Control of Raccoon Rabies Using RABORAL V-RG® from Merial

www.raboral.com
Merial - World Leader in Rabies Vaccines

Merial, one of the world’s largest research, development, and manufacturer of vaccines for animal health, has a unique combination of outstanding products, unparalleled technical expertise, and a history of individualized customer care.

• IMRAB® and its overseas counterpart, RABISIN®, are the world’s leading rabies vaccines, with millions of successful doses administered across the globe. IMRAB provides a three-year duration of immunity against rabies in dogs, cats and sheep, and one year for cattle, horses and ferrets.

• PUREVAX® Feline Rabies is the first viral-vectored rabies vaccine for cats. This genetically engineered recombinant vaccine, which eliminates the need for chemical adjuvants, is available as a monovalent and in multivalent combinations that may reduce the number of injections needed for comprehensive vaccination.

• RABORAL V-RG® is the world’s first oral, vaccinia-vectored rabies vaccine. Since its development, it has become one of the most extensively tested animal vaccines ever developed, and it has shown extraordinary success against wildlife rabies under actual field conditions.

The Spread of Raccoon Rabies: A Case History

Rabies is a serious concern and is responsible for nearly 92% of the reported rabies cases in the United States. Raccoons account for a significant portion of total wildlife rabies cases each year. Thus, it is particularly instructive to review the history of raccoon rabies along the eastern coast of the United States.

Raccoons (Procyon lotor) have been recognized as a reservoir for rabies in the southern states since the 1950s. For many years, rabies was considered to be a wildlife disease in rural areas, posing little threat to human populations. Rabies cases were monitored, but little else was — or realistically could have been — done. At that time no practical means of effective wildlife rabies control was available to prevent an outbreak.

Looking back, it was apparent that the stage was set for a large rabies outbreak in raccoons called an epizootic (see page 6). Contributing factors to this outbreak were: increasing raccoon populations in rural and urban environments, intentional or unintentional transportation of raccoons from the south and human behavior of treating raccoons more as semi-wild pets than true wildlife.

Suddenly, the burgeoning raccoons began a relentless march northward through the coastal states. As raccoon rabies invaded the mid-Atlantic region, it began to move through populated areas, and human exposure to rabies increased.

In 1989, a new orally active recombinant rabies vaccine, RABORAL V-RG, began field testing in the United States for use in wildlife. After successful large-scale use in Europe and extensive testing in various states in the United States, it was conditionally approved for use in New Jersey in 1994. Soon, other states began to follow suit. Full licensure of RABORAL V-RG was received for raccoon in April of 1997, followed by a coyote claim in May of 2002.

As a powerful component of a total rabies control program that includes the veterinary vaccination of domestic animals, RABORAL V-RG currently offers the most promising way to stop the rapid spread of wildlife rabies in North America.

A Proud History

Merial’s company roots reach back to the time when 19th century pioneers in microbiology discovered vaccination — a radical new way to prevent infectious disease by inoculating a person or animal with a less virulent form of the infecting agent. One of these pioneers was French chemist Marcel Merieux, who had developed special dyes to color silk. Louis Pasteur and Merieux formed a bond of friendship as they devised ways to use these silk dyes to identify bacteria.

Mérieux founded Institute Merieux in Lyon, France in 1897. The company became a world leader in human and animal health, creating the French Institute of Foot and Mouth Disease, which produced early vaccines to prevent the disease, and developed rabies and polo vaccines. As it grew, Institute Mérieux formed two operating companies: Pasteur Mérieux to manufacture and market products for human health and Rhone Mérieux for research, development and manufacturing of animal health products. Both of these companies continued to grow. In 1997, Rhone Mérieux joined Merck AG and became Merial. In 2011, Merial became the animal health division of Sanofi.

Merial is proud to continue research with the dedication that drove Marcel Mérieux to excellence in France more than a century ago. It is reflected in our outstanding technology, state of the art facilities, research leadership, committed professionals, a strong sense of responsibility, service to the veterinarian, and an innovative spirit that expanded into wildlife. These have combined to form a powerful force in the animal health industry — Merial, dedicated to the improvement of animal health and well-being, worldwide.
The Evolution of Orally Active Recombinant Rabies Vaccines

More than twenty years ago, new ground was broken in the field of veterinary medicine with the development of a different sort of rabies vaccine — a vaccine designed specifically to orally vaccinate wildlife in their natural habitat. It began with a most appropriate step. Looking back for inspiration to pioneering studies in immunization, researchers started with the same carrier virus (vector) that had been used successfully in the worldwide campaign to eradicate smallpox. Employing the latest genetic engineering techniques, scientists combined this vector with a single very important part of the rabies virus — the glycoprotein gene that elicits immunity to rabies disease. Because only a portion of the rabies virus gene was included, the vaccine can not cause rabies disease. The new vaccine was effective when given orally. It also proved very stable, even under wide temperature fluctuations as would be found in the field. Even before development of the new vaccine was complete, wildlife biologists and other researchers began looking for an attractive, stable, cost-effective bait with which to deliver the vaccine. Several edible substances were found to work well. For raccoons, researchers chose fish meal. Wild raccoons seem to find it palatable. This fish meal and a special polymer were mixed to form a hardy bait into which a sealed vaccine-filled package, called a sachet, could be inserted. A raccoon eagerly biting down on the bait would puncture the sachet and immunize itself as the vaccine was released into its mouth and throat. Trials demonstrated up to 85% raccoon bait acceptance. Bait contact has been reported as high as 99% on day-two post-deployment. Tests in Virginia and Pennsylvania, under the direction of the United States Department of Agriculture-Animal and Plant Health Inspection Service (USDA-APHIS), demonstrated the vaccine was environmentally safe.

In 1997, the USDA granted license to RABORAL V-RG for oral rabies vaccination (ORV) in raccoons. Its utility for controlling raccoons in European red foxes was well established.

RABORAL V-RG has been successfully used in Florida, Massachusetts, Maryland, New Jersey, New York, Ohio, Pennsylvania, Texas, Vermont, Alabama, West Virginia, Georgia, Tennessee, Maine, Virginia, North Carolina, Arizona, New Mexico and New Hampshire. In 2002, based on successful trials in Texas against the canine strain in coyotes, RABORAL V-RG was granted license for use in coyotes. In the American Southwest, under experimental use, the oral vaccine was demonstrated to be effective against gray fox variant raccoons.®
RABORAL V-RG® FISHMEAL POLYMER BAIT

Introduction
RABORAL V-RG is a product developed and manufactured using state-of-the-art biotechnology. The product is specifically designed to impede or prevent the spread of lethal rabies disease in raccoons. Since raccoons are spread by animal-to-animal contact, vaccination of a significant number of raccoons may effectively establish a barrier between raccoons enzootic and uninfected areas. Over time, repeat vaccination campaigns may reduce the reservoir of susceptible raccoons.

While a program to vaccinate raccoons and/or coyotes against rabies may reduce the rate of infection in wild animals, the main objective of any rabies vaccination program is to limit the exposure of domestic animals to rabid wild animals. Because people are more likely to come in contact with domestic animals, the ultimate goal is to protect the human population from rabies.

An ORV program does not and is not intended, in any way, to eliminate the need for vaccination of pets or other domestic animals. RABORAL V-RG is not intended nor approved for use in pets. All animal owners are encouraged to have their animals vaccinated in accordance with local, state, or federal regulations by licensed veterinarians.

Indications
RABORAL V-RG is recommended for the oral vaccination of raccoons and coyotes against disease caused by the pathogenic rabies virus. The vaccine is restricted for use in raccoons control programs approved and directed by an appropriate federal or state agency. Control of the use of the vaccine rests with the sponsoring agency which has the responsibility for defining conditions for proper use in its program. Assessment of such factors as target species population, baiting densities, competitive species, habitat, methods and frequency of distribution, public awareness, safety procedures, and any appropriate parameter is the responsibility of the sponsoring state or federal agency.

RABORAL V-RG is composed of vaccine-filled plastic sachets contained in fishmeal polymer baits or coated in wax and fishmeal crumbles. The vaccine is a Type III recombinant virus which means it contains a live virus vector which carries and expresses a foreign gene. In this case, the viral vector is vaccinia virus, and the expressed gene product is rabies virus glycoprotein. This vaccine cannot cause rabies because it expresses only the antigen which is important in inducing immunity. It has been demonstrated to be safe in more than 60 species of animals including primates. It also has been shown to be effective in protecting raccoons against virulent rabies challenge in controlled studies in the United States.

Route of Administration
This vaccine is effective when administered by the oral route.

Packaging and Storage
Slipped refrigerated. Store refrigerated 2-7°C (35-45°F). Do not freeze. Each bait contains one single-dose sachet ready for field use.

Quality Control
The quality of RABORAL V-RG is confirmed by testing under guidelines put forth by USDA-APHIS (9CFR) for:

- **PURITY** - Tested for bacteria, fungi, and mycoplasma to assure no detectable contaminants.
- **POTENCY** - Tested to assure each lot meets or exceeds the viral content required in accordance with Production Outline specifications.
- **SAFETY** - Tested for safety to assure no adverse effects are attributable to the vaccine.

IDENTITY - Tested to ensure the vaccinia virus identity and to confirm the expression of rabies.

Precautionary Measures
Labels are printed on each bait, clearly identifying the recombinant vaccine and listing a toll-free phone number to contact the appropriate public health authorities. Public education should be conducted prior to distribution of the baits to inform local communities the purpose of distribution, the type of vaccine, times and areas of distribution, public health concerns, and reasons for not disturbing the baits. This education may include newspaper articles, local television and radio reports, public meetings, and the distribution of brochures and posters. In certain areas, it may be appropriate to post signs at the periphery and at strategic points within the distribution area notifying visitors of rabies control efforts and warning them not to disturb the vaccine-filled baits.

The local public health authorities in the areas where the recombinant raccoons vaccine is used should be notified prior to the distribution of the baits. This notification should include instructions for addressing animal and human exposure to the vaccine.

The key personnel conducting the raccoons control programs should be trained in the appropriate precautions and techniques for handling and distributing the vaccine-filled baits. All personnel who will be handling the vaccine should be nonpregnant adults at least 18 years of age, who are free of any known immunosuppressive conditions.

Tetracycline Biomarker
The fishmeal polymer bait contains the antibiotic tetracycline hydrochloride.

After a raccoon, or non-target animal, eats the bait, the antibiotic binds to calcium in growing bones and teeth. This interaction creates a detectable line in the bone that can be seen microscopically by ultraviolet light detection. This “biomarker” line is a permanent record of bait consumption. Tooth and bone samples collected from animals within the baited zones demonstrate bait uptake. Such post-baiting surveillance data can be used to determine the percentage of raccoons in a given area that may have been vaccinated.

Rabies incidence rates and serum antibodies against rabies are the primary tools used to determine the success of an ORV campaign. Biomarker analysis is useful but requires additional laboratory cost and technical support. Since the biomarker is a permanent record of yearly bait consumption, the number of lines detected in a single animal’s tooth or bone shows the number of baits consumed over time.

Note: RABORAL V-RG is one of the most extensively tested animal vaccines ever developed. During the approval process prior to the release of RABORAL V-RG to the environment, numerous laboratory studies were conducted at the Walter Reed Institute and Thomas Jefferson University, two of the world’s premier rabies research centers. These experiments demonstrated that inadvertent contact with the vaccine would not harm these species but does not constitute approval for use. A 2, 3, 5, 14 American porcupine Arctic fox Bank vole Black bear Bobcat Canis lupus Castle Chimpanzee Common buzzard Common vole Cotton rat Coyote Daubenton bat Deer mouse Domestic cat Domestic dog Domestic pig Duck European badger Ferret Field vole Flying squirrel Gapper’s vole Great homed owl Gray fox Gray squirrel Grey homed mule Green mouse Groundhog Haplopod cotton rat Horse Jay Kestrel Laboratory mouse Laboratory rabbit

Safety Tested in More Than 40 SPECIES
Vaccine Vector

Vaccinia vaccines.
Glycoprotein
Sylvatic rabies
Reservoir
Enzootic
Barrier

While an effective ORV program begins with the availability of an efficient, efficacious vaccine, it doesn’t end there. Success depends on decisions about area of coverage, time and method of vaccination, and a host of epidemiological, geographic, climatic, biologic, and economic factors. Timing and spacing of bait deliveries are particularly important, because they often determine what proportion of the population will be successfully vaccinated.

The cycle of disease in a rabies-infected population can be broken if enough of its animals are immunized and if rabid animals do not come into contact with susceptible animals. Ideally, the disease will die out in the population. Rabies can be kept from penetrating into a new area in the same way. In either case, the immunized proportion of the target animal population presents a barrier against rabies that is as real and effective as a physical barrier would be.

The barrier concept for raccoons is similar to — and complementary to — the current philosophy of rabies control in domestic animals. This strategy is based on producing a buffer of immunized animals around humans. Because pets are the animals with the most day-to-day-contact with people, such programs usually focus on canine and feline rabies vaccination. For effective raccoon rabies control, concurrent domestic animal vaccination programs must be continued. Additional measures which help to increase the effectiveness of pet vaccination include reducing contact among pets, reducing the population of free-ranging pets, and reducing pet contact with raccoons.

RABORAL V-RG can be a very efficient system for immunizing raccoon populations when combined with effective vaccine distribution strategies. These strategies, in turn, are based on the status of raccoon rabies in the targeted area, e.g., Is rabies already entrenched at a low enzootic level? Has it exploded onto the scene as a major animal epizootic? Or is it absent now but threatening to move into the area? The next page contains some possible distribution scenarios.

Barrier programs: Keeping rabies out

Generally, a population of animals immunized against rabies is effective in preventing the spread of the disease. Immune barriers may be created in multifaceted fashions which depend upon the area threatened with rabies (see opposite page for some examples). Scientific experiences and field use of RABORAL V-RG suggest that successful barrier programs depend on:

1. Designating the area of the barrier — must include sufficient area to impede the spread of rabies.
2. Achieving vaccination of greater than 50% of the target species within the barrier.
3. Using vaccine densities of greater than 75 baits per square kilometer.
4. Continued vaccine delivery as long as the threat of rabies is in the region.
5. Contingency plans for additional vaccination in case the barrier is breached.

Confronting an epizootic in raccoon habitats

Dealing with an epizootic front of rabies requires a campaign which includes several phases. Short term and long term planning includes:

1. Vaccinating the target species ahead of and within the advance of the epizootic front.
2. Creating a barrier of immunity to prevent the advancement of the front.
3. Vaccinating behind the barrier to eliminate the establishment of enzootic rabies.
4. Determining if vaccine should be administered once or twice per year to gain control.
5. Vaccine densities must be established to vaccinate greater than 50% of the target species.
6. Surveillance to ensure that the outbreak has been stopped.
7. Developing an exit strategy after the epizootic has been wiped out.

Baiting in a rabies enzootic area

Enzootic rabies may be established following the progression of an epizootic front. If no other control measures are taken. Whether the disease becomes enzootic is dependent on the residual population of the target species which may be extremely low or rising. This allows for an entire area to be designated for vaccination. The following aspects must be considered in developing such a program:

1. The area to be covered must be clearly designated and defined.
2. A surveillance program for the target species should be established.
3. Vaccine densities, frequencies, and targeted habitats must be determined.
4. Designate a barrier surrounding the area in which rabies will be controlled.
5. Maintain or expand the barrier to meet the original objectives.

Terms and Definitions

Barrier — Anything that bars passage or access to the disease.
Enzootic (en-zo-ot’ik) — A disease that is entrenched in an animal population, existing with predictable regularity and with only relatively minor fluctuations in its frequency over time.
Epizootic (ep’-iz-o-ot’ik) — A disease that affects a larger than expected number of animals in the same geographical area at the same time. The spread of the disease in an animal population, often with the implication that it may also affect human populations.
Glycoprotein — A class of compounds in which a protein is combined with a carbohydrate group. The compound’s synthesis is directed by the single rabies gene incorporated in RABORAL V-RG which triggers development of an immune response to rabies.
Recombinant vectored vaccine — A vaccine made of low or non-pathogenic microorganisms that have been genetically altered to contain the part of a virus or bacterium responsible for stimulating immunity to a disease.
Vaccinia — The virus used to vaccinate humans against smallpox and now commonly manipulated for use as a vector in recombinant vaccines.
Vaccine — A safe carrier or reservoir of a virus or bacterium in a recombinant vaccine.
Variant — A subtype or strain of rabies virus that can be distinguished from others by laboratory methods and that has one or more specific natural hosts.
Vaccinia Vector — A safe carrier organism used to transmit genes encoding the immunogenic part(s) of a virus or bacterium in a recombinant vaccine.

Keys to a Successful ORV Program

Merial can assist you in developing a specific program tailored to control raccoon rabies in your area. What follows is a brief overview of the steps in a typical vaccination program, using the various resources that might be available to the sponsoring organization within your state.

1. Gather pertinent background information

Detailed information on the target species and the rabies problem in your area is vital to the design and implementation of a successful vaccination program to control rabies in raccoons or other wildlife species.

- Status of rabies in the proposed control area — Number of rabies cases reported in the targeted area; species in which these cases have occurred; when were first cases reported or is the disease endemic; methods currently used to report rabies cases. Similar data for adjacent areas also will be useful.
- Population information — Estimates of the human population and populations of both domestic and wild animals; concentration or dispersal of the targeted wildlife population; local laws concerning confinement or movement of domestic animals.
- Habitat information — Physical and demographic maps of the targeted geographical area which are necessary to determine how and where the rabies vaccine and baits will be dropped.
- Activities of target species — Local biological data on behavioral seasonal activity of the target species, including such factors as breeding cycles and animal movement associated with seasonal variations in food supply, will help determine the timing of the campaign.

2. Determine what you want to accomplish and who may be able to help

The objectives and rationale of your Rabies Control Program must be clearly stated at the outset. Include a description of methods for assessing the outcome of the program.

Identify the types of civic, service, educational, medical, and governmental organizations that might be supportive and useful in helping carry out your program. Contact the leaders of these organizations to solicit their assistance and support.

3. Learn about orally-administered rabies vaccine and baits

Those administering the ORV program must know the properties of the vaccine and the baits.

4. Begin program development

Depending upon the status of wildlife rabies in the targeted area, your program may be a customized version of one of three basic approaches: 1. Vaccination to develop a barrier against the intrusion of the rabies virus; 2. Vaccination of the local wildlife population; and 3. Vaccination of a target species potentially already exposed to rabies virus because the disease is enzootic within the targeted area. Sample scenarios appear under “Baiting Patterns” in this brochure.

5. Establish cooperation with appropriate agencies

An ORV program must be approved by a State or Federal Rabies Control Program, but obtaining that approval is just the beginning. The most successful programs have been widely cooperative in nature.

There are many potential partners to consider in an ORV program. The United States Department of Agriculture - Wildlife Services (USDA-WS) is the lead federal agency in controlling wildlife rabies. Protecting the public against transmissible diseases is the responsibility of the U.S. Centers for Disease Control and Prevention (CDC). You may also want to work with organizations such as: your State Veterinarian’s Office, your state departments of Health, Agriculture, and Fish and Wildlife; state veterinary schools or veterinary science departments; state and local medical and veterinary medical associations; state and local animal control officials; wildlife rehabilitators or law enforcement officials.

6. Estimate the budget and identify funding sources

After the scope of the program has been determined, the cost estimates of conducting such a program will have to be developed. Vaccine and bait costs can be obtained directly from Merial. Other budget items will have to be derived according to local costs and available personnel.

Typical ORV programs require funding over multiple years, as no ORV program will be successful from a single baiting. Depending on the scope of the program, useful guidance might be obtained from data on costs incurred in the implementation of other on-going programs.

7. Cultivate positive public relations

It’s vitally important — and never too early — to set up a framework for distributing information regarding a planned ORV program. All successful programs have included a variety of communications to organizations, groups, and the general public. An informed public is usually a supportive public. Please see www.raboral.com.

Much of the information to be disseminated will involve potential benefits from baiting, but possible safety issues that may be raised by various individuals and groups should also be addressed.

- The medical community — Letters should be sent to the physicians, hospitals, and veterinarians in the community, informing them of the public health significance of the program. Include answers for commonly asked questions.
- Public officials — Letters, brochures, and news clippings should be sent to public officials so that they can be knowledgeable on the vaccination program when interacting with their constituents.
- Organizations identified in your historical data base — Members of these groups will help spread your message to others.
- Newspapers — Plan an orchestrated release of information regarding program planning, targeted areas, supporting organizations, interviews with personnel, vaccine information, pictures of baits, method of distribution, etc. Most newspapers will be willing to print several preliminary informational articles, cover the distribution of the vaccine, and communicate the results of the program.
- Radio — Many programs interview people with various public concerns. Control of rabies is a popular topic when a community is threatened. Areas targeted for control, the extent of the disease, the number of baits to be dropped, precautions to be taken, and the timing of events are pertinent topics.
- Television — Stations want visually graphic news. Some stations have presented special news features on the problem of raccoon rabies and the dangers it presents to the community, pets, and livestock. Invite local televi-
sion stations to film the distribution of the baits and interview the personnel associated with the distribution, along with the program administrators, and public health officials.

- Schools — Give special presentation in schools using video clips that describe the program, and distribute informative brochures to the students. The children can take the brochures home to tell their parents what they learned in school.

8. Distribute baits according to a well-designed plan, with continuous evaluation and fine-tuning

This step, which everyone generally thinks of first, actually comes quite late in the overall campaign, after much detailed planning. The actual distribution requires a surprisingly large amount of careful coordination and follow-up.

A comprehensive ORV control program is complex, but its potential benefits can be correspondingly great. Program success is measured by a decline in reported rabies cases in the target species, serology results, and other parameters. Armed with an effective oral rabies vaccine and guided by experience with other successful programs, Merial stands ready to help you in this endeavor. Working together we can control the raccoon rabies which is threatening your area.

9. ORV Programs Network

Becoming an expert in ORV programs is a matter of time, study, patience, setting achievable and meaningful goals, and most importantly, the adaptability to work as part of a team, not only in your geographical area but in conjunction with other states. Taking advantage of the experience already gained by other states, regions, counties, and agencies using RABORAL V-RG, is a key factor for the success of a new program.

Any adverse reactions observed in the areas where the recombinant rabies vaccine is used should be reported immediately to Merial, who will forward this information to the USDA-APHIS, Center for Veterinary Biologics.

Mail or fax the reports to:

Merial Veterinary Technical Solutions
3239 Satellite Boulevard
Duluth, GA 30096

Telephone: 1-888-637-4231 option 3
Fax: 1-888-424-2079

Related Web Sites

The following links are provided only as a means of learning more about rabies or communicating with State Health Organizations about rabies. Note that these sites are current as of the date of publication, and their content may not be devoted entirely to rabies. Merial does not endorse, nor is it affiliated with, any of the links or their sponsors.

GENERAL RABIES INFORMATION
http://www.rabiesawareness.com
http://www.cdc.gov/rabies/
http://www.rabiescontrol.org
http://www.worldrabiesday.org
http://www.cdc.gov/rabiesandkids/
http://www.who.int/rabiesandkids/en/

U.S. BY STATE
Florida
http://www.doh.state.fl.us/environment/medicine/rabies/rabies-index.html
North Carolina
New York
http://www.health.state.ny.us/diseases/communicable/zoonoses/rabies/
http://www.wadsworth.org/rabies/index.htm
http://www.health.state.ny.us/cd/disease/rabies/orvp/
http://www.dshs.state.tx.us/idcu/disease/rabies/orvp/
Texas
http://www.dshs.state.tx.us/idcu/disease/rabies/orvp/
http://www.wadsworth.org/rabies/index.htm
Tennessee
http://www.health.state.tn.us/FactSheets/raccoon.htm
http://www.rabiescontrol.org/
Virginia
http://www.vdh.virginia.gov/Epidemiology/DEE/Rabies/
1. Based on product label for IMRAB®.