

Canine Research in the Department of Veterans Affairs



On behalf of the Office of Research and Development,
Veterans Health Administration, Department of Veterans Affairs:

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VA Canine Research

- Has helped millions of people in its 70 year history.
- Under sustained attack based upon false statements and false assertions that dogs are not needed, that such research is “expensive”, and that test tube and other non-animal techniques can substitute for dog research.
- The future of life-saving research on spinal cord injury and heart disease is in question.
- We understand fully it is sensitive, and have the strictest, most thorough monitoring measures in place of any United States institution.
- *VSO support was critical to allowing this research to continue in 2017, and VSO support is now needed again in the face of continued threats of legislative termination.*

Huge Payoff from VA Biomedical Research Involving Dogs

- Handout 1 - *Selected VA Research Accomplishments with Dogs, 1960's to Current Decade*
- Handout 2 – *Publications from the Last 10 Years Stemming from VA Research with Dogs*
- Collectively, VA dog research projects have saved countless lives, and will continue to do if allowed to continue:
 - Cardiac pacemaker development
 - Organ transplant procedures
 - Link between smoking and lung cancer and emphysema
 - Cardiac ablation technique refinement
 - Treatments for narcolepsy
 - New treatments to non-invasively repair intervertebral discs
 - Development of new therapies to prevent heart disease
 - Cough enhancement for Veterans with SCI

Seven VA Canine Studies are Currently Approved by Sec Wilkie- Handout 3

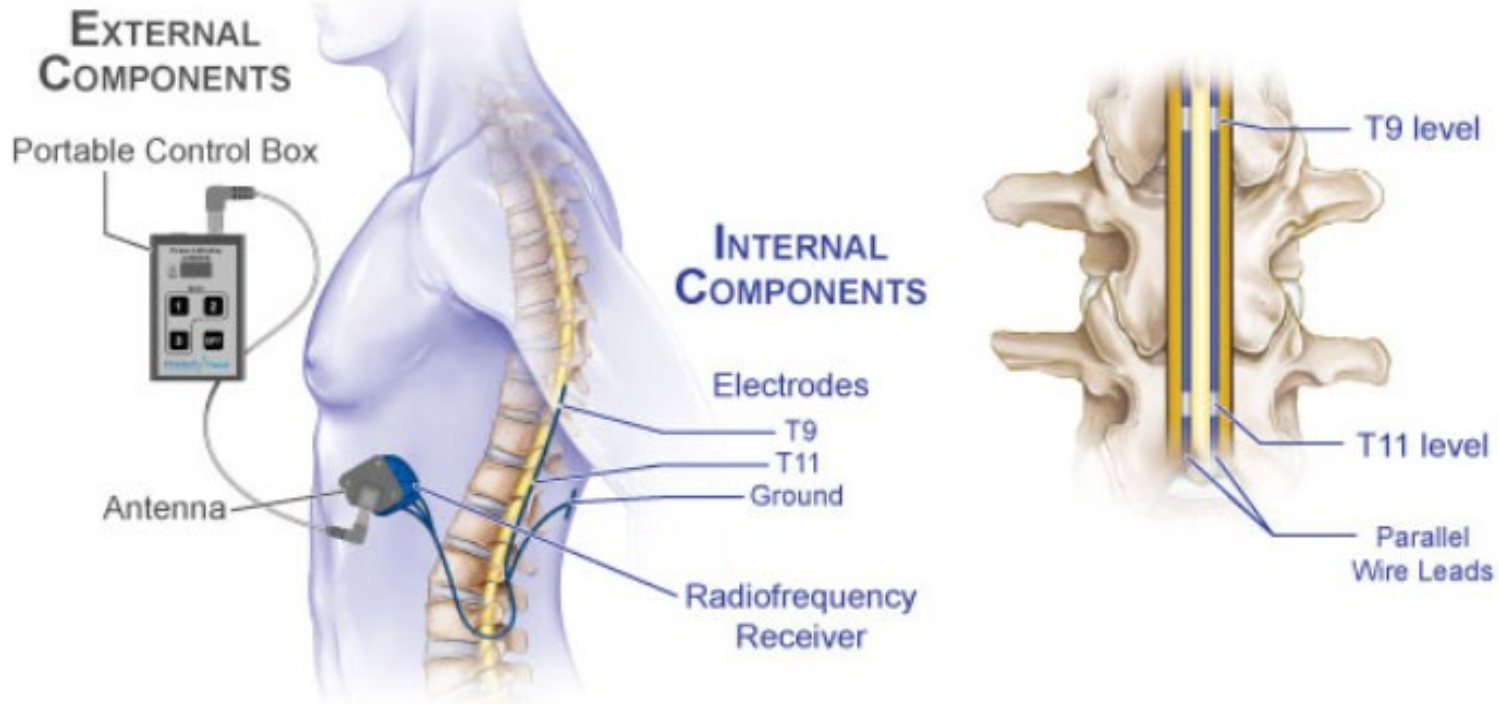
Dog Project No.	Protocol	Funding Source	Purpose of Research	VA Location	Status as of March 2019
1	High Frequency Spinal Cord Stimulation to Restore Cough	VA	Veterans with spinal cord injuries that impair their ability to cough are vulnerable to potentially fatal respiratory infections. This study evaluates how electrical stimulation of the spinal cord could be optimized to activate respiratory muscles appropriately to generate effective coughing.	Cleveland, OH	Active
2	Neuropharmacology of Pontine Control of Breathing Frequency	VA	Veterans with certain head or neck injuries, or who suffer from pain that can only be controlled with potent analgesics, often experience impaired control of breathing and coughing. This work is to increase understanding of that control, which is fundamental to developing better ways to help these veterans.	Milwaukee, WI	The PI has retired; no further work expected unless manuscript reviewers require it
3	Mechanistic Insight of Premature Ventricular Contractions-induced Cardiomyopathy	NIH	Premature Ventricular Contractions (PVCs) interfere with proper beating of the heart. This is research into the cellular mechanisms involved, which we need to understand in order to develop better ways to manage PVCs.	Richmond, VA	Active
4	Autonomic Nerve Activity and Cardiac Arrhythmias	American Heart	Premature ventricular contractions (PVCs) interfere with nerve signals to the heart, and can damage heart muscle. This is research into how the loss of nerve signals might be responsible for the damage, which we need to understand in order to develop better ways to protect the heart.	Richmond, VA	Active
5	Effect of Chronic Premature Ventricular Contractions on the Remodeled Ischemic Heart	American Heart	Heart attacks injure heart muscle and makes it more prone to premature ventricular contractions (PVCs), which can cause further damage. This is research into how the injury produced by a heart attack interacts with PVCs to impact heart function, which we need to understand in order to improve heart function after heart attacks.	Richmond, VA	Study complete as of September 2018; study is now closed.
6	Nanoparticle Injection into Ganglionated Neural Plexi to Prevent Atrial Fibrillation	Other- Virginia Commonwealth	Atrial fibrillation (AF) increases the risk of stroke, heart failure, hospitalization, and death, but current treatments for AF are risky. This is research into new ways to treat AF with less risk than is currently possible.	Richmond, VA	Active
7	A Comparison of Canine Anesthetic Regimens to Optimize Electrophysiologic and Neurophysiologic Data Acquisition	Other- internal funds	Sedatives and anesthetics commonly affect how the heart works. This study is designed to sort out how to improve anesthesia for future studies of cardiac function.	Richmond, VA	Active

Why Are Dogs Necessary for These Studies?

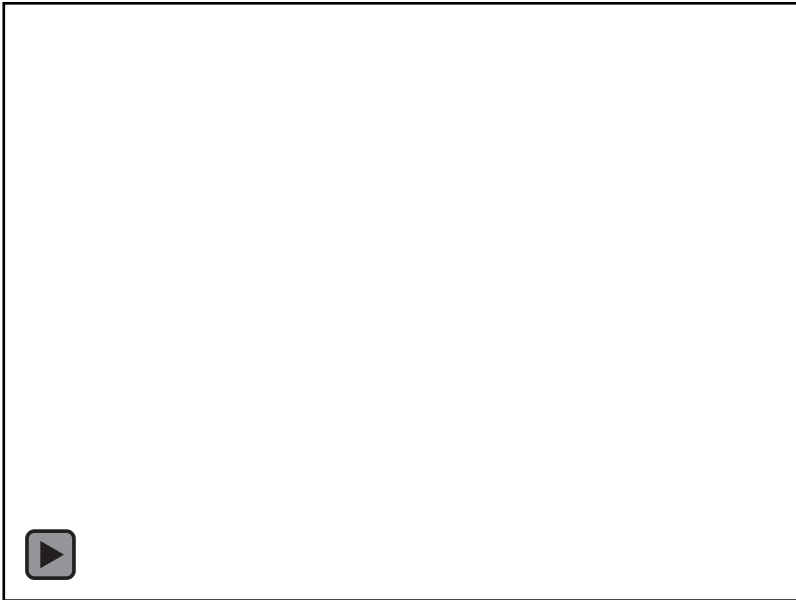
- Cleveland spinal cord injury studies- to determine proper wire lead and device design and placement, an animal with a spinal cord about the size of a human's with a very similar anatomy is needed. The dog is the only available species for such work at this time. Some limited studies in pigs were conducted to determine if the device components would be safe in a human over an extended period of time because the tissue reaction of pigs is similar to that of humans.
- Richmond heart disease studies- the dog heart electrical conduction system is the most similar to the human heart, and the way the dog heart reacts to PVCs closely mimics changes in the human heart. However, if some baseline studies are conducted in pigs, it might be possible to transition from dogs to pigs. VA is committing over \$2M to study this possibility.

How Does it Work?

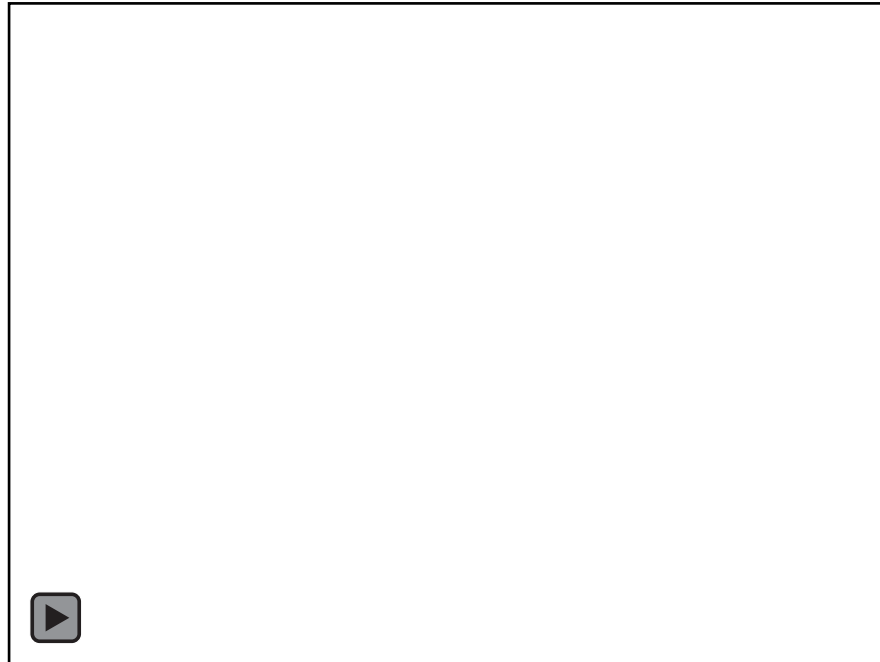
COUGH STIMULATOR



VA-Funded Dog Research at Cleveland- A Patient With and Without the Cough Stimulator



Words from the Recipient of a Cough Stimulator



Words from a Veteran's Family

Dr. Kowalski -

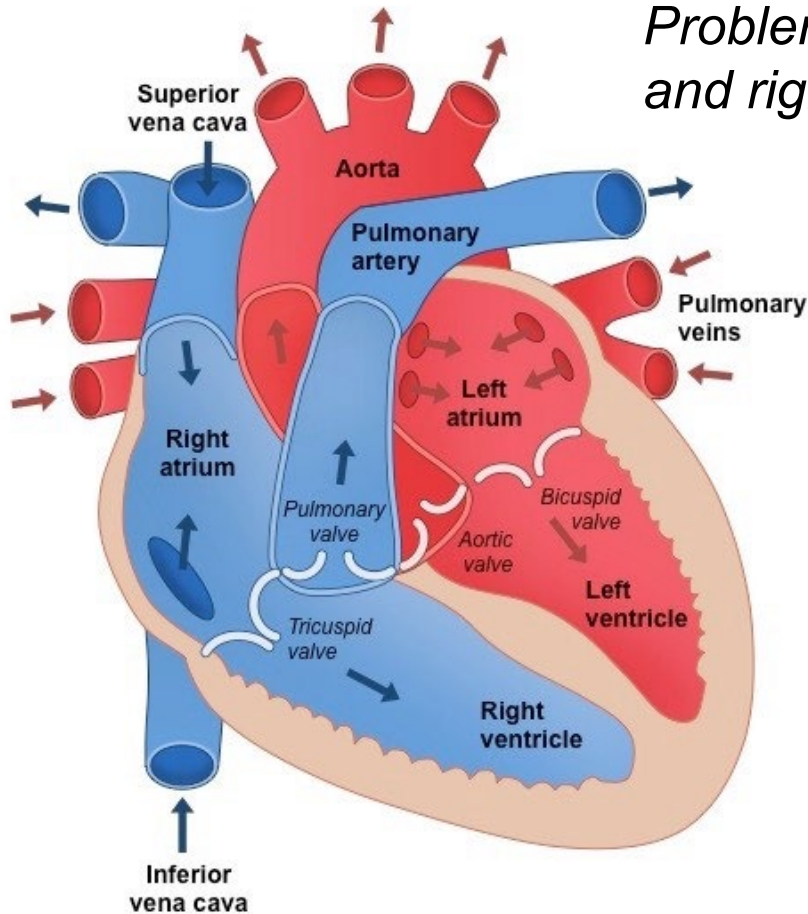
I did want to say "Thank you" again:

This device has been a life-saver for David.

This is the best thing that we have done since David's injury.

VA Dog Research at Richmond- Reducing Heart Disease/Sudden Death in Veterans

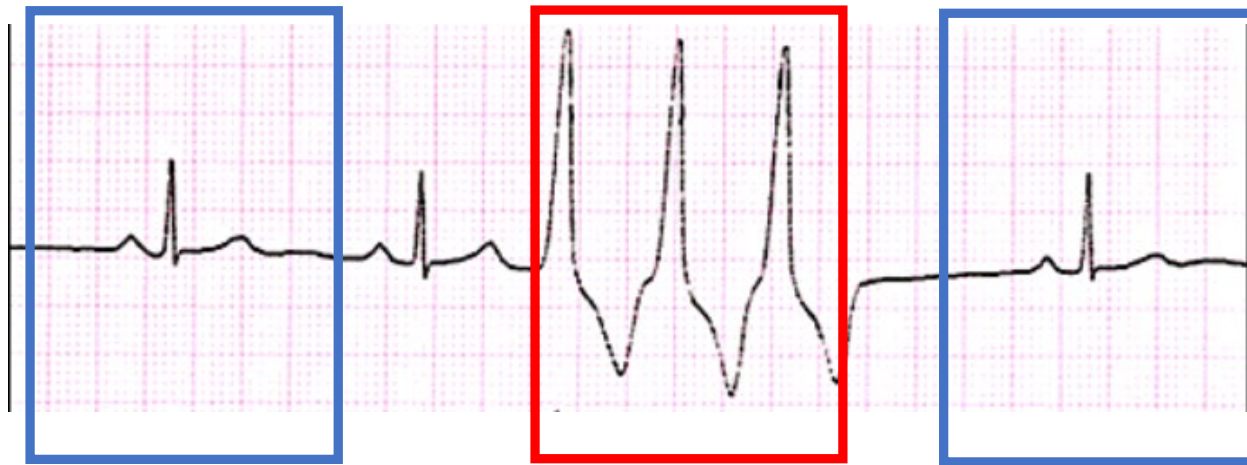
Problems with “top” of heart, the left atrium and right atrium



Problems with “bottom” of heart, the left ventricle and right ventricle

Heart disease caused by premature ventricular contractions (PVCs)

- Normally the top and bottom of the heart beat in a rhythm that efficiently pumps oxygen-depleted blood through the lungs and oxygenated blood from the lungs to the body.
- Many people have extra beats in the ventricles (bottom portion of heart)

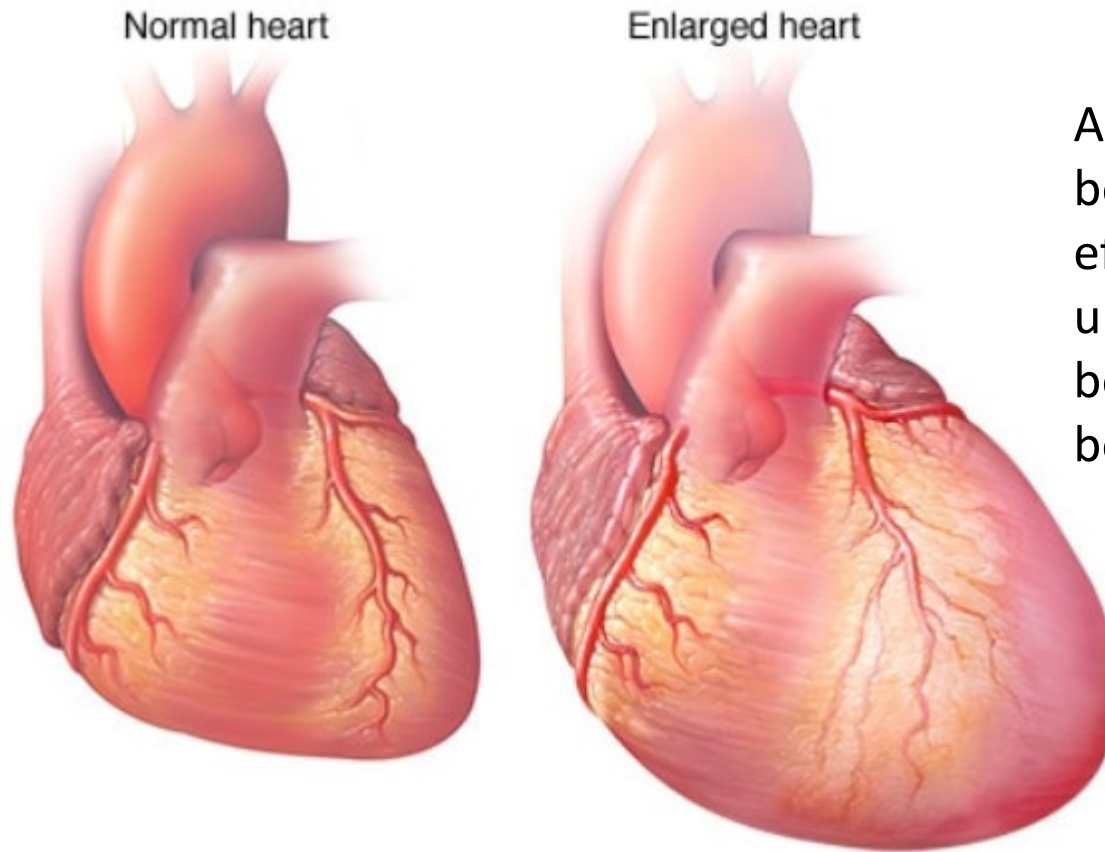


A normal
heart beat

Three extra
Ventricular beats

A normal
heart beat

The Outcome- “Cardiomyopathy”, and Sometimes Sudden Death

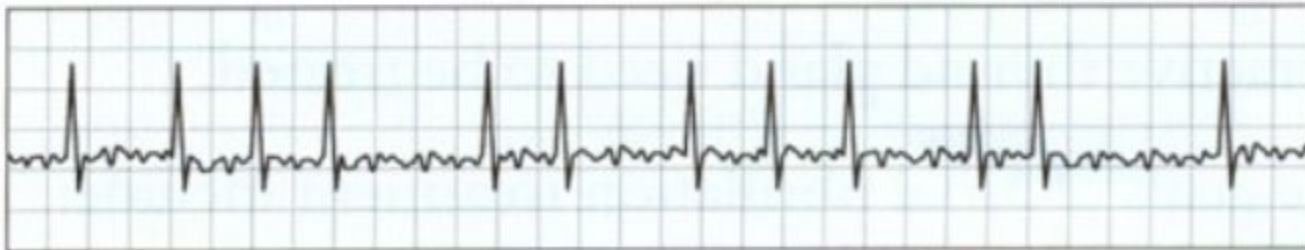


As the heart stretches, it becomes less and less efficient pumping blood until not enough blood can be pumped to keep the body supplied

Complications cause by Atrial Fibrillation



ECG tracing of a normal heart rhythm.



In atrial fibrillation, the tracing shows tiny, irregular "fibrillation" waves between heartbeats. The rhythm is irregular and erratic.

- Most commonly encountered arrhythmia after cardiac surgery.
- Important predictor of increased patient morbidity, mortality, and increased health care costs.

Why is this Research Important to Veterans?

The number of Heart-Failure-related hospitalizations in the VA health care system increased from 74,000 in FY2002 to 96,000 in FY2009.

- 120,000 Veterans were admitted a diagnosis of heart failure in 2010
- Annual cost to VA is about \$30,000 per patient, which is greater than \$3.6 Billion in 2010 alone.*
- Cardiovascular disease is the leading cause of hospitalization in the VA health care system.

***Yoon J. JACC Heart Failure 2016;4(7):551**

Richmond Dog Studies Recognized by American Heart Association, and NIH

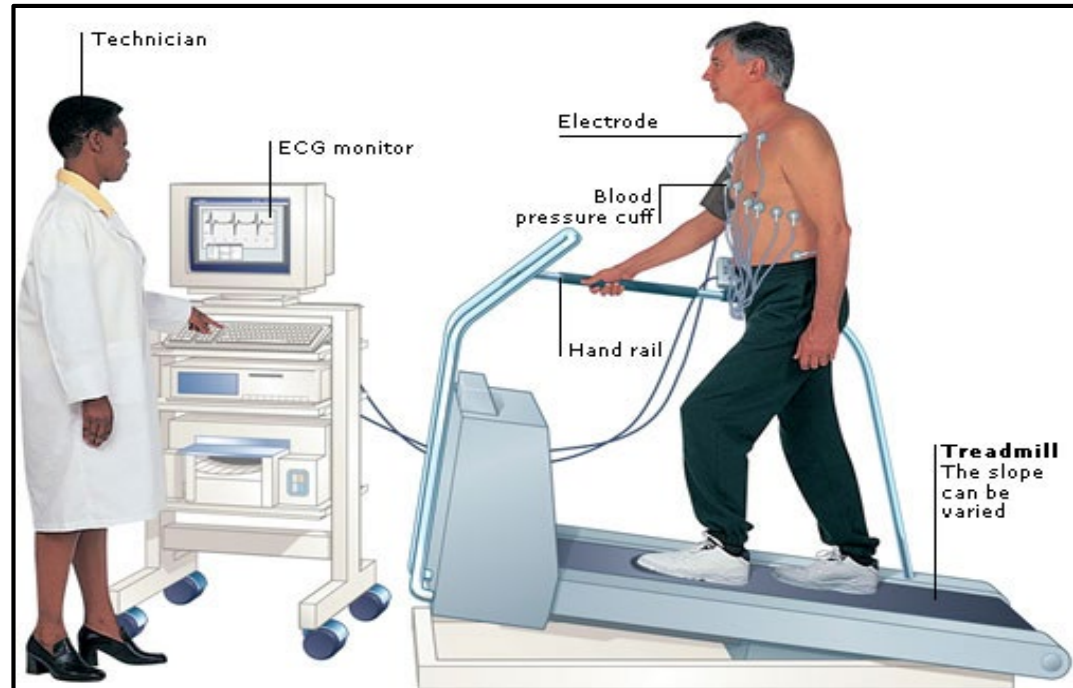
- The Richmond work on PVC-induced heart disease was referenced twice in the American Heart Association's 2016 Scientific Statement on the link between premature ventricular contractions and heart disease.*
- The group was awarded an NIH-R34 (Clinical Pilot Study) on “Prospective Assessment of PVC Suppression in Cardiomyopathy (PAPS): A Pilot Study”; this is a multicenter randomized study (11 centers in US & Canada) made possible through advances in understanding the problem provided by both canine research and human clinical observations.

*Bozkurt B, et.al, *Circulation* 2016;134:e479-e646

Treadmill Stress Test



https://www.valleyvet.com/group_images/29075_A.jpg



<http://www.vitalsdiagnostics.com/img/TreadMill-Test.jpg>

Alleged Canine Treadmill Stress Test

“Forced to run on a treadmill until they collapse.”

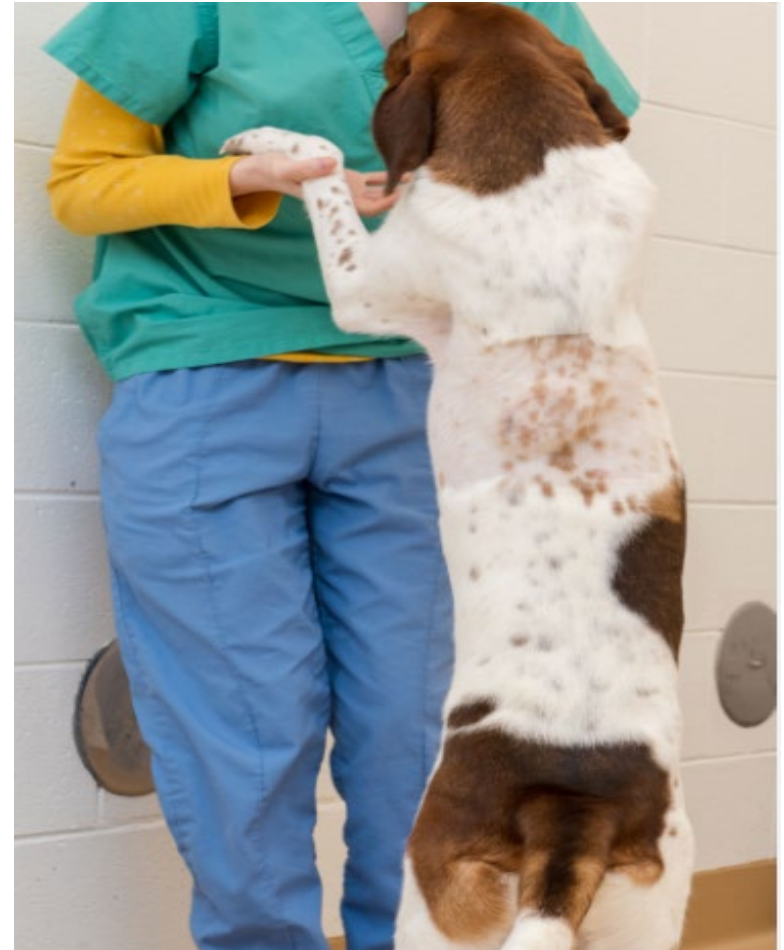
- WRIC ABC News



Actual Canine Treadmill Stress Test



Dogs are Given Love and Respect



Military Working Dogs and VA Research Dogs

Both types of dogs give their lives to protect and save Veterans.



VA Policy: Dogs Must Be Adopted Whenever Possible

- If the scientific goals of the study do not require collection of tissues for analysis and dogs are available for adoption after the study, they must be adopted.
- VA has a written agreement with Homes for Animal Heroes to assist with adoptions.
- 100% of eligible dogs have been adopted, most recently three narcoleptic Dobermans maintained as potential breeders, but released from research in 2018.

The Start of the Controversy

- In late 2015 and 2016, complications in surgical outcomes in dogs at the Richmond program occurred:
 - A researcher reported that several dogs developed nausea after an experimental surgery. The surgery was performed to isolate the heart from different sources of nerve impulses by resecting some nerves. Unable to adequately control the nausea, staff humanely euthanized the dogs. The IACUC (ethics committee) and researcher agreed that fewer nerves would be resected, which solved the problem.
 - After a chest surgery, the lungs of a dog adhered the chest wall. When the researcher attempted to repair it, a blood vessel in the lung burst, and unfortunately the dog died under anesthesia.
- These incidents were all self-reported by the program to the NIH Office of Laboratory Animal Welfare, as required by VA Policy and Public Health Service Policy.
- The self-reports were obtained via a FOIA request by an animal rights group.
- **NO problems in surgical outcomes have occurred since 2016.**

External NIH Review: VA Canine Research

The NIH Office of Laboratory Animal Welfare visited all VA dog research programs in 2018 and released a report on January 3, 2019. Findings:

- “Hunter Holmes McGuire VAMC responded appropriately to the allegations of animal welfare concerns, recordkeeping and reporting inconsistencies. In compliance with the PHS Policy, the institution investigated, self-reported to OLAW, and ensured that appropriate corrective measures were taken after deficiencies were identified. During the site visit OLAW found that the facility not only executed and implemented, but has consistently maintained, the appropriate corrective measures in response to the animal welfare concerns.”
- “OLAW determined that the visited VAMCs are effectively supporting the humane programs of animal care and use at their institutions and conducting research with dogs and other vertebrate species in compliance with the PHS Policy, and applicable rules and regulations.”

VA Canine Research-Congressional and External Reviews

- Currently governed by Section 254 of the FY2018 and Section 247 of the FY2019 VA funding legislation
 - Review by CVMO's office and other VACO offices required for any new proposed dog research
 - VA Secretary's approval required before VA funds can be used for any dog research projects. We have voluntarily extended this restriction to the use of any funds, VA or non-VA.
 - Annual reports to Congress.
- External reviews:
 - All VA program must be accredited by AAALAC; those with dog research are visited twice as frequently, every 18 months (only VA does this)
 - VA has contracted with the National Academies of Science to perform a detailed external review of the VA canine research program

Allegation- VA's Ongoing Dog Research can be Replaced by Alternate Methods

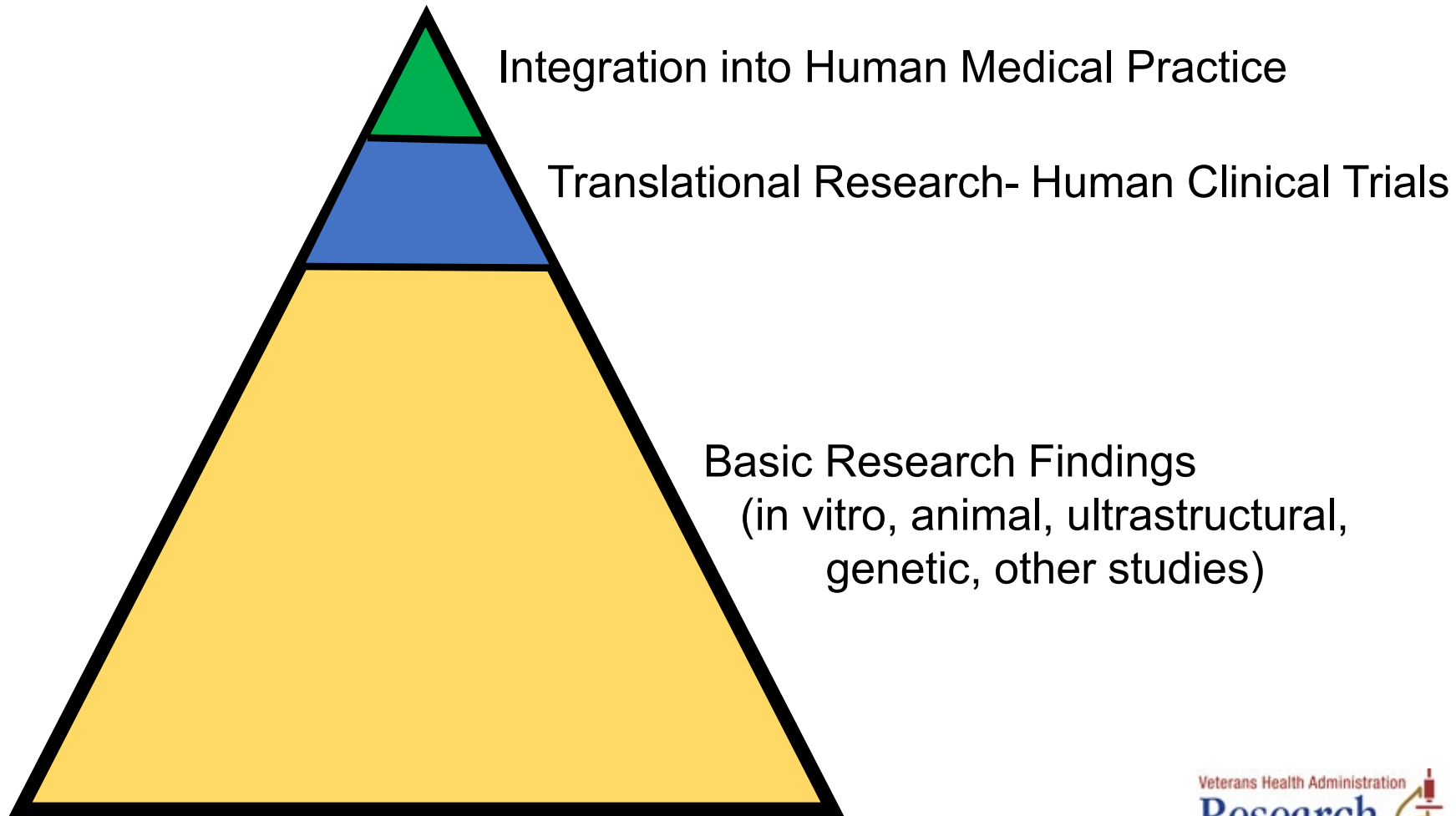
- The availability of alternatives to current animal models is frequently claimed, but actual methods don't materialize.
- If in vitro, computer simulation or organoid/"organ on a chip" techniques can be used instead of animals, VA will not allow the use of animals. This issue is evaluated very carefully prior to allowing use of dogs.
- FACT: currently, in vitro alternatives cannot replace most animal research projects, but do have great potential to replace animals in toxicity testing of new drugs and compounds.

Allegation-VA Dog Research is “Expensive”

- The VA Research budget for FY2018 was ~\$720,000,000.
- In FY2018, a total of about \$100,000 was spent on purchasing, maintaining, and caring for VA research dogs:

0.014 % of the VA research budget

Overlooked/Misunderstood Fundamental Biomedical Research Concepts



Why doesn't every study produce a human treatment breakthrough?

Research advances are like solving a puzzle....



A Perspective: The Number of Dogs Used in VA Research

- Yearly, VA uses about 100 dogs in research per year.
- According to a 2018 analysis by Rowan and Kartal, 775,000 dogs annually are euthanized in shelters in the US, which is over 2100 per day.
- In 2016 according to USDA, 64,707 dogs were used nationwide in research; VA used about 100 in FY16, which is 0.15% of 64,707.
- 99% of animals used in VA research are mice and rats. For a very few studies, VA allows the use of dogs, which represent <0.05% of the animals used.

Components to VA Dog Research Review before Studies can Start

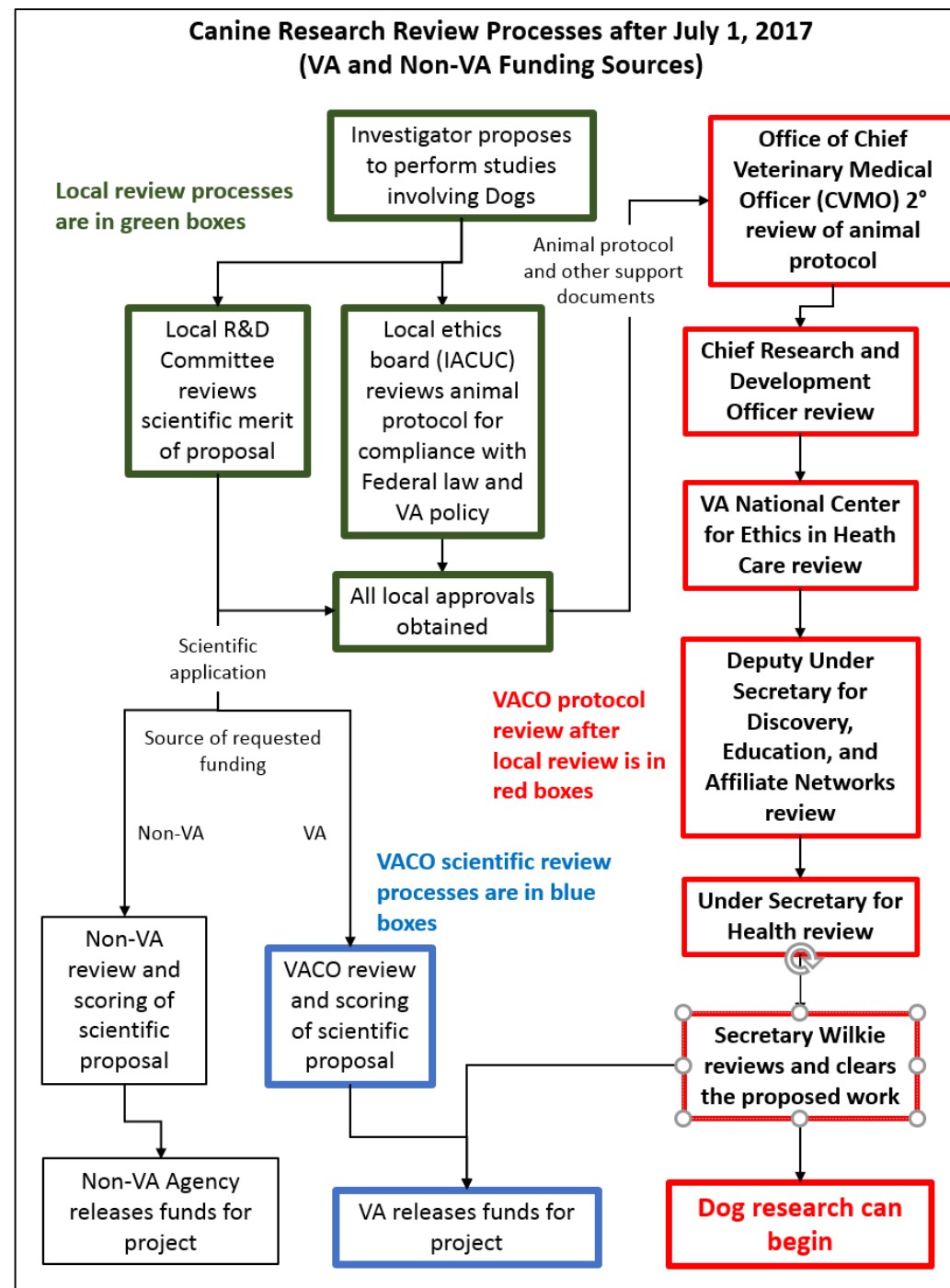
1. VACO Scientific review- VA peer-review system very similar to NIH scientific review system:

- Reviewers are specifically asked to evaluate the requirement for dogs in the proposed research
- VA is also looking for opportunities to fund parallel studies in other species if lack of background data in another species is the impediment to validating a non-canine species model

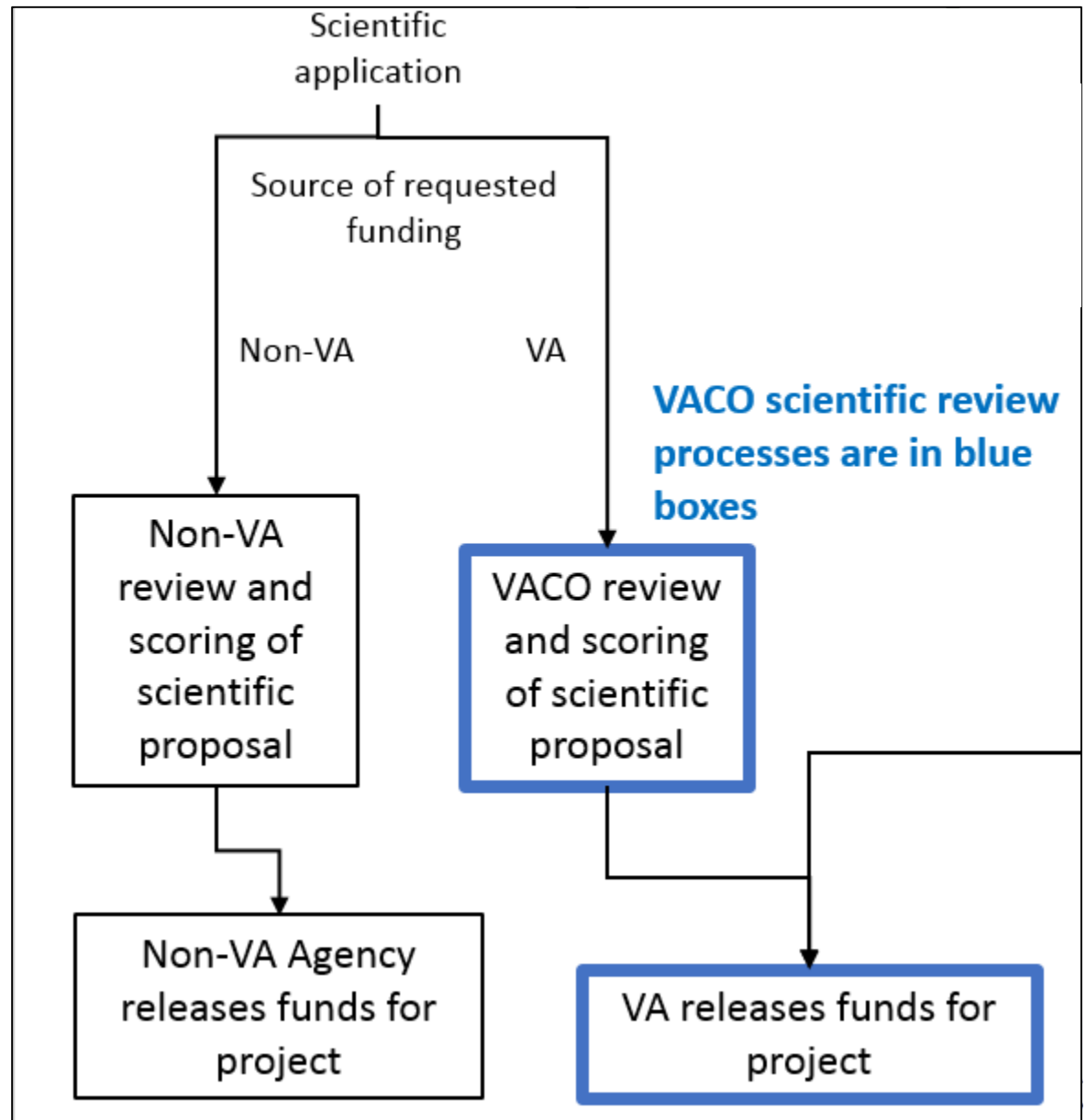
2. Local review- follow USDA, PHS, and VA rules and regulations

3. VACO Review- unique to the VA, a secondary veterinary review of local protocols has been in place at VA since the 1970s

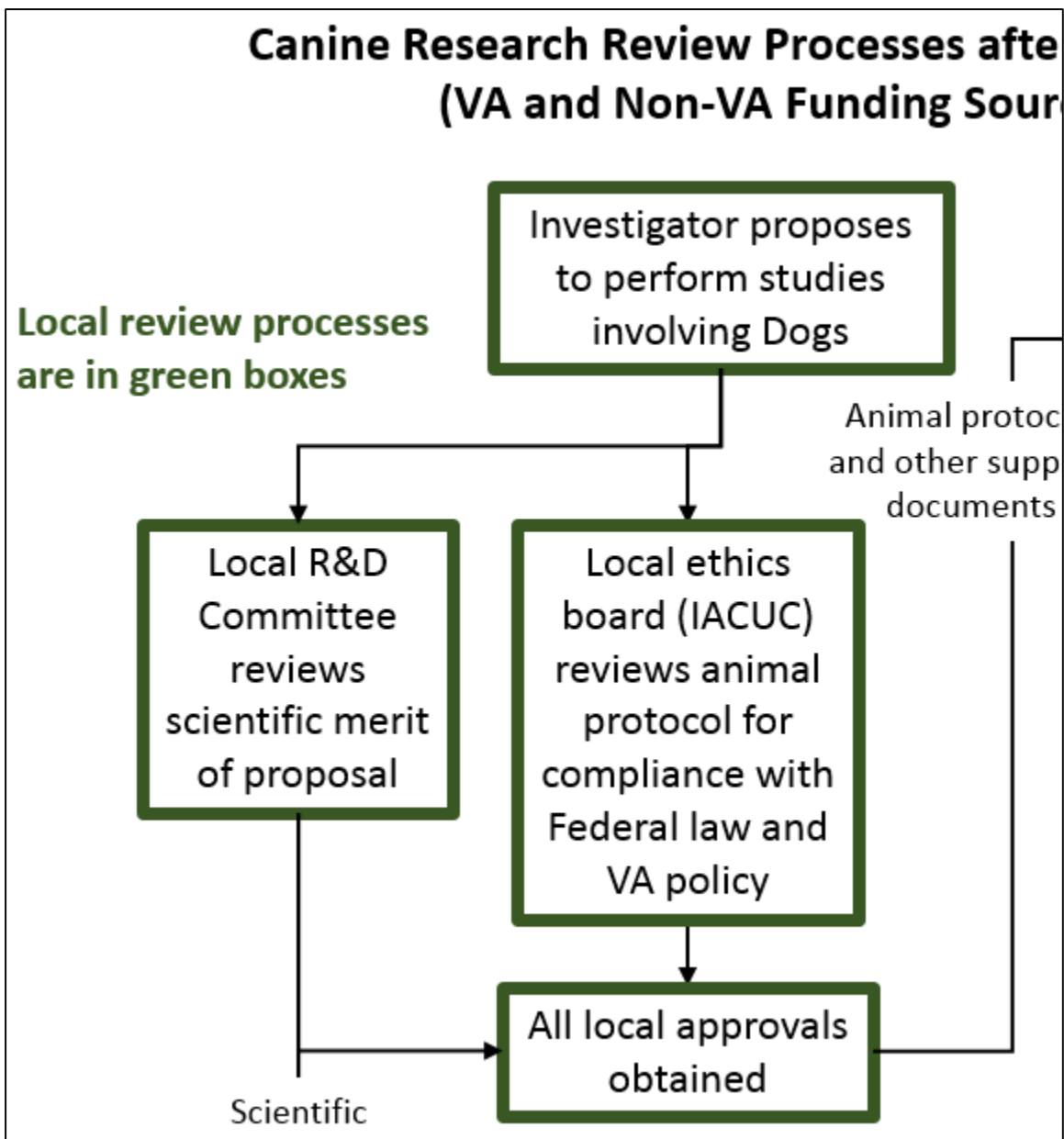
The VA Dog Research Review Process



VACO Scientific Review



Local Review

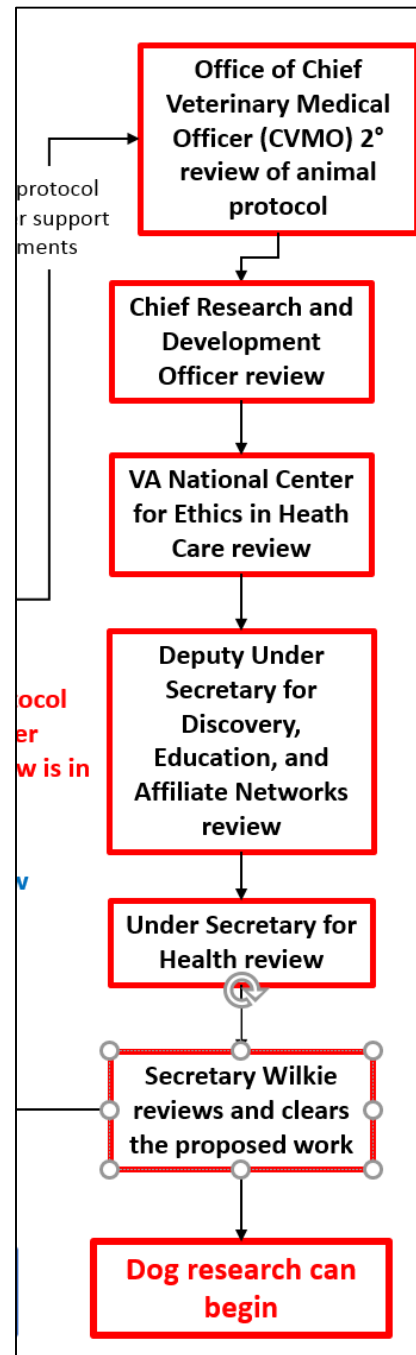


IACUC Membership

Designed to Include All Important Voices

- A Doctor of Veterinary Medicine, specializing in laboratory animal science and medicine
- A Non-Affiliated Member (NAM) – voice of the general community
- A practicing scientist experienced in research with animals
- A Non-Scientific Member (NSM) – perspective unbiased by scientific training
- At least one other member
- (One member other than the veterinarian and the NAM serves as Chair)

VACO Secondary Review



Secondary Veterinary Review by office of the Chief Veterinary Medical Officer

Outcomes of SVR

ACORPs must be reviewed and cleared by the CVMO before funding is released.

- **Level 0** – No concerns; may include informational suggestions. Cleared by CVMO.
- **Level 1** – Some concerns; local IACUC determines response to concerns. Cleared by CVMO.
- **Level 2** – More serious concerns, requires revisions to the ACORP. Note: If revised ACORP is not satisfactory, additional revisions will be required before clearance by the CVMO is given.

What does the SVR look for?

- Why is this research needed?
- Is harm/benefit addressed?
- Why is it necessary to use dogs?
- Is the experimental plan clear?
- Are the dogs well-cared for?
- How will potential pain and distress be minimized?



After the SVR, Multiple Other Reviews

- The Chief Research and Development Officer reviews materials and meets with an expert reviewer who can answer questions about scientific necessity and whether only dogs can be used to achieve needed scientific goals.
- Only after all scientific questions are answered, and there is confidence that dogs are necessary, will the CRADO approve.
- Drs. Clancy and Stone must then approve, then finally Secretary Wilkie must approve before new work can begin.

Diabetes



The death sentence of diabetes was lifted through the discovery of insulin in dogs-
some medical advancements will continue to rely on dogs.

Figure 1. Effects of Insulin Therapy. These photographs from 1922, in a case described by Geyelin,¹¹ show a young girl with insulin-deficient diabetes before treatment with insulin (Panel A) and after treatment (Panel B).

The Past 200 Years In diabetes. KS Polonsky. New England Journal of Medicine October 4, 2012

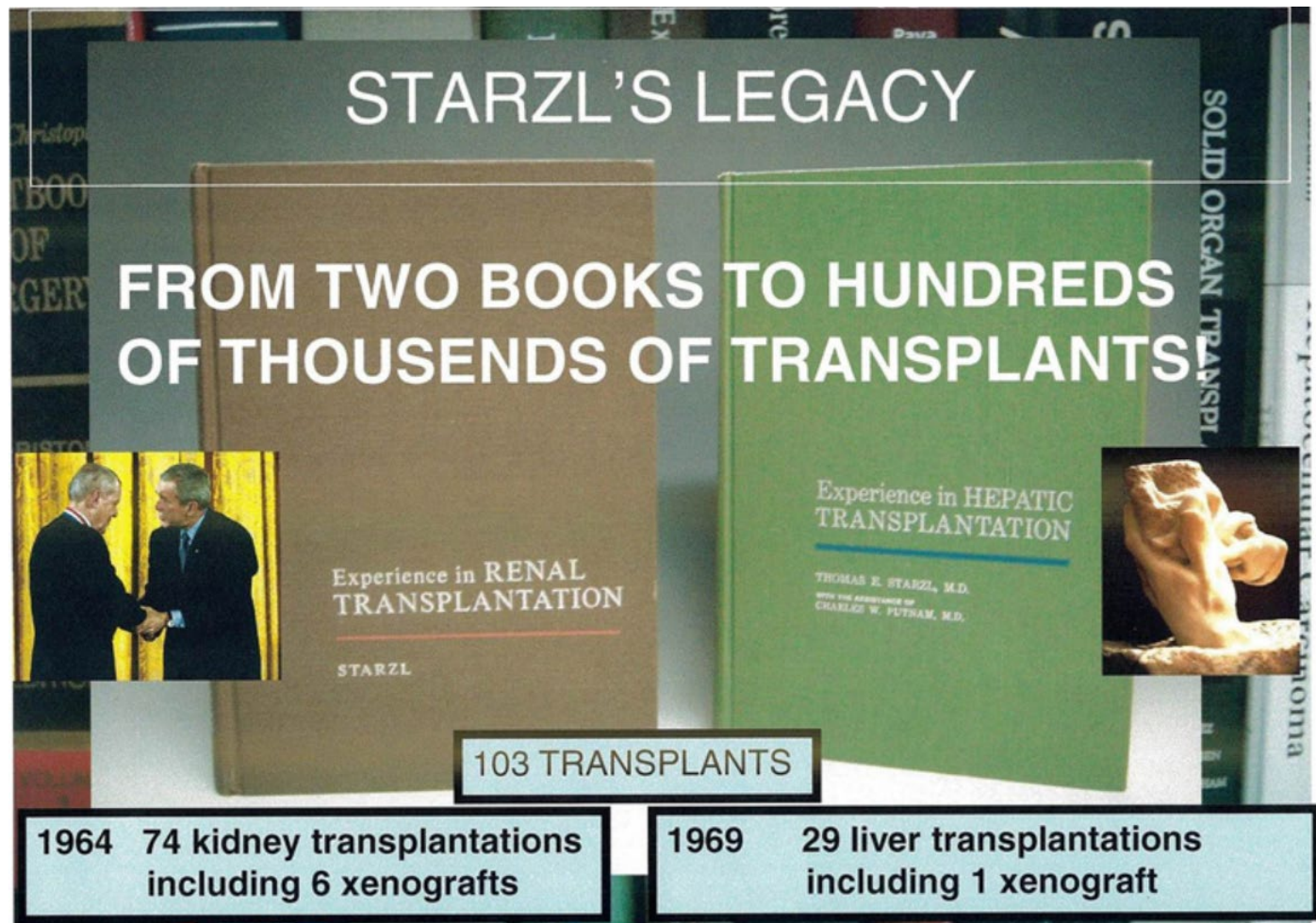
Polio



Our children and other loved ones will never have to experience an iron lung- all due to life-saving breakthroughs from animal research, which provides an understanding of the immune system as well as the development of effective vaccines.

Organ Transplant

200,000+
lives saved



The procedures and drugs needed to transplant organs and stop the body from rejecting them were developed initially by Dr. Thomas Starzl, who conducted much of the early groundbreaking work in dogs as a VA physician scientist.

IN SUMMARY:

VA does not tolerate abuse of animals. VA supports the humane use of animals in scientifically necessary, ethically conducted studies. VA dog research will continue to provide life-saving advances for Veterans unless extreme animal rights groups succeed in stopping it...

Thank Research

If.  you take  medicine to treat allergies • your  doesn't have fleas • your grandmother has a new hip • you've taken medicine to stop an ache • you've never had the measles • you've never breathed with the help of an iron lung • you don't know what bubonic plague is • you control your diabetes with insulin • you take vitamins • your dad has recovered from a heart attack • your great aunt survived breast cancer • your  doesn't have feline leukemia • your grandpa has had bypass surgery • your friend has had a stem cell transplant • you've had a broken  repaired • your don't have ulcers • you've had an operation and you slept through the whole thing • **you feel great today!** 

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