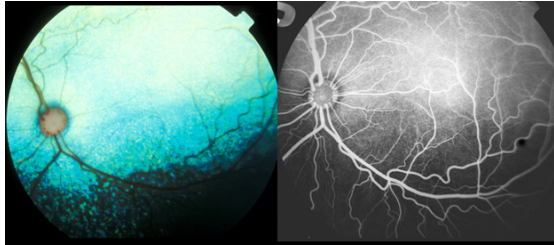


COMPONENTS OF AN OPTHALMIC EXAMINATION

The components of an ophthalmic examination vary depending on the species involved and the specific objective of testing. Sedation or general anesthesia for routine exams may or may not be required depending on the species and individual animal. If the purpose of testing is to screen for adverse effects on any ocular tissue, examination must include, at a minimum:

Slit-lamp Biomicroscopy: use of a microscope to examine the lens, anterior segment and vitreous in vivo; the slit beam provides accurate localization within the ocular media

Ophthalmoscopy: examination of the retina, retinal vasculature, and optic nerve



Fundus photograph and fluorescein angiogram - cat²

Reference Textbooks

Assessing Ocular Toxicology in Laboratory Animals (Molecular and Integrative Toxicology). Weir, AB and Collins, M, Springer, New York, 2013.

Ocular Pharmacology and Toxicology. Gilger, BC, Humana Press, New York, 2013.

¹Images courtesy of Midwest Animal Eye Associates, LLC

²Images courtesy of Ocular Services on Demand, LLC (OcularServices.com)

SPECIALIZED OPTHALMIC EXAMINATION TECHNIQUES

Corneal staining (fluorescein, rose bengal): evaluation of the surface integrity of the cornea in vivo

Corneal ultrasound pachymetry: measurement of corneal thickness in vivo

Specular microscopy: evaluation of corneal endothelial cell number and morphology

Tear function tests: Schirmer tear test, phenol red thread test, tear fluorophotometry to provide quantitative and qualitative assessments

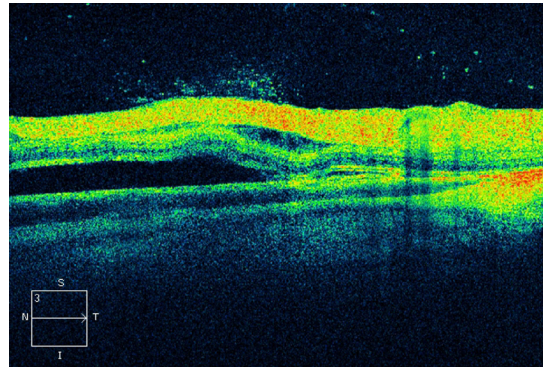
Tonometry: measurement of intraocular pressure

Aqueous humor dynamic studies: measurement of aqueous humor production, outflow, episcleral venous pressure

Gonioscopy: visualization and assessment of the iridocorneal angle

Electroretinography (ERG): quantitative assessment of electrical responses of retinal cells, including photoreceptors, bipolar and amacrine cells and ganglion cells

Ultrasonography: the use of ultrasound waves to create an image of the structures within the eye



Experimental retinal separation viewed by OCT³

Optical coherence tomography (OCT): the use of long wavelength energy to capture micrometer-resolution, three-dimensional images in vivo

Fluorescein angiography: photographic technique for examination of the circulation of the retina and choroid

THE ROLE OF VETERINARY OPHTHALMOLOGISTS IN PHARMACEUTICAL AND TOXICOLOGICAL TESTING

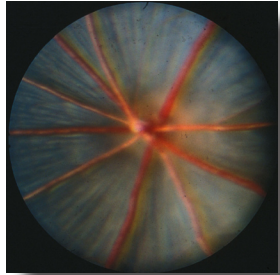


ACVO

AMERICAN COLLEGE OF VETERINARY OPHTHALMOLOGISTS

WHAT IS A VETERINARY OPHTHALMOLOGIST?

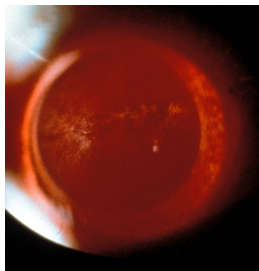
A Diplomate of the American College of Veterinary Ophthalmologists (Diplomate, ACVO), in addition to being a licensed veterinarian, has completed a minimum of 3-5 years of post-graduate specialty training in veterinary ophthalmology. This training encompasses the diagnosis and treatment of eye conditions in a variety of animal species, including those commonly used in toxicological testing. The American



Normal pigmented rat fundus¹

Board of Veterinary Ophthalmology (ABVO) is the only credentialing body in the United States that supervises the training and certification of those qualified to perform ophthalmic diagnosis in animals, awarding ACVO diplomate status.

Sponsors engaging the services of a Contract Research Organization (CRO) should be advised of the participation or lack thereof by veterinary ophthalmologists and the potential limitations that may arise if such studies do not involve veterinary ophthalmologists.

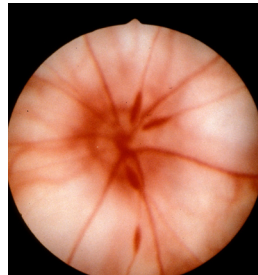


Corneal dystrophy - rat¹

DOES MY STUDY NEED A VETERINARY OPHTHALMOLOGIST?

A board certified veterinary ophthalmologist is uniquely qualified to consult in the development of the experimental design, including the species selected, appropriate diagnostic tests, and frequency of exams. Coordination between the testing agency and the ophthalmologist is essential throughout the process, to include protocol development, Standard Operating Procedures (SOP), and assessment of the outcome of testing. If ocular abnormalities are identified, communication between the ophthalmologist and the pathologist will allow correlation of clinical and histopathologic findings.

Veterinary ophthalmologists have the necessary skills for administration of test article directly into the eye, including *subconjunctival*, *anterior chamber*, *intravitreal* and *subretinal injection*. In these studies, precise placement of the test article is critical. Collateral damage to adjacent ocular structures can easily eliminate an animal from the study. Implantation of



Retinal vascular aneurysm¹

devices including intraocular lenses, intravitreal and subretinal implants are examples of procedures which require the skill of a veterinary ophthalmologist. Laser photocoagulation is used in a number of animal models to induce choroidal neovascularization as a model of age-related macular degeneration (AMD).

Scoring systems are designed to provide a semi-quantitative assessment of ocular inflammation and abnormalities observed in vivo. These include the Hackett McDonald, McDonald-Shadduck, Standardization of Uveitis (SUN) and others. Veterinary ophthalmologists are uniquely qualified to render the consistent observations and assessments necessary for such systems to yield useful results.

HOW DO I FIND A VETERINARY OPHTHALMOLOGIST?

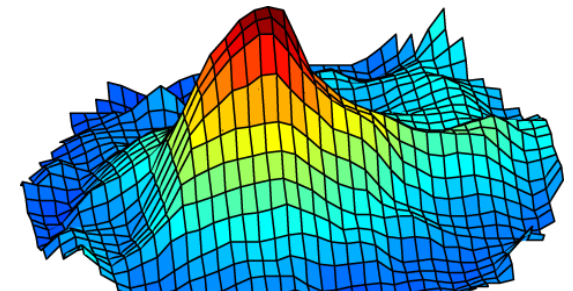
Within the Diplomates of the ACVO is a smaller group of individuals who regularly consult with the pharmaceutical industry and Contract Research Organizations. These individuals have years of experience evaluating laboratory animal eyes and offer a valuable resource. Qualified veterinary ophthalmologists are present throughout the United States and Canada and travel as needed.

Contact information for ACVO consultants can be obtained by contacting the ACVO office directly at:

ACVO.org

PO Box 1311, Meridian, ID 83680

208-466-7624



Multifocal electroretinogram - nonhuman primate²

As a sponsor, you should be informed about the qualifications of those performing ophthalmic examinations.

¹Images courtesy of Midwest Animal Eye Associates, LLC

²Images courtesy of Ocular Services on Demand, LLC (OcularServices.com)