HUMANE USE OF ANIMALS POLICY

(EXHIBIT A)

The mission of American Kennel Club Canine Health Foundation, Inc. (the "Foundation") is to advance the health of all dogs and their owners by funding sound scientific research and to support the dissemination of health information to prevent, treat and cure canine disease. As such, Foundation funded research often requires the involvement of animals in research studies. All studies receiving funding from the Foundation must follow the Foundation's Humane Use of Animals Policy. This policy ensures that every animal involved in a Foundation-supported project will receive compassionate care throughout the study. Per general policy, the Foundation does not fund projects which require euthanasia of any animal as an endpoint, or induction of disease or injury. This includes samples acquired from matings whose purpose is to induce a genetic disease in the offspring or to perpetuate a disease-causing genetic mutation. Furthermore, the Foundation will not fund any project that induces or allows pain or distress in any animal, other than short-term minor pain or distress that can be controlled by appropriate anesthetics, analgesics, and/or nursing care. The Foundation and/or a designated party shall evaluate each proposal for scientific merit, relevance for optimizing canine health, impact and significance to canine health, research environment and consideration of animal welfare (minimizing discomfort, distress, and pain).

The Foundation Humane Use of Animals Policy is as follows:

1. IACUC. The Foundation requires that all proposals have the approval of the Institutional Animal Care and Use Committee (IACUC), or equivalent, at the relevant institution for any Foundation-supported study regardless of the Institution's requirements. If IACUC approval is pending at time of application, any awarded funds will not be dispersed until proof of approval has been provided to the Foundation. Use of animals shall be humane and consistent with applicable laws and regulations and with standards established by local governing bodies whose function is the oversight of animals in research (e.g., IACUC). When a standard IACUC is unavailable (e.g., foreign country, private or corporate veterinary practice, animal clinic, shelter or sanctuary, etc.), the Foundation requires the review of the proposed animal use by an equivalent institutional review committee/agency or an established collaborating institution's IACUC. All animal care and IACUC member structures shall, at a minimum, meet or exceed the guidelines set forth in the U.S. Government's Animal Welfare Act (Title 9 CFR Subchapter A – Animal Welfare) and/or further required regional and institutional regulations.

2. Colony Animals. The Foundation will not fund any project that involves research colony animals of any species.

3. Owner Consent. The Foundation shall require informed owner/responsible agency consent in all studies. An informed owner/responsible agency consent form of acceptable standards must be submitted for review concurrent with a research grant proposal and must be approved by the IACUC (or institutional equivalent) and the Foundation prior to approval

and release of funding.

4. Biological Samples. A description of biological samples including tissues, blood, cell lines, and others must be included in the grant application and detail a) how they will be used, b) where and how they will be, or were, responsibly acquired, and c) IACUC approval under which such samples will be / were collected.

5. Archived Samples. If a study utilizes archived samples, they must have been collected with informed owner consent or with owner permission in the course of veterinary care and have IACUC or equivalent approval covering the original collection of those samples and comply with the above requirements for humane animal care and use. If archived tissue or body fluid samples are to be used, the project(s) and protocol(s) under which those samples were collected also must comply with the Foundation's Humane Use of Animals Policy. For example, stored tissue samples from projects involving research colony animals, induction of disease or injury, or those where euthanasia was an elective endpoint may not be used.

6. Live Animals. If a project involves live animals, the following must be addressed:

    a. Details of the animals involved and justification of the number of animals required for the project. All dogs participating in studies should be client-owned and with owner consent;
    b. Statistical evidence that the number of animals proposed in the study is appropriately justified and adequate to achieve the proposed results. It is also imperative that scientists requesting support shall review relevant literature (both USA and international) to prevent unnecessary replication of research or unnecessary utilization of animals;
    c. Explanation of how the animals will be recruited and verification that the animals are suitable for the study (e.g., have no physiologic, physical, or pharmacologic issues that would interfere with results);
    d. Inclusion and exclusion criteria; justification for the breed, sex, health status and other inclusion / exclusion criteria. A review of the literature should be conducted to demonstrate that the animals chosen are the best model to answer the question posed, and that there are no better in vitro, in silico or in vivo options. Frequency and monitoring criteria must be included and clearly outline financial responsibility for costs incurred as part of the study.
    e. If the project causes transient pain or distress, the following must also be addressed:
        i. Defense of the experimental design;
        ii. Information on the nature of any pain or distress and criteria for how it will be monitored, controlled and treated; financial responsibility for such treatment must be clearly defined, i.e., whether owner or study will be expected to cover costs;
        iii. Justification that no alternative can be used to accomplish the project objectives.
        iv. Demonstration of the critical significance of the disease or condition to be studied for improving the health of dogs.

7. Clinical Trials. The Foundation accepts the AVMA language on the use of an institutional Veterinary Clinical Studies Committee (VCSC) for review of clinical trials involving client-owned dogs (see references). The Foundation does not support clinical trials performed at institutions or clinics that are not overseen by Veterinary Clinical Studies Committees (VCSC), or equivalent, such as a Clinical Review Board. At institutions, the VCSC should work closely with the IACUC for clinical trial oversight and administration as established by AVMA policy. In general, owners must be informed of alternate options for treatment and that their dog's care will not be diminished by declining or choosing to stop study participation. They should also understand the potential for side effects and how potential adverse events will be monitored and managed, including clear statement of their/or institution's financial responsibility for medical management of side effects/adverse events. (see Page, et al, in references section). A component of the VCSC, or other, should be responsible for monitoring and reporting adverse events.

8. Control Population. Control dogs should come from a population that is similarly representative of the population being studied and be demonstrated to be healthy controls.

    a. The Foundation considers dogs belonging to students and/or staff to be vulnerable subject populations. Consequently, a principal investigator who plans to actively recruit student- and/or staff-owned dogs must clearly define the rationale for such participation, and include dogs owned by this population into both the control and experimental groups, as appropriate. In addition, all recruitment strategies must be stated, and owner consent forms reviewed and completed.
    b. If/when student- and/or staff-owned dogs are enrolled in a study, the proposal must be accompanied by a letter from a department head or other appropriate institutional official attesting to the fact that the project is acceptable and documenting how coercion has been minimized, and a statement should be in place that guarantees staff or students will not be involved in the medical management of their animal while on study. Such assurance will be a condition of approval, but the availability of such assurance is not a guarantee of approval. In general, students and staff should only be asked to participate in a research study by someone to whom they do not directly report; alternatively, staff or students may respond to a posted ad recruiting study participants and be assigned an anonymous participant ID number in these instances.

9. Care. Every animal shall have timely, compassionate care, be provided comfort and protection from abuse and unnecessary pain and distress. Investigators also shall minimize stress and fear in animals.

10. Research, Veterinary and Care Staff. Investigators and staff who are involved with animal care shall have appropriate qualifications and experience for conducting procedures on living animals per IACUC or institutional protocols. Each investigator on the study shall include in their biographical sketch details of their animal care qualifications and experience specific to the proposal. They shall further document appropriate qualifications of staff

associated with the funded research in a 'Key Personnel Justification' document. Approval by an IACUC, or institutional equivalent, does not guarantee that the project will be acceptable to the Foundation.

11. Procedures. The Foundation discourages health studies that require unnecessarily invasive procedures. Invasive procedures are only permissible when 1) the nature of the disease or condition to be studied is of such significance for improving animal health that an invasive procedure is justified (investigators shall be required to address invasive procedures in all Foundation grant applications including all related methodologies, including an adverse event reporting plan, and clear outline of medical management and financial responsibility for management of pain/distress and adverse events, and criteria for removal of an animal from a study); 2) meaningful information can be obtained no other way (i.e. alternative models have been thoroughly evaluated). Examples of permissible procedures include those standard, yet invasive, medical procedures, such as laparoscopic or endoscopic biopsy, or any procedure such as imaging or sample collection requiring general anesthesia (e.g., CSF, bone marrow, MRI).

12. Treatment. The Foundation does not fund projects which subject healthy or unhealthy dogs to potentially harmful treatment not indicated for their medical or surgical conditions.

13. Euthanasia. The Foundation only considers medically-necessary and humane euthanasia acceptable as set forth by the AVMA, with informed consent of the owner or responsible agent, when an animal develops unanticipated illness or injury that results in pain and suffering that cannot be alleviated with standard treatments. When necessary, the criteria and endpoints must be described.

14. Funding Termination. The Foundation reserves the right to terminate funding of a study if there are concerns about animal welfare.

15. Site Visits. The Foundation reserves the right to perform announced or unannounced site visits and/or independent audits for program assessment and/or to investigate concerns or institutional/investigator whistleblower communications on animal welfare issues.

Questions regarding compliance with the Foundation's Humane Use of Animals Policy should be directed to chfgrants@akcchf.org.

References:

1. U.S. Government's Animal Welfare Act (Title 9 CFR Subchapter A - Animal Welfare) https://www.gpo.gov/fdsys/pkg/CFR-2013-title9-vol1/pdf/CFR-2013-title9-vol1-chapI-subchapA.pdf
2. National Research Council's Institute for Laboratory Animal Research (ILAR) Guide for the Care and Use of Laboratory Animals (2011), 8th ed. Washington DC: National Academies Press.

3. Page, R., Baneux, P., Vail, D., Duda, L., Olson, P., Anestidou, L., ... & Hardy, C. (2016). Conduct, oversight, and ethical considerations of clinical trials in companion animals with cancer: report of a workshop on best practice recommendations. *Journal of veterinary internal medicine*, *30*(2), 527-535.
4. AVMA Animal Welfare Principles (https://www.avma.org/KB/Policies/Pages/AVMA-Animal-Welfare-Principles.aspx)
5. Establishment and Use of Veterinary Studies Committee. https://www.avma.org/KB/Policies/Pages/Establishment-and-Use-of-Veterinary-Clinical-Studies-Committees.aspx
6. Institutional animal care and use committee review of clinical studies
Lon V. Kendall, Nicolette Petervary, Valerie K. Bergdall, Rod L. Page, and Philippe J. R. Baneux (2018). *Journal of the American Veterinary Medical Association* 253:8, 980-984
7. Regan, D., Garcia, K., & Thamm, D. (2019). Clinical, pathological, and ethical considerations for the conduct of clinical trials in dogs with naturally occurring cancer: A comparative approach to accelerate translational drug development. *ILAR Journal*, https://doi.org/10.1093/ilar/ily019

I have read and will abide by the Foundation's Humane Use of Animals Policy:

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Principal Investigator Name (Please Print)

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Signature Date

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Grantee Research Administrative Official Name (Please Print)

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Signature Date

Approved by the American Kennel Club Canine Health Foundation, Inc. Board of Directors 6/9/2019.