ Survival Surgerie(s)
- Species: Macaque, rats (RFC 4)
- Surgerie(s): Intracranial injection
- Multiple Major?: ☐ Yes ☒ No

☒ Hazardous Agents
- Biological (list agent and hazard level): AAV
- Chemical (note category – toxicant, toxin, irritant, carcinogen, etc.): 4% Formaldehyde
- Physical (note type - radiation, UV light, lasers, noise, magnetic fields, etc.): MRI (magnetic fields and up to ~110 dB noise)

☐ Non-Centralized Animal Housing
- Location:
- Maximum duration:

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

IACUC Protocol Trackable Components Checklist

☐ Decapitation

☐ USDA-covered Species exempt from USDA reporting

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

Institutional Animal Care and Use Committee (IACUC)
Office of Research Integrity and Assurance
Arizona State University
[redacted]

Animal Protocol Review

ASU Protocol Number: 21-1867R RFC 9
Protocol Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics
Principal Investigator: [redacted]
Date of Action: 8/11/2022

The animal protocol review was considered by the Committee and the following decisions were made:

The request for changes was approved by Designated Review to alter previously approved procedures.

NOTE: If you have not already done so, documentation of Level III Training (i.e., procedure-specific training) will need to be provided to the IACUC office before participants can perform procedures without supervision. For more information on Level III requirements see https://researchintegrity.asu.edu/animals/training, or contact Research Support Services within DACT at [redacted]

Additional requirements:

☐ This protocol requires that Research Support Services group within DACT provide supervision for the first time a procedure is conducted. Contac[redacted]o schedule.
☐ This protocol indicates that there are surgical procedures. A surgical checklist may be required to be submitted to Research Support Services within DACT[redacted] rior to starting surgeries.
☐ Other requirements:

Total # of Animals: 26
Species: NHP — **Pain Category:** D - 18
Species: Rats — **Unalleviated Pain/Distress:** No

Protocol Approval Period: 8/26/2021 – 8/25/2024

Sponsor: National Institutes of Health
ASU Proposal/Award #: [redacted]
Title: Differential diagnosis of Parkinson's and multiple system atrophy in nonhuman primate models using a novel a-synuclein retinal contrast agent and AI assisted analytics

Signature: [redacted] Date: 8/12/2022
IACUC Chair or Designee
Cc: IACUC Office; IACUC Chair

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

ARIZONA STATE UNIVERSITY

Institutional Animal Care and Use Committee

REQUEST FOR CHANGES TO AN APPROVED PROTOCOL

Protocol No. 21-1867R RFC 9
Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics

Principal Investigator: [redacted] Email Address [redacted]
If not PI, whom should we contact for questions related to this amendment: [redacted] Email Address: [redacted]

☒ Funded ☐ Unfunded

Requested Change (check all that apply):

☐ New procedures to be performed – complete Part A, and Appendix 1 and/or 2 as applicable, and sign assurance.
☐ New species and or an increase in the number of animals to be used – complete Part A and sign assurance.
☐ New location of housing or procedures – complete Part A and sign assurance.
☐ New personnel – complete Part B and sign assurance.
☒ Other (includes changes in dosages, funding, etc.) – complete Part A and sign assurance.

A. Description of Requested Changes

For new procedures or additional animals that are USDA-covered species (all mammals EXCEPT mice and rats bred for research), list the **Category of Pain:**

For new procedures or additional animals that are not USDA-covered species, will there be the potential to involve more than slight or momentary pain or distress that will NOT be relieved with anesthetics, analgesics, tranquilizer drugs, or other methods for relieving pain or distress (e.g., negative conditioning, unrelieved post-surgical pain, death without euthanasia)? ☐ No ☐ Yes

If yes, describe and justify:

If you are adding a procedure that could create pain or distress, you need to include a **literature search** for alternatives.
If you are adding a new survival surgery, submit a surgical checklist.
If you are requesting an increase in animal numbers, provide justification with supportive statistics.
If you are adding additional funding sources, provide the grant agency, grant title and ASU proposal or award number.

Describe the changes you are requesting. To facilitate retinal imaging, we would like to administer mydriatic drops at the beginning of each imaging session (e.g., Phenylephrine 2.5% ± Tropicamide 1%, one drop per eye; Tropicamide 1%, two drops per eye, 5-10 min apart). During the imaging session, an ophthalmic solution (e.g., artificial tears, one drop per eye) will be administered to lubricate the eyes approximately every 5-10 minutes. All eye drops will be pharmaceutical grade and are not DEA controlled.

B. Addition of Personnel

All personnel who work with animals are required to have animal care training within the last four years. ASU IACUC training modules can be completed at https://asu.co1.qualtrics.com/jfe/form/SV_b2b2XRXRRs1309f. Personnel are required to have Level III training certification on file with the IACUC office in order to perform procedures independently (without supervision). Training can be received from DACT staff or PIs can have a member of their lab approved by DACT to be a Certified Trainer who can then train others. Simply being Level III certified does not allow the training of others. See the IACUC web site (https://researchintegrity.asu.edu/animals/training) for more information on training and Level III forms.

*** Procedures other than husbandry, handling, or behavioral testing MUST be performed under supervision unless the person is Level III certified to conduct the procedure independently. Personnel are not Level III certified until the IACUC has reviewed and approved the Level III training documentation. The PI is responsible for ensuring that personnel who are not Level III certified are supervised at all times.**

Name	Title	ASURITE	What activities will each person perform	What activities will each person be	Species with which individual will have	IACUC

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Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

		name	animals ONLY while under direct supervision?	allowed to perform independently (including appropriate Level 3 certification*) at the time of protocol submission?	d rect contact ("a " or list species) *	USE ONLY Training (mm/yy)

For each individual, describe the individual's training and years of experience with all listed species and procedures they will be conducting under this protocol. For procedures for which they are not yet trained, but will likely be trained to do during the activity period of this protocol, provide a description of who will provide such training:

Assurance

As Principal Investigator of this protocol, I assure that all procedures will be conducted as described in this request for changes and that personnel will receive appropriate additional training prior to conducting any new procedures that are not listed above.

[redacted] 8/5/2022

Principal Investigator Date

For IACUC use only:

☐ Administratively approved - Approving administrator: Date of approval:

☐ Administratively handled by VCV - Veterinarian providing verification: Date of verification:
Sources used for verification:

☒ Approved by Designated Review – Designated reviewer: Karen K bler Date of approval: 8/11/2022

☐ Approved by Full Committee Review – Primary reviewer: Date of approval:

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

From: Karen Kibler
To: [redacted]
Cc: IACUC@asu.edu
Subject: RE [redacted]21-1867R RFC 9 - Ready for Assignment
Date: Tuesday, August 9, 2022 9:28:25 AM
Attachments: image001.png

Hello [redacted]

Please send for DR process approval with me as the DR. If the process is approved, I approve the RFC as written.

Thanks,
Karen

From: [redacted]
Sent: Tuesday, August 09, 2022 8:24 AM
To: Karen Kibler [redacted]
Cc: IACUC@asu.edu
Subject [redacted] 21 1867R RFC 9 Ready for Assignment

Hello Karen,

The attached RFC has cleared vet review. Who would you like to assign as the DR/PR?

Sincerely,

[redacted] Compliance Coordinator, Office of Research Integrity & Assurance
Arizona State University | Knowledge Enterprise | Operations
[redacted]480-965-777
[redacted] | http://researchintegrity.asu.edu
How am I doing? Email m[redacted]or send a Sun Award
[redacted](ASU Users Only)

This message may contain information that is privileged, confidential and exempt from disclosure under applicable law. Please do not copy or forward this message without permission. If you are not the intended recipient, please delete all copies and notify me immediately by reply e-mail or by telephone[redacted]so we may correct our records

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

[redacted]

To: [redacted]iacuc@asu.edu
Subject: RE: Action Required: Designated Review for [redacted]21 1867R RFC 9

From: [redacted]
Sent: Tuesday, August 9, 2022 9:49 AM
To: [redacted]Dale DeNard [redacted]Karen Kibler [redacted]
Cc: [redacted]
Subject: Action Required: Designated Review for [redacted]21-1867R RFC 9
Importance: High

Designated Reviewer: Karen Kibler
Principal Investigator: [redacted]
Peer Reviewer: N/A
Protocol Number: [redacted]21-1867R RFC 9

Tracking:	Recipient	Response
	[redacted]	Yes: 8/9/2022 10:15 AM
	Dale DeNardo	Yes: 8/9/2022 10:10 AM
	[redacted]	Yes: 8/9/2022 10:30 AM
	Karen Kibler	Yes: 8/10/2022 7:57 AM
	[redacted]	Yes: 8/9/2022 10:16 AM
	[redacted]	Yes: 8/9/2022 11:17 AM
	[redacted]	Yes: 8/9/2022 3:29 PM
	[redacted]	Yes: 8/9/2022 10:14 AM
	[redacted]	Yes: 8/10/2022 5:06 PM

A request for an amendment to the referenced protocols has been submitted. The request for amendment is attached and the various related protocols are available at the SharePoint site. The Designated Review process allows IACUC members, by voting, to permit the Designated Reviewer to approve or disapprove an amendment request.

Select "**YES**" if you approve the use of the designated review process for this amendment.

Select "**NO**" if you disapprove the use of designated review process regarding this amendment request. The amendment will then be reviewed at the next monthly IACUC meeting.

Select "**Abstain**" if you would like to abstain from the vote for any reason.

Select "**Recuse**" if you have a conflict of interest.

Please indicate your approval or disapproval of the request for designated review by using the YES or NO button in the toolbar at the top of this message. The use of "YES or NO" buttons allows you to submit comments along with your choice. **You may also send your comments to me directly or to the primary reviewer without using the selection buttons. Please copy me on all correspondence and email related to this request.**

Sincerely,

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

PRR22-11_0433

IACUC Protocol Trackable Components Checklist

Protocol #: 21-1867R If for amendment, amendment #: 9

PI: [redacted]

Species: Macaque, Rats (RFC 4) Highest Category of Pain: Macaques – D

Rats - no unalleviated pain

Completed by: [redacted] Date completed: 8/8/22

☐ No trackable components in this document

Exceptions to the Guide:

☐ Food/Fluid Regulation
- Species:
- What Restricted:
- Parameters:

☐ Prolonged Restraint
- Species:
- Details:

☒ Husbandry Deviation from the Guide
- Species: Macaque; rats (RFC 4)
- Deviation: macaques single housing if suitable pairing partners are not available; rats singly housed under non-research related circumstances (e.g., fighting, unexpected death, early end point euthanasia of cagemate)

☐ Other:

Other Trackable Components:

☒ Survival Surgerie(s)
- Species: Macaque, rats (RFC 4)
- Surgerie(s): Intracranial injection
- Multiple Major?: ☐ Yes ☒ No

☒ Hazardous Agents
- Biological (list agent and hazard level): AAV
- Chemical (note category – toxicant, toxin, irritant, carcinogen, etc.): 4% Formaldehyde
- Physical (note type - radiation, UV light, lasers, noise, magnetic fields, etc.): MRI (magnetic fields and up to ~110 dB noise)

☐ Non-Centralized Animal Housing
- Location:
- Maximum duration:

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

IACUC Protocol Trackable Components Checklist

☐ Decapitation

☐ USDA-covered Species exempt from USDA reporting

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

Date: 5/24/22

ARIZONA STATE UNIVERSITY
IACUC ANNUAL REVIEW

I. Currently approved protocol

Protocol Number: 21-1867R
Protocol Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics

Principal Investigator: [redacted]
☒ Funded ☐ Unfunded

II. Status of Project

A. Were the animal activities conducted?

i. ☐ **Yes, they were conducted.** If yes,

1. Were there any significant animal welfare issues (morbidity or mortality, complications, etc.) encountered over the past 12 months?
   a. ☐ Yes. Describe (include the problem, approximate number of animals affected, and resolution).

   b. ☐ No. Proceed to item II B.
2. Were all unanticipated welfare issues reported?
   a. ☐ Yes. Proceed to item II B.
   b. ☐ No. Describe. Proceed to item II B when completed.

ii. ☒ **No, they were not conducted.** If the protocol will be terminated, complete the Final Review form.

1. If the protocol will remain active, why were animal activities not conducted?
   We are finalizing the purchase of 18 macaques for this study to be imported into the US in the summer of 2022.

   Proceed to Section II B.

B. Have there been any recent findings, either from this study or a related study that would change the planned use of animals?

- Species Used
- Animal Numbers
- Procedures
- Criteria to Measure/Monitor Pain or Distress
- Alternatives to Painful Procedures
- Restraint
- Amelioration and Control of Painful Procedures
- Estimation of Potential Postoperative/Intervention Pain
- Preoperative/Postoperative/Chronic Care
- Euthanasia/Disposition of Animals
- Animal Care and/or Use Sites

i. ☐ Yes. Complete a separate Request for Changes form describing all proposed changes as well as the scientific rationale for these changes. Proceed to item III.

ii. ☒ No. Proceed to item III.

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

III. Updated Information

A. Did the pain status stated on the protocol remain appropriate for the procedures performed?

i. ☒ Yes. Proceed to item III B.
ii. ☐ No. If no, please describe: Proceed to item III B when completed.

B. Has there been new funding added to the project?

i. ☐ Yes. Provide new grant(s) information:
Granting Agency:
Title:
ASU Proposal or Award number:

☒ No.

IV. Progress Report (for research or teaching protocols only)

Provide a statement on progress under this protocol over the past 12 months. Include any presentations or publications that have resulted from this protocol during the past 12 months.

We are finalizing the purchase of 18 macaques for this study to be imported into the US in the summer of 2022.

V. Personnel

All personnel who work with animals are required to have animal care training within the last four years. ASU IACUC training modules can be completed at https://asu.co1.qualtrics.com/jfe/form/SV_b2b2XRXRRs1309f. Personnel are required to have Level III training certification on file with the IACUC office in order to perform procedures independently (without supervision). See the IACUC web site (https://researchintegrity.asu.edu/animals/training) for more information on training and Level III forms.

*** Procedures other than husbandry, handling, or behavioral testing MUST be performed under supervision unless the person is Level III certified to conduct the procedure independently. Personnel are not Level III certified until the IACUC has reviewed and approved the Level III training documentation. The PI is responsible for ensuring that personnel who are not Level III certified are supervised at all times.**

A. List the names, titles, affiliations, and roles of **ALL** persons currently involved in the research or teaching activity.

Name	Title	ASURITE name	Role in Protocol: What activities will each person perform on live animals ONLY while under direct supervision?	Role in Protocol: What activities will each person be allowed to perform independently (including appropriate Level 3 certification*) at the time of protocol submission?	Species with which individual will have direct contact ("none" "all" or list species)	FOR IACUC USE ONLY: Training Confirmation
[redacted]	PI	[redacted]		Intracranial surgery, MRI, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under	All	7/2021 9/2021 Rodents OHSP

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

				direct supervision until certified).		
[redacted]	Laboratory Manager	[redacted]		Intracranial surgery, MRI, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified).	All	11/2021 OHSP
	Laboratory Coordinator			Intracranial surgery, MRI, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified).	All	11/2021 OHSP
	Research Specialist			Intracranial surgery, MRI, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified).	All	11/2021 12/2021 Rodents OHSP
	Graduate Student			Intracranial surgery, MRI, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified).	All	11/2021 12/2021 Rodents OHSP
	Research Specialist			Intracranial surgery, MRI, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified).	All	5/2019 OHSP
	Research Specialist			Intracranial surgery, MRI, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified).	All	7/2022 OHSP
	Research Specialist			Intracranial surgery, MRI, blood/CSF collection, behavioral tests, administration	All	7/2022 OHSP

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

				of medications, and necropsy (all under direct supervision until certified).		

B. If any of the above listed personnel are new to the protocol, describe their years of experience with all listed species and procedures they will be conducting under this protocol. For procedures for which they are not yet trained, but will likely be trained to do during the activity period of this protocol, provide a description of who will provide such training:
N/A

C. List the names of any individuals no longer involved with the research (these individuals will be removed from the protocol and DACT will be notified):
N/A

VI. Certification

By signing this report, I certify that, to the best of my knowledge, the information included herein is accurate and complete. I understand that continued animal use past the scheduled termination date of the protocol requires IACUC approval. I also understand that should the animal use under this protocol require ANY change from that stated in the protocol, prior approval by the IACUC is required.

[redacted]

Principal Investigator's Signature

5/26/22
Date

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

FOR IACUC USE ONLY
Annual Review Determination

ANNUAL REVIEW APPROVAL SIGNATURES:

[redacted] 08/25/2022

Chair, IACUC (or Designee) Date

[redacted] 08/25/2022

Attending Veterinarian (or Designee) Date

[redacted] 08/25/2022

IACUC Member Date

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

Institutional Animal Care and Use Committee (IACUC)
Office of Research Integrity and Assurance
Arizona State University
[redacted]

Animal Protocol Review

ASU Protocol Number: 21-1867R RFC 10
Protocol Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics
Principal Investigator: [redacted]
Date of Action: 9/2/2022

The animal protocol review was considered by the Committee and the following decisions were made:

The request for changes was administratively approved to add [redacted] as additional personnel to the protocol.

NOTE: If you have not already done so, documentation of Level III Training (i.e., procedure-specific training) will need to be provided to the IACUC office before participants can perform procedures without supervision. For more information on Level III requirements see https://researchintegrity.asu.edu/animals/training, or contact Research Support Services within DACT at [redacted]

Additional requirements:

☐ This protocol requires that Research Support Services group within DACT provide supervision for the first time a procedure is conducted. Contac[redacted] to schedule.

☐ This protocol indicates that there are surgical procedures. A surgical checklist may be required to be submitted to Research Support Services within DACT [redacted], prior to starting surgeries.

☒ **Other requirements: IBC approval of new personnel is required before work with biohazardous materials may begin.**

Total # of Animals: 26
Species: NHP — **Pain Category: D - 18**
Species: Rats — **Unalleviated Pain/Distress: No**

Protocol Approval Period: 8/26/2021 – 8/25/2024
Sponsor: National Institutes of Health
ASU Proposal/Award #: [redacted]
Title: Differential diagnosis of Parkinson's and multiple system atrophy in nonhuman primate models using a novel a-synuclein retinal contrast agent and AI assisted analytics

Signature: [redacted] Date: 9/7/2022
IACUC Chair or Designee
Cc: IACUC Office; IACUC Chair

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 08/15/2023

PERSONNEL MODIFICATION FORM
IACUC and IBC

This form can be used to add or remove participants from both an IACUC protocol and an IBC disclosure. Please submit only one form to Research.Integrity@asu.edu and it will be processed by both committees.

Principal Investigator Name: [redacted]	Phone [redacted]
Dept: [redacted]	Email: [redacted]

Participant #1	**Add to:** ☒ **IBC #**SPROTO202100000070 ☒ **IACUC #** 21-1867R, 22-1872R, 22-1873R, 22-1880R, 22-1886R, 22-1887R, 22-1898R, 22-1901R, 22-1903R, 22-1918R **Delete from:** ☐ **IBC #** ☐ **IACUC #**	**FOR ORIA USE ONLY** **Training Verification**
Name: [redacted]	**ASURITE** [redacted] **Email:** [redacted]	
Project Responsibilities in IBC: Will handle AAV viral vectors, alpha-synuclein preformed fibrils, Human Lewy Body extracts, and mouse/rat/nonhuman primate blood/CSF/brain tissue.		Being added in ERA
Experience/Training in These Responsibilities: No previous experience		
What procedures are they responsible for on the IACUC protocol (please note which procedures are being done independently and which are done under supervision: Macaques: Intracranial surgery, intracarotid surgery, MRI, PET scan, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified). Rats: Intracranial surgery, blood/CSF collection, behavioral tests, administration of any medications, and necropsy (all under direct supervision until certified). Mice: Intracranial surgery, blood/CSF collection, behavioral tests, administration of any medications, and necropsy (all under direct supervision until certified).		8/2022 OHSP
Species: Macaques, Rats, Mice **Experience and training with species and procedures:** 1 year experience working with rats in research		

Assurance

As Principal Investigator, I assure that personnel will receive appropriate training prior to working with animals or biological materials as applicable.

Principal Investigator Signature: [redacted] Date: 9/1/22

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Revised 11/20/12

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Institutional Animal Care and Use Committee (IACUC)
Office of Research Integrity and Assurance
Arizona State University
[redacted]

Animal Protocol Review

ASU Protocol Number: 21-1867R RFC 11
Protocol Title: Differential diagnosis of Parkinson's and multiple system atrophy in non-human primate models using a novel a-synuclein retinal contrast agent and AI-assisted analytics
Principal Investigator: [redacted]
Date of Action: 9/23/2022

The animal protocol review was considered by the Committee and the following decisions were made:

The request for changes was administratively approved to add [redacted] and [redacted] as additional personnel.

NOTE: If you have not already done so, documentation of Level III Training (i.e., procedure-specific training) will need to be provided to the IACUC office before participants can perform procedures without supervision. For more information on Level III requirements see https://researchintegrity.asu.edu/animals/training, or contact Research Support Services within DACT at [redacted]

Additional requirements:

☐ This protocol requires that Research Support Services group within DACT provide supervision for the first time a procedure is conducted. Contac[redacted]to schedule.

☐ This protocol indicates that there are surgical procedures. A surgical checklist may be required to be submitted to Research Support Services within DACT[redacted] prior to starting surgeries.

☒ **Other requirements: IBC approval of new personnel is required before work with biohazardous materials may begin.**

Total # of Animals:	**26**	
Species:	**NHP**	**Pain Category: D - 18**
Species	**Rats**	**Unalleviated Pain/Distress: No**

Protocol Approval Period: 8/26/2021 – 8/25/2024
Sponsor: National Institutes of Health
ASU Proposal/Award #: [redacted]
Title: Differential diagnosis of Parkinson's and multiple system atrophy in nonhuman primate models using a novel a-synuclein retinal contrast agent and AI assisted analytics

Signature: [redacted] Date: 9/27/2022
IACUC Chair or Designee
Cc: IACUC Office; IACUC Chair

Obtained by Rise for Animals.
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PERSONNEL MODIFICATION FORM
IACUC and IBC

This form can be used to add or remove participants from both an IACUC protocol and an IBC disclosure. Please submit only one form to Research.Integrity@asu.edu and it will be processed by both committees.

Principal Investigator Name: [redacted]	Phone: [redacted]
Dept: [redacted]	Email: [redacted]

Participant #1	**Add to:** ☒ **IBC #**SPROTO202100000070 ☒ **IACUC #** 21-1867R, 22-1872R, 22-1873R, 22-1880R, 22-1886R, 22-1887R, 22-1898R, 22-1901R, 22-1903R, 22-1918R **Delete from:** ☐ **IBC #** ☐ **IACUC #**	**FOR ORIA USE ONLY** **Training Verification**
Name: [redacted]	**ASURITE** [redacted]	**Email:** [redacted]
Project Responsibilities in IBC: Will handle AAV viral vectors, alpha-synuclein preformed fibrils, Human Lewy Body extracts, and mouse/rat/nonhuman primate blood/CSF/brain tissue.		Already on IBC in ERA
Experience/Training in These Responsibilities: No previous experience		
What procedures are they responsible for on the IACUC protocol (please note which procedures are being done independently and which are done under supervision: Macaques: Intracranial surgery, intracarotid surgery, MRI, PET scan, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified). Rats: Intracranial surgery, blood/CSF collection, behavioral tests, administration of any medications, and necropsy (all under direct supervision until certified). Mice: Intracranial surgery, blood/CSF collection, behavioral tests, administration of any medications, and necropsy (all under direct supervision until certified).		8/2022 OHSP
Species: Macaques, Rats, Mice **Experience and training with species and procedures:** No previous experience		
Participant #2	**Add to:** ☒ **IBC #**SPROTO202100000070 ☒ **IACUC #** 21-1867R, 22-1872R, 22-1873R, 22-1880R, 22-1886R, 22-1887R, 22-1898R, 22-1901R, 22-1903R, 22-1918R **Delete from:** ☐ **IBC #** ☐ **IACUC #**	**FOR ORIA USE ONLY** **Training Verification**
Name: [redacted]	**ASURITE:** [redacted]	**Email:** [redacted]
Project Responsibilities in IBC: Will handle AAV viral vectors, alpha-synuclein preformed fibrils, Human Lewy Body extracts, and mouse/rat/nonhuman primate blood/CSF/brain tissue.		Being added in ERA
Experience/Training in These Responsibilities: No previous experience		
What procedures are they responsible for on the IACUC protocol (please note which procedures are being done independently and which are done under supervision: Macaques: Intracranial surgery, intracarotid surgery, MRI, PET scan, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified). Rats: Intracranial surgery, blood/CSF collection, behavioral tests, administration of any medications, and necropsy (all under direct supervision until certified). Mice: Intracranial surgery, blood/CSF collection, behavioral tests, administration of any medications, and necropsy (all under direct supervision until certified).		10/2018 9/2022 NHP OHSP
Species: Macaques, Rats, Mice **Experience and training with species and procedures:** 3 years experience working with mice in research		
Participant #3	**Add to:** ☒ **IBC #**SPROTO202100000070 ☒ **IACUC #** 21-1867R, 22-1872R, 22-1873R, 22-1880R, 22-1886R, 22-1887R, 22-1898R, 22-1901R, 22-1903R, 22-1918R	**FOR ORIA USE ONLY** **Training Verification**

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	Delete from: ☐ IBC # ☐ IACUC #	
Name: [redacted]	ASURITE: [redacted] Email: [redacted]	
Project Responsibilities in IBC: Will handle AAV viral vectors, alpha-synuclein preformed fibrils, Human Lewy Body extracts, and mouse/rat/nonhuman primate blood/CSF/brain tissue.		Need to add in ERA
Experience/Training in These Responsibilities: No previous experience		
What procedures are they responsible for on the IACUC protocol (please note which procedures are being done independently and which are done under supervision: Macaques: Intracranial surgery, intracarotid surgery, MRI, PET scan, blood/CSF collection, behavioral tests, administration of medications, and necropsy (all under direct supervision until certified). Rats: Intracranial surgery, blood/CSF collection, behavioral tests, administration of any medications, and necropsy (all under direct supervision until certified). Mice: Intracranial surgery, blood/CSF collection, behavioral tests, administration of any medications, and necropsy (all under direct supervision until certified).		9/2022 OHSP
Species: Macaques, Rats, Mice **Experience and training with species and procedures:** No previous experience		

Assurance

As Principal Investigator, I assure that personnel will receive appropriate training prior to working with animals or biological materials as applicable.

Principal Investigator Signature: [redacted] Date: 8/25/22

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Revised 11/20/12

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