APPLICATION FOR APPROVAL OF RESEARCH PROJECTS AT DEPARTMENT OF VETERINARY CLINICAL SCIENCES (IKV)

This form should be filled in and accepted before starting a research project. **This procedure is practiced to secure the research strategy and ethical policies of IKV**. The responsible researcher fills this form and sends it to: ikv-sekretariat@sund.ku.dk

A decision will be taken as soon as possible and no later than 2 weeks after application).
To speed up the application fell free to take advice in advance from the heads of hospitals, in case your research involves the hospitals (patients, clients, staff, equipment, facilities etc.)

1. Is the project/main applicant allocated to Taastrup or Frederiksberg Campus?	Frederiksberg	X	Taastrup	
2. Project title				
3. Responsible researcher - state education and status on experimental animals course	Sophie Agger, DVM, Ph.D student No experimental animal course			
4. Other participants - list and state education and status on experimental animals course	Maja L. Arendt FELASA C qualified in 2005			

5. Purpose of the project	The purpose is to investigate genetic aspects of cancer development in dogs as a comparative model for human disease by different genetic methods. The project consists of three (Work package 1-3) parts*, only WP 2-3 require recruitment of patients from the University Hospital for Companion Animals: **WP2:** Identification of somatic variants by comparing whole genome, whole exome or SNP genotyping sequencing data from tumor and normal tissue and the relationship between the mutation burden and tumor stage, grade and clinical outcome. **WP3:** Identification of cell-free DNA and circulating tumor cells from mammary tumor liquid biopsies and the use of these for diagnosis, monitoring disease relapse and progression.

* WP1 takes place at Uppsala University.

6. Project description (max 1 page). Include the information needed for assessment of the application such as patient population, inclusion/exclusion criteria, recruitment of patients, specific procedures conducted, use of medicine etc. If comprehensive, please enclose a detailed plan

The full PhD project description has been attached to this application.

Patient population:

Canine cancer patients with malignant mammary tumors, lymphoma, or osteosarcoma (WP2). Patients will only be enrolled in the study after informed consent by the owner (proposal for consent form attached).

Inclusion criteria:

Samples will only be taken if it is possible without compromising diagnosis or animal welfare (typically histopathological evaluation of tumor margins or biopsies where additional samples could increase risk of adverse events).

Only patients weighing > 2 kg will be included to ensure that < 2 % of blood volume is collected, other blood samples will not be calculated into this volume, but a total maximum of 5 % will be obtained. If the dog is severely anemic blood will not be collected.

Exclusion criteria

WP3: Only patients deemed able to tolerate the 8 follow up visits to the hospital will be included.

Recruitment of patients:

Patients will be recruited over a two-year period from both surrounding private practices, the certified oncology veterinarians and through the University Hospital for Companion Animals. As many study relevant canine cancer patients as possible will be recruited but a minimum of 10 is expected.

Specific procedures:

Information collected on each patient includes electronic record information and routine history and physical examination. Samples planned to be collected include blood and tumor tissue. All procedures are part of the routine diagnostic work up for canine cancer patients, including blood sampling (venipuncture), fine needle aspiration for cytology and collection of a biopsy under sedation or anesthesia will be conducted.

The blood collected will be collected either during routine blood sampling, from an already placed venous catheter. If this fails, the blood sample can be collected with a venipuncture while the dog is anesthetized. The amount of blood collected will be < 2 % of blood volume.

7. Ethical considerations concerning the project.

All procedures are part of the routine diagnostic work up for canine cancer patients, including blood sampling (venipuncture), fine needle aspiration for cytology and collection of a biopsy under anesthesia will be conducted.

The investigators will aim to reduce the discomfort to patients by:

1) When possible, tissue sampling will be performed when the patient is sedated or anesthetized. Extra venipunctures will only be performed while the dog is anesthetized.
2) Using surplus biopsy material or material taken post mortem*
3) Only patients in the WP3 study deemed able to tolerate the 8 follow up hospital visits during an 18-month period will be enrolled. WP3: Only canine cancer patients with relevant malignant and aggressive tumors, who will benefit from being monitored closely (patients with high risk of local recurrence or metastasis) will be enrolled.

Blood collection and cytology sampling is associated with minimal discomfort and part of routine diagnostic procedures for any canine cancer patient.
Specifically, for WP3, the disposition and temperament of the patient will be considered. If the patient is deemed to not tolerate frequent clinical exams at the hospital or venipunctures well, it will not be enrolled into the study.

In cases where biopsies are obtained, these will be taken under sedation or general anesthesia and in conjunction with diagnostic work up for cancer staging and grading, or surgery. These procedures, are part of routine work up and treatment of cancer patients. Intra- or postoperative needle aspirates of the tumor are alternatives in cases where tumor margins will be compromised by biopsies.
In cases where owners opt for euthanasia without prior diagnostics or surgery, postmortem tumor sampling is possible and blood can be collected antemortem from the venous catheter used for euthanasia. If it is impossible/impractical to collect blood antemortem a muscle biopsy obtained post mortem can be used as an alternative.

Advantages of participating:
WP2: For the client: free physical exam conducted by either Sophie Agger or Maja L. Arendt. Our experience is that clients to canine cancer patients are quite keen on contributing to research which can benefit both future canine and human cancer patients.
WP3: The patients will receive free physical examinations and disease progression monitoring at each visit during the course of the study and potentially free cytology and imaging if indicated. Hematology and biochemistry will not routinely be performed on the blood samples, but in case they are needed the owner will not pay for the utensils associated with sampling.
The patients will contribute to the advancement of veterinary oncology. Discovery of mutational patterns can improve the diagnosis and staging procedures of canine cancer patients in the future. Furthermore, improving canine cancer patients as a model for human cancers will facilitate further translational research which will benefit both canine and human cancer patients.

Disadvantages of participating:
No major disadvantages are associated with participation in WP2. Minor disadvantages include extra fine needle aspirates and collection of additional blood in connection with routine blood sampling. For WP3 the disadvantages are minor discomfort associated with the additional venipunctures and potential fine needle aspirates if evidence of recurrence is suspected.

Steps taken to minimize disadvantages:
Use of lidocaine spray or ointment for all needle sticks. Only performing extra venipunctures during anesthesia.
Use of ≥ 23 g needles when possible.
Only experienced veterinary technicians and veterinarians will perform blood collections, fine needle aspirates, and biopsies.
Minimizing student contact if deemed necessary, due to added time and/or stress.
Biopsies only performed if there is no risk of compromising tumor margins.
For WP3: Only including canine cancer patients who will benefit from close monitoring and which are deemed able to tolerate frequent hospital visits.

8. Animals - number and species. If animals are involved, please state if the animals are categorized as teaching animals, research animals, client owned animals, whether general hospital population or specially recruited for the project.				
WP2: Client-owned canine cancer patients with either osteosarcoma, lymphoma or mammary tumors. Patients will be recruited over a two-year period from both surrounding private practices, the certified oncology veterinarians and through the University Hospital for Companion Animals. As many study relevant canine cancer patients as possible will be recruited but a maximum of 120 patients will be enrolled. **WP3:** Up to 30 client-owned canine cancer patients with malignant mammary tumors will be recruited over a two-year period from both surrounding private practices, the certified oncology veterinarians and through the University Hospital for Companion Animals.				
9. If permission from The Animal Experimentations Committee is needed for the study, please enclose approval. Also, state if permission is not obtained yet, but you plan to apply for this.				
Not relevant				
10. Time schedule (including starting time and expected duration) - if a detailed plan exists, please enclose				
Jan 2019 - Dec 2021				
11. If laboratory facilities are required Has a request been sent to the lab staff. (In Taastrup please consult Lise Berg)	Yes	KU VETLAB for centrifugation, preparation and storage of samples.	No	
12. Are files or patients from the hospital required? - If yes, please fill in app 1	Yes	X	No	
13. Are hospital facilities required? - If yes, please fill in app. 2	Yes	X	No	
14. Is hospital personnel required? - if yes, please fill in app. 2	Yes		No	X

Appendix 1

APPLICATION FOR THE USE OF MATERIALS, FILES AND/OR PATIENTS FROM THE HOSPITAL

Materials/Files/Patients requested, please describe the use. This section is a supplement to the project description on page 1, so it should only add specific extra information
Blood collection: sampling utensils Tumor samples: Cytology: Needles, and syringe(s) Biopsy: Utensils. Storing of samples: Access to biobank/CUBE. Cryo-tubes, and RNA-later Patients Canine cancer patients with mammary tumors, osteosarcoma, or lymphoma.
Budget for the above-mentioned activities
The project is funded from the National Institutes of Health (NIH), PI Associate professor Maja L. Arendt (partially funded). The funding includes utensils and technician salary (Mette Rasmussen). Sophie Agger has a fully paid PhD stipend from the Dean.

Is an owner consent form necessary? - If yes, please attach a draft of your information folder	Yes	X	No	

If Confidential data – please attach a plan for handling confidential data
The patients will only be marked with a record number (pseudonymized).
The application is accepted under the following conditions:
The application is ***not*** accepted for the following reasons:

Date	Head of hospital
Date	Responsible researcher

Appendix 2

APPLICATION FOR THE USE OF HOSPITAL FACILITIES AND/OR HOSPITAL PERSONNEL FOR PROJECTS

Hospital facilities requested
Examination room as part of routine oncology patient work up. Tumor sampling will be performed in our own laboratory. VETLAB (sample centrifugation) Biobank storage (CUBE)
Budget For the requested facilities
The project is funded from the National Institutes of Health (NIH), PI Associate professor Maja L. Arendt (partially funded). The funding includes utensils and technician salary (Mette Rasmussen). Sophie Agger has a fully paid PhD stipend from the Dean.
Hospital personnel requested In case of requests for specific skills, please specify
For any project related procedures, the oncology research technician Mette H. Rasmussen
Budget For the requested hospital personnel
Technician salary covered by NIH grant (Mette H. Rasmussen)
The application is accepted under the following conditions:
The application is ***not*** accepted for the following reasons:

Date	Head of hospital
Date	Responsible researcher