CALIFORNIA COMPENDIUM OF RABIES CONTROL AND PREVENTION, 2004

CALIFORNIA DEPARTMENT OF HEALTH SERVICES
VETERINARY PUBLIC HEALTH SECTION
(916) 552-9740

The purpose of these recommendations is to provide information on rabies to California's public health officials, medical professionals, practicing veterinarians, animal control officers, and other parties concerned with rabies control in the State. The recommendations below are reviewed and updated on a periodic basis to reflect the current status of rabies and rabies prevention activities in California. Updates are based on a review of current rabies research and scientific literature, and rabies prevention guidelines published by the Advisory Committee on Immunization Practices (ACIP)[1] and by the National Association of State Public Health Veterinarians, Inc[2].

Part I.
Rabies Control

A. Principles of Rabies Control:

1. Human Rabies Prevention:

Human rabies can be prevented by: (1) eliminating exposure to rabid animals, (2) providing appropriate rabies preexposure prophylaxis, and (3) prompt local treatment of wounds combined with appropriate rabies postexposure prophylaxis (PEP). Human rabies preexposure and postexposure prophylaxis is addressed in Part II of the compendium.

2. Domestic Animal Rabies Control Program:

The California Rabies Control Program is a multifaceted approach to the control of an age-old disease. The primary components of the California Rabies Control Program include companion animal immunization and licensing; stray animal control; animal bite reporting, investigation, and animal isolation; and public education. The California Health and Safety Code (HSC), Section 121690, mandates that the governing body of each city, city and county, or county shall maintain or provide a rabies control shelter system and a rabies control program. Animal shelters and animal control authorities should establish policies to ensure that adopted animals are vaccinated against rabies.

3. Wildlife Rabies Control:

Rabies is well-established in skunk and bat populations in California. Today, wildlife accounts for >90% of reported animal rabies cases[3]. Every opportunity should be taken to educate the public on the risks of trauma and infectious diseases associated with contact with wild animals. The control of rabies in bats and terrestrial mammals is very difficult. Selective population reduction may be useful in terrestrial rabies outbreaks, but the success of these efforts depend on the circumstances surrounding each rabies outbreak episode. It is generally not feasible or desirable to attempt wild carnivore or bat population reductions as a means of rabies control. Control efforts for bats should concentrate on exclusion from dwellings and other buildings. The Veterinary Public Health Section (VPHS) should be contacted for assistance with wildlife rabies control efforts in outbreak situations. Translocation of infected wildlife has contributed to the spread of rabies; therefore, the translocation or importation of a known rabies reservoir species should be prohibited.

B. Rabies Control Methods in Domestic and Confined Animals:

1. Animal Bite Reporting (Title 17, California Code of Regulations [CCR], Section 2606):

The local health officer or designee shall be immediately notified of any person or animal bitten by or potentially exposed to a rabid or suspected rabid animal. In addition, the local health officer or designee shall be notified when any person is bitten by a mammal. Potential human rabies exposures are then evaluated and rabies PEP recommendations made.

2. Isolation of Biting Animals (17 CCR 2606):

(a) Dogs and Cats:

Domestic dogs or cats that bite or otherwise expose humans must be isolated in strict confinement and in compliance with the local health officer's isolation order. The biting dog or cat must be observed daily for signs of rabies for **ten (10) days** following the exposure date regardless of the animal's vaccination status, or be euthanized immediately and tested for rabies in an approved public health laboratory. If an isolated dog or cat is healthy at the end of the ten-day period, there is no risk of a rabies exposure from the original bite wound.

(b) Ferrets:

While pet ferrets are currently illegal in California, bites from these animals do occur. If a ferret bites a human in California, it must be isolated in strict confinement and in compliance with the local health officer's isolation order. The biting ferret must be observed daily for signs of rabies for **ten (10) days** following the exposure date regardless of the animal's vaccination status, or be euthanized immediately and tested for rabies in an approved public health laboratory. Biting ferrets must be confiscated by the animal control agency and isolations conducted under the direction of the local health officer in an animal control shelter or veterinary hospital. If an isolated ferret is healthy at the end of the ten-day period, there is no risk of a rabies exposure from the original bite wound. Because pet ferrets are illegal, any ferret isolated for a human bite must be reported to the California Department of Fish and Game for disposition following the isolation.

(c) Isolation Considerations:

If the bite is judged by the local health officer to be unusual or to represent an increased risk for rabies (e.g., unprovoked attacks, bites to the face, or attacks on children), the animal should be euthanized and tested immediately. If an animal under isolation develops clinical signs suggestive of rabies, the animal should be humanely euthanized and the head immediately submitted for rabies testing through the local health department. Any unwanted or stray animal that bites a human may be euthanized and the head promptly submitted to the local health department for rabies testing. Protocols for submitting samples for rabies testing are available from the local health department. Rabies or other immunizations should **not** be administered to a dog, cat, or ferret during bite isolations since adverse reactions may be misinterpreted as clinical signs of rabies.

In the case of a dog, cat, or ferret bitten by another dog, cat, or ferret, the biting animal(s) may be placed in isolation for a period of at least 10 days. Should an isolated animal show signs clinically suggestive of rabies, that animal should be euthanized and tested for rabies. If the biting animal tests positive for rabies, the animal that was bitten must be placed in isolation as provided for in section B. 3. (a) below. If an isolated dog, cat, or ferret is healthy at the end of the ten-day period, there is no risk of a rabies exposure from the original bite wound.

(d) Other Domestic and Nondomestic Species:

There is little data on rabies incubation, clinical presentation, and viral shedding in domestic animal species other than dogs, cats, and ferrets. The period of virus shedding in the saliva of infected domestic, wild or nondomestic animals prior to showing clinical signs of rabies is generally not known. Therefore, isolation and observation of animal species other than dogs, cats and ferrets that bite humans is not appropriate. Biting domestic, wild, or nondomestic animals other than dogs, cats, and ferrets should be euthanized and tested for rabies immediately.

While isolation of biting animals other than dogs, cats and ferrets is not recommended for the reasons given above, local health officers have an alternative to euthanizing and testing the animal in special circumstances: In the situation where the biting animal has a comprehensive history that minimizes the potential for rabies infection, and the risk of rabies in the biting animal is judged by the health officer to be acceptably low, the health officer may offer the option of instituting a prolonged (30-day) isolation of the biting animal. Under the care of a physician, the bite victim could be started immediately on rabies postexposure prophylaxis. This special exemption can be considered due to the low risk for exposure, the high efficacy of rabies postexposure treatment, and the low incidence of serious adverse reactions with that treatment.

3. Isolation of Animals Exposed to Rabies (17 CCR 2606):

Any animal bitten by, scratched by, or having direct contact with a wild mammal (especially bats and skunks) that is not available for rabies testing should be regarded as having been exposed to rabies.

(a) Dogs, Cats, and Ferrets:

Unvaccinated dogs, cats, and ferrets exposed to a rabid or suspect rabid animal should be euthanized immediately. An alternative to euthanasia is immediate vaccination of the animal and placement in a strict isolation for **six months (180 days)**. Isolation provisions are at the discretion of the local health officer and must preclude contact between the isolated animal and other animals or the public. Euthanasia is strongly recommended for unvaccinated juvenile animals due to their higher susceptibility to rabies infection. Protocols for the postexpsoure vaccination of previously unvaccinated animals have not been validated, and there is evidence that the use of vaccine alone will not prevent the disease. Dogs, cats, and ferrets that are currently vaccinated should be revaccinated immediately and placed in strict isolation for **30 days**. Ferrets must be confiscated by the animal control agency and isolation conducted under the direction of the health officer in an animal control shelter or veterinary hospital. Since pet ferrets are illegal to possess in California without a permit, any ferret isolated must be reported to the California Department of Fish and Game for disposition following the isolation.

(b) Livestock:

All livestock species are susceptible to rabies infection. Cattle and horses are the most common livestock species diagnosed with rabies. Unvaccinated livestock bitten or exposed to a rabid or suspect rabid animal should be euthanized. If the animal is slaughtered within **seven days** after being exposed, the tissues may be consumed without risk of infection, provided liberal portions of the exposed area are discarded. However, the slaughtered animal cannot be used commercially as a source of food; federal (United States Department of Agriculture [USDA]) meat inspectors are required to reject for slaughter any animal known to have been exposed to rabies within the past **eight months**. Neither tissue nor milk from a rabid animal should be used for human or animal consumption. However, the virus is susceptible to heat inactivation, and drinking pasteurized milk or eating fully cooked meat does not constitute an exposure to rabies.

An alternative to euthanizing exposed livestock is to vaccinate the animal immediately and to place it in a strict isolation for **six months** during which time the animal may not be transported, sold, or slaughtered unless approved by the local health officer and the California Department of Food and Agriculture. Livestock that are currently vaccinated should receive a rabies booster

immediately and be placed in isolation for **30 days** under the same restrictions cited above. In general, an isolation order for the entire herd is not indicated unless the animals have been held in close confinement that would allow for multiple animals exposed to the same rabies source (e.g., a wild animal). It is unusual to have more than one rabid animal in a herd. In such cases, multiple animals were usually exposed by a single rabid wild animal or canine source rather than herbivore to herbivore transmission. Animals in a herd where a rabies death has occurred should be examined for evidence of bite exposures immediately.

(c) Wildlife, Nondomestic and Other Species:
Wild, nondomestic, and other animal species bitten by or exposed to a rabid or suspect rabid animal should be euthanized immediately.

4. Animal Rabies Vaccination:

(a) Rabies Vaccine Administration (HSC 121690, 121700):
All animal rabies vaccines shall be restricted to use by, or under the supervision of a California-licensed veterinarian. The level of supervision shall be consistent with Title 16, CCR, Sections 2034-2036.5 of the California Veterinary Medicine Practice Act (http://www.calregs.com/). The administration of rabies vaccinations is restricted to veterinarians or registered veterinary technicians (RVT) under direct or indirect supervision. Lay personnel are restricted to performing tasks in an "animal hospital setting." Therefore, a lay person may only administer rabies vaccinations when working in an animal hospital setting under the direct or indirect supervision of a California-licensed veterinarian. Any veterinarian signing a rabies certificate should assure that the person administering the vaccine is identified on the certificate and is appropriately trained in vaccine storage, handling, administration, management of adverse events, etc. This practice ensures that a qualified and responsible person can be held accountable to assure that the animal has been properly vaccinated.

In addition, the sale of animal rabies vaccines is restricted to licensed veterinarians or government agencies conducting rabies control programs. Rabies vaccine should be administered in a new, previously unused, sterile needle and syringe. The use of cleaned, sterilized, recycled needles and syringes is strongly discouraged. The theoretical risk of chemical residues in recycled needles and syringes adversely affecting the immunogenicity of rabies vaccine makes it prudent to avoid even the potential for such a problem. Single use of the needle and syringe is consistent with vaccine manufacturers' recommendations. Rabies vaccines must be administered in accordance with the specifications of the vaccine product label or package insert.

(b) Accidental Human Exposure to Rabies Vaccine:
Accidental human inoculation may occur during administration of an animal rabies vaccine. Such exposure to inactivated rabies vaccine does not constitute a risk for rabies infection.

(c) Adverse Events:
Currently, there is no epidemiologic association between a particular licensed vaccine product and adverse events including vaccine failure. Adverse reactions or rabies in a currently vaccinated animal should be reported to the USDA, Center for Veterinary Biologics (at http://www.aphis.usda.gov/vs/cvb/ic/adverseeventreport.htm, by telephone at 800-752-6255, or by e-mail to CVB@usda.gov).

(d) Canine Rabies Vaccination (HSC 121690, 17 CCR 2606.4):
The owner of every dog over the age of four months shall ensure that his or her pet is currently vaccinated for rabies by a licensed veterinarian and secure a license for the pet as provided by local city or county ordinance.

Within 28 days after primary vaccination, a peak rabies antibody level is reached and the animal can be considered immunized. Dogs less than four months of age must be confined at home or kept under close leash supervision by the owner. A current rabies vaccination certificate must accompany dogs over four months of age entering the State.

Regardless of the age of the animal at initial vaccination, a second rabies booster vaccination should be given one year later, and the three-year booster schedule followed thereafter. Because a rapid anamnestic response is expected, an animal is considered currently vaccinated immediately after a booster vaccination. An animal that is overdue for a rabies vaccine should receive a booster as soon as possible and then be placed on a three-year booster schedule.

Only canine rabies vaccines licensed by USDA and approved by the California Department of Health Services (DHS) can be used in the California Rabies Control Program (see Part III of the Compendium). There is no laboratory or epidemiologic data to support the annual or biennial administration of 3-year vaccines following the initial immunization series.

(e) Feline Rabies Vaccination:

Cats are now the most frequently reported domestic rabid animals in the United States (U.S.). Because of the rabies risk to cats and their owners, feline rabies vaccination is strongly recommended for ALL cats. A USDA licensed feline rabies vaccine should be administered according to the vaccine label instructions (see Part III of the Compendium). Feline licensing and identification programs at the local level and the use of triennial vaccines are strongly endorsed by VPHS.

In recent years, epidemiologic studies have suggested that the administration of various vaccines may be a risk factor for the development of cancer (sarcoma) in some cats. However, this risk appears to be extremely low. The public health significance of rabies far outweighs the extremely low risk of a sarcoma developing at a vaccination site. Therefore, feline rabies immunization in California is strongly indicated and may be mandatory according to local ordinances.

(f) Ferret Rabies Vaccination:

Although possession of pet ferrets is currently illegal in California, DHS is aware that owners of illegally kept ferrets may seek veterinary care in some situations. As a public health measure, these animals should be vaccinated against rabies when encountered using a USDA licensed rabies vaccine administered according to vaccine label instructions (see Part III of the Compendium).

(g) Livestock Rabies Vaccination:

There are limited economic or public health justifications to vaccinate all livestock against rabies. However, vaccination of horses and livestock with a USDA licensed vaccine (see Part III of the Compendium) should be considered in areas where wildlife rabies is highly endemic, especially for valuable animals, for horses kept in boarding stables or racetracks, or for other animals having frequent contact with humans. Horses traveling interstate should be currently vaccinated against rabies.

(h) Rabies Serologic Testing:

Rabies serologic testing is **not** a substitute for rabies vaccination. Several laboratories offer rabies virus neutralizing antibody titer testing for animals. Such titers measure the animal's response to vaccine or infection and is not an indicator of protection. Several studies have shown that sometimes animals with high serologic titers will succumb to rabies, and sometimes animals with low or undetectable serologic titers will be protected. An ability to measure and interpret the other immunologic factors that play a role in protecting against rabies is not well developed. Therefore, serologic evidence of rabies neutralizing antibodies in an animal cannot substitute for

current rabies vaccination in managing rabies exposures or determining the need for booster vaccinations.

(i) Wildlife Vaccination and "Hybrids":

Vaccination of nondomestic animals or wildlife is not routinely recommended since there are no rabies vaccines licensed for use in animal species other than dogs, cats, cattle, horses, sheep, and ferrets in the U.S. The effectiveness of rabies vaccination in other species is unknown. Because of their susceptibility to rabies, wild or nondomestic carnivores, and bats should not be kept as pets. Newly imported exhibit animals that are susceptible to rabies should be strictly isolated for at least 180 days since wild animals may be incubating rabies when captured. Due to the special rabies risk, the trapping, transport, sale, or exchange of skunks in California is prohibited. Bats and certain carnivore species representing a high risk for rabies may not enter California without an importation permit from DHS (17 CCR, Sections 30070-86). Carnivores and bats must be housed in a manner that precludes direct contact with the public. Zoos or research institutions may establish vaccination programs, which attempt to protect valuable animals, but these should not replace appropriate public health activities that protect humans.

The effectiveness of rabies vaccination of the offspring of domestic dogs or cats bred to wild animals (e.g., wolf-dog hybrids, civet-cat hybrids) and their subsequent generations is unknown. Vaccination may afford some rabies protection to the animal; however, there are no rabies vaccines currently licensed for use in wild animals or in wild-domestic animal hybrids. Complete rabies vaccine challenge and viral shedding studies have not been conducted with these animals. There is no definitive evidence that the vaccine is protective in these animals. Vaccination of these animals is considered an extra label use of a biologic.

State law does not prohibit the use of rabies vaccines in domestic-wild animal hybrids. However, it is illegal to license domestic dog-wild animal hybrids **as dogs** under the California Rabies Control Program. A rabies vaccine certificate issued for a vaccinated hybrid must identify the animal as a "domestic-wild animal hybrid." Local jurisdictions are free to institute domestic dog-wolf hybrid permitting programs and issue such permits in order to identify these animals in the community. Canine or feline hybrids previously rabies vaccinated cannot be recognized as "rabies immunized" in the event of a human bite or contact with a rabid or suspect rabid animal. The hybrid will be considered a "wild animal" under these circumstances, and managed accordingly.

(j) Canine Licensing and Vaccination Procedure (17 CCR 2606.4):

The vaccination of all dogs four months of age or older is a prerequisite to licensing. Completion of the licensing procedure consists of issuing a license tag or vaccination tag bearing the license data only after presentation of a current valid official rabies vaccination certificate. Official rabies vaccination certificates must show the following:

(a) Name, address and phone number of the dog's owner;
(b) description of the dog, including breed, color, age, and sex;
(c) date of immunization;
(d) type of rabies vaccine administered;
(e) name of the manufacturer, product, and lot number of the rabies vaccine used.

Each certificate must bear the signature of the veterinarian administering the vaccination or a signature authorized by him or her. The certificate must be stamped, printed or typed with the vaccinating veterinarian's name, address and telephone number.

6. Rabies Immunization Exemptions:

A rabies immunization exemption may be issued by the local health officer upon the written recommendation of a California-licensed veterinarian where illness or a veterinary medical condition in a dog warrants. The exempted animal shall be maintained in strict rabies isolation, under conditions that

are at the discretion of the local health officer, until such time as the medical condition has resolved, and the animal can be rabies immunized.

7. "Actual Cost" Rabies Vaccination Clinics (HSC 121690):

Each city, city and county, or county shall provide or arrange for canine rabies vaccination clinics in the community. No charge in excess of the actual cost may be made for vaccination administration. The current DHS approved "Actual Cost" vaccination fee has been increased to $6.00.

Part II.
Human Rabies Prevention

A. Rabies Postexposure Prophylaxis (PEP):

The essential components of rabies PEP are immediate local wound cleaning and treatment, and the appropriate administration of human rabies immune globulin (HRIG) and rabies vaccine. Persons who are bitten by, or have significant exposure to the saliva or nervous system tissue of a confirmed rabid animal should begin rabies PEP immediately. Persons exposed to a *suspected* rabid animal should begin treatment if rabies testing on the animal is not immediately available. To appropriately manage *potential* human exposure to rabies, the risk of infection must be accurately assessed. It is important to remember that administration of rabies PEP is a medical urgency, not a medical emergency. There is time for assessment, but a decision on whether or not to start rabies PEP should not be delayed. Rabies PEP is occasionally complicated by adverse reactions, but these reactions are rarely severe.

Extensive field experience from many parts of the world indicate that prompt wound treatment, passive immunization, and vaccination are uniformly effective when administered appropriately. However, rabies has developed in humans where key elements of the rabies PEP were omitted or incorrectly administered according to the World Health Organization (WHO) recommendations (http://www.who.int/emc-documents/rabies/whoemczoo966c.htm). Rabies PEP should not be denied due to a prolonged time interval between exposure and starting treatment. There have been many instances in which rabies PEP was not initiated until months after exposure due to delays in recognition of the exposure. Incubation periods well in excess of one year have been reported.

1. Rabies Exposure: In addition to the classic bite exposure (teeth penetrating the skin), nonbite exposure (contamination of open wounds, abrasions, mucous membranes, or scratches) to saliva or nervous system tissue of a rabid animal resulting in human rabies has been documented. Therefore, such nonbite exposures constitute sufficient reason to consider rabies PEP. Other contact (e.g., petting a rabid animal with no saliva contact; or contact with blood, urine, feces, or skunk spray) does not constitute an exposure. Rabies virus is inactivated by exposure to ultraviolet radiation and by desiccation, though the exact time required in different environmental conditions is not fully known. Dried saliva or neurologic tissue is generally considered noninfectious.

2. Bats and Human Rabies Exposure: Bats are increasingly implicated as important reservoirs for rabies transmitted to humans. Epidemiologic data suggest that transmission of rabies virus can occur from very minor or even unrecognized bites from bats. The limited injury inflicted by a bat bite (in contrast to lesions caused by carnivores), and limited recall of the exact exposure history can hinder a health-care provider's ability to assess the risk of rabies resulting from an encounter with a bat. Bite marks may not be evident even on close examination. Human and domestic animal contact with bats should be prevented.

On the basis of the available information from the 28 bat rabies variant associated cases of human rabies reported in the U.S. from 1990-2003, only 3 cases had a history of a definite bat bite, 11-13 cases had

apparent bat contact but no bite was detected, and in 10-12 cases, no exposure to bats was reported but an undetected or unreported bat bite remains the most plausible hypothesis[3].

In all instances of potential human exposures involving bats, the bat in question should be safely collected, if possible, and submitted for rabies testing. Rabies PEP is recommended for all persons with bite, scratch, or mucous membrane exposure to a bat, unless the bat is available for testing and is negative for evidence of rabies. Rabies PEP may be appropriate even if a bite, scratch, or mucous membrane exposure is not apparent when there is reasonable probability that such exposure might have occurred.

Rabies PEP should be considered when direct contact between a bat and a human has occurred, unless the exposed person can be certain a bite, scratch, or mucous membrane exposure did not occur. In instances in which a bat is found indoors and there is no history of bat-human contact, the likely effectiveness of rabies PEP must be balanced against the low risk such exposures appear to present. In this setting, rabies PEP can be considered for persons who were in the same room as the bat and who might be unaware that a bite or direct contact had occurred (e.g., a sleeping person awakens to find a bat in the room or an adult witnesses a bat in the room with a previously unattended child, mentally disabled person, or intoxicated person) and rabies cannot be ruled out by testing the bat. Rabies PEP would not be warranted for other household members.

3. **Local Treatment of Wounds:** Immediate and thorough washing of any bite or scratch wound with soap and water may be one of the most important measures in preventing rabies. Simple local wound cleaning has been shown to markedly reduce the likelihood of rabies in animal experiments. Tetanus and antibiotic prophylaxis should be given as indicated.

4. **Active Immunization - Vaccine:** Human Diploid Cell Vaccine (HDCV), Purified Chick Embryo Cell Vaccine (PCEC), or Rabies Vaccine Adsorbed (RVA) is administered in conjunction with HRIG at the beginning of postexposure treatment. A regimen of five 1-ml doses of HDCV, PCEC, or RVA is given intramuscularly. The first dose should be given as soon as possible following an exposure (day 0). The other doses are given on days 3, 7, 14 and 28 after the first dose. Vaccine should always be administered by the IM route in the deltoid area (lateral aspect of the upper arm). For pediatric patients, intramuscular administration in the anterolateral aspect of the thigh is recommended. It is important that the needle length be adequate to ensure intramuscular delivery of vaccine[4]. **Rabies vaccine should never be administered in the gluteal region.** Administration in the gluteal area may result in lower or inadequate neutralizing antibody titers.

   Rabies PEP should always include both vaccine and HRIG except in persons who have previously received complete prophylaxis regimens (pre- or postexposure prophylaxis) with a cell culture vaccine, or persons previously vaccinated with other types of vaccine that have documented and adequate rabies virus neutralization antibody titers. These persons should immediately receive a 1-ml booster vaccination of HDCV, PCEC, or RVA administered intramuscularly, and a second booster three days later.

   Because antibody response in persons receiving the currently recommended rabies PEP schedule has been universally satisfactory, post-treatment serologic testing is not routinely recommended. Serology testing may be indicated in unusual circumstances, such as when the patient is known to be immunosuppressed. Immunosuppressive agents should not be administered during rabies PEP unless essential for the treatment of other conditions. The DHS Division of Communicable Disease Control [(916) 552-9740, (510) 540-2566, or (510) 540-2308 after hours] may be contacted for recommendations in these cases.

5. **Passive Immunization - HRIG:** HRIG is administered only once (i.e., at the beginning of rabies PEP) to previously unvaccinated persons to provide immediate antibodies until the patient responds to rabies vaccination by actively producing antibodies. If HRIG is not given with the first dose of vaccine, it can be given through the **seventh day** following administration of the first vaccine dose. Beyond the seventh

day, HRIG is not indicated since an antibody response to cell culture vaccine is presumed to have occurred. HRIG should be administered at a dose of 20 IU/kg body weight for all age groups. No more than the recommended dose should be used due to a potential partial suppression of active immunization by HRIG. If anatomically feasible, the full dose of HRIG should be infiltrated into the subcutaneous tissue and/or muscle around the wound site(s), and any remaining volume administered intramuscularly at an anatomical site distant from vaccine administration. HRIG should never be administered in the same syringe or at the same anatomical site as vaccine and should never be administered in the gluteal area unless that is the site of exposure.

The combination of HRIG and vaccine is recommended for both bite and nonbite exposures in persons not previously rabies immunized regardless of the interval between exposure and initiation of PEP.

B. Preexposure Prophylaxis:

In California, preexposure vaccination should be offered to persons at increased risk of rabies exposure. This "frequent risk" category includes veterinarians, animal handlers, animal control officers, laboratory workers potentially exposed to rabies virus, and persons traveling to and spending time (e.g., >1 month) in foreign countries where canine rabies is endemic. Preexposure vaccination should be considered for other persons, such as wild mammal rehabilitators, whose vocations or avocations bring them into frequent contact with potentially rabid dogs, cats, skunks, bats or other species at risk of having rabies.

Preexposure vaccination for persons at risk has several potential advantages. Most importantly, it may protect persons with unrecognized exposures to rabies. Second, it simplifies and saves money on required treatment following a rabies exposure by eliminating the need for HRIG and decreasing the number of vaccine doses to be given. Finally, preexposure vaccination may protect persons exposed in areas where immunizing products are not available, carry a high risk of adverse reactions, or where treatment may be delayed (e.g., travelers).

1. Primary Preexposure Vaccination:

Intramuscular Primary Immunization: Three 1.0 ml injections of HDCV, PCEC, or RVA should be given intramuscularly in the deltoid area (lateral aspect of the upper arm) on days 0, 7, and 21 *or* 28. Development of antibodies in patients vaccinated using this regimen has been 100% successful in several studies conducted. Based on results of these studies, routine post-primary immunization serologic testing is not necessary except for persons suspected of being immunosuppressed. Persons who are immunosuppressed due to medication or illness should postpone preexposure vaccination if possible. Immunosuppressed persons who are at risk of rabies exposure can be vaccinated and should have their antibody titers measured following completion of the regimen.

Intradermal Primary Immunization: Three 0.1 ml intradermal (ID) injections of HDCV have also been recommended as an alternative to the intramuscular primary immunization regimen. Injections of Imovax® Rabies I.D. are accurately administered intradermally (i.e., raising a visible bleb within the epidermis) in the area over the deltoid (lateral aspect of the upper arm) on days 0, 7 and 21 *or* 28. The 1.0 ml HDCV vial is not approved for multi-dose ID use and **should not be administered in this way**. RVA and PCEC are **not** to be given by the ID route.

Chloroquine phosphate used for malaria chemoprophylaxis (and possibly related antimalarial drugs - e.g., mefloquine) can interfere with the antibody response to Imovax® Rabies I.D. HDCV should not be administered by the intradermal route to persons receiving such drugs for malaria chemoprophylaxis. For further information, please refer to the Recommendations on Human Rabies Prevention published by the Advisory Committee on Immunizations Practices [*MMWR* January 8, 1999;48(RR-1):1-21].

2. Booster Vaccination:

Persons classified as having "frequent risk" for rabies exposure include rabies diagnostic laboratory workers, spelunkers, veterinarians and their staff, animal control officers, wildlife officers and international travelers visiting areas where canine rabies is endemic. Such persons should receive preexposure immunization and have a serum sample tested for rabies antibody every two years (every six months for laboratory workers). If the titer is less than complete neutralization at 1:5 or 1:8 (depending on dilution method used by the testing laboratory) by the Rapid Fluorescent Focus Inhibition Test (RFFIT), the person should receive a booster dose of rabies vaccine.

Several commercial sources for RFFIT testing are currently (Jan. 2004) available at a cost of approximately $25-$35 per sample (RFFIT testing through other laboratories may be available). Instructions for submission of samples and pricing are available by calling the numbers below.

Department of Veterinary Diagnostics
Veterinary Clinical Science Building
Kansas State University
Manhattan, KS 66506-5600
(785) 532-4483 Phone, (785) 532-4474 Fax
http://www.vet.ksu.edu/depts/rabies/

Atlanta Health Associates, Inc.
309 Pirkle Ferry Road, Suite D300
Cumming, GA 30040
(770) 205-9091, (800) 717-5612
(770) 205-9021 Fax
http://www.atlantahealth.net/

Maryland State Rabies Laboratory
Maryland Department of Health
201 W. Preston Street
Baltimore, MD 21201
(410) 767-6177

C. Rabies Immunizing Products Available in the United States:

1. Human Rabies Vaccine: Produces an active immune response including production of neutralizing antibodies. This antibody develops in approximately 7-10 days and usually persists for at least 2 years.

(a) Human Diploid Cell Vaccine (HDCV) - Intramuscular (Imovax® Rabies) and Intradermal (Imovax® Rabies I.D.)

HDCV is prepared from the Pitman-Moore rabies virus strain grown in MRC-5 human diploid cell culture. The vaccine is concentrated by ultrafiltration and inactivated with beta-propiolactone. Imovax® Rabies and Imovax® Rabies I.D. are manufactured and distributed by Aventis Pasteur, Inc., phone [(800) VAC-CINE {822-2463}].

Intramuscular (IM) Administration:

A single dose vial containing lyophilized vaccine (Imovax® Rabies) that is reconstituted with diluent to a volume of 1.0 ml just before administration.
http://www.vaccineshoppe.com/US_PDF/LE4733_Imovax_IM_VS.pdf

Intradermal (ID) Administration:

A single dose syringe containing lyophilized vaccine (Imovax® Rabies I.D.) that is reconstituted to a volume of 0.1 ml just before administration. The manufacturer discontinued sales of this product in 2001.

(b) Purified Chick Embryo Cell Culture (PCEC)

PCEC is prepared by growing the Flury LEP fixed-virus strain in primary culture of chicken embryonic fibroblasts. The virus is inactivated with beta-propiolactone, and further processed

with zonal centrifugation in a sucrose density-gradient to separate the final product from media and cell culture antigens. The vaccine is then lyophilized after addition of a stabilizer solution. RabAvert® is manufactured and distributed by Chiron Vaccines, phone [(800) CHI-RON8 {244-7668}]. http://www.rabavert.com/

(c) Rabies Vaccine Adsorbed (RVA)

RVA is prepared from the Kissling strain of Challenge Virus Standard rabies virus adapted to fetal rhesus lung diploid cell culture. The vaccine is inactivated with beta-propiolactone and concentrated by adsorption to aluminum phosphate to form a final 1.0 ml liquid dose. RVA is manufactured and distributed by BioPort Corporation, phone (877) BIO-THRAX {246-8472}. http://www.bioportcorp.com/default.asp

All three types of vaccine are considered equally efficacious and safe when used as indicated. The 1.0 ml dose of either HDCV, PCEC, or RVA can be used for both preexposure and postexposure prophylaxis. Imovax® Rabies I.D. has been approved for intradermal administration for **preexposure vaccination only**, and is not to be used in postexposure rabies prophylaxis. The intramuscular dose (Imovax® Rabies) should **NOT** be split into multiple doses for intradermal administration.

The safety and efficacy of RVA and PCEC administered by the intradermal route have not been studied; therefore, RVA and PCEC are not to be used intradermally.

2. Rabies Immune Globulin - Human: Provides immediate passive immunity that persists for only a limited time (half-life of approximately 21 days).

BayRab™, Imogam® Rabies-HT

Human rabies immune globulin (HRIG) is available from Aventis Pasteur, Inc., (Imogam® Rabies-HT), phone (800) VAC-CINE {822-2463}, http://www.vaccineshoppe.com/US_PDF/190-10_4125.pdf, and Bayer Corporation, Pharmaceutical Division, Biological Products (BayRab™), phone (800) 288-8370, http://www.bayerbiologicalsusa.bayerhealthcare.com/prod_hype_brab.asp. HRIG is an antirabies gamma globulin concentrated by cold ethanol fractionation from plasma of hyperimmunized human donors. Rabies neutralizing antibody content is standardized to 150 international units (IU) per ml. HRIG is supplied in 2 ml and 10 ml vials for pediatric and adult use, respectively. Imogam® Rabies-HT is heat treated but has no preservatives. It must be administered within an hour once the seal is broken. Both HRIG preparations are considered equally efficacious and safe when used as indicated.

D. Adverse Reactions to Rabies Immunizing Products:

1. Vaccine:

Reactions after vaccination with HDCV, PCEC, and RVA are less serious and common than with previously available vaccines. Local reactions such as pain, erythema, and swelling or itching at the injection site were reported in approximately 30-75% of patients receiving HDCV or PCEC. Mild systemic reactions such as headache, malaise, dizziness, muscle aches, nausea, and abdominal pain have been reported in 5-50% of recipients. Anaphylactic, encephalitic or neuroparalytic events are extremely rare, but have been reported.

An "immune complex-like" reaction has been reported to occur in approximately 6% of persons receiving booster doses of HDCV. The illness, characterized by onset 2-21 days postbooster, presents with a generalized urticaria and may also include arthralgia, arthritis, angioedema, nausea, vomiting, fever, and malaise. In no cases were the illnesses life-threatening. This reaction occurs much less frequently in persons receiving primary immunization. The reaction appears to be associated with the presence of betapropiolactone-altered human serum albumin in HDCV and the development of IgE to this allergen. This reaction appears to be less common in persons immunized with RVA, and has not been reported in

persons immunized with PCEC. An alternative vaccine product should be considered for patients with a history of adverse reactions following administration of one of the licensed vaccines. Please refer to the package insert or the manufacturers for more information on vaccine safety and adverse reactions.

2. Rabies Immune Globulin, Human:

Local pain and low-grade fever may follow receipt of HRIG. Although not reported specifically for HRIG, angioneurotic edema, nephrotic syndrome, and anaphylaxis have been reported after injections of immune globulin (IG). These reactions have occurred predominantly in persons receiving large and frequent doses of IG for various dysgammaglobulinemias. These reactions occur so rarely that the causal relationship between IG and these reactions is not clear.

BayRab™ and Imogam® Rabies-HT undergo multiple viral clearance procedures during preparation. There is no evidence that hepatitis B virus, human immunodeficiency virus or other viruses have ever been transmitted by commercially available HRIG in the U.S.

3. Management of Adverse Reactions:

Once initiated, rabies PEP should not be interrupted or discontinued because of local or mild systemic adverse reactions to rabies vaccine. Usually such reactions can be successfully managed with non-steroidal anti-inflammatory and antipyretic agents (ibuprofen or acetaminophen, for example). For more severe reactions, consideration should be given to switching from one product to another. When a person with a history of hypersensitivity must be given rabies vaccines, antihistamines may be given; epinephrine should be readily available to counteract anaphylactic reactions, and the person should be carefully observed immediately after immunization.

Systemic anaphylactic or neuroparalytic reactions occurring during the administration of rabies vaccines, though rare, pose a serious dilemma for the attending physician. A patient's risk of developing rabies must be carefully considered before deciding to discontinue vaccination. The use of corticosteroids in the treatment of life-threatening neuroparalytic reactions carries the risk of inhibiting the development of active immunity to rabies. It is especially important in these cases that the serum of the patients be tested for rabies antibodies following vaccination.

All serious systemic, neuroparalytic, or anaphylactic reactions to a rabies vaccine should be immediately reported to the DHS Division of Communicable Disease Control ([510] 540-2566 during working hours or [510] 540-2308 at other times), the Vaccine Adverse Event Reporting System (VAERS) via a 24-hour toll-free telephone number ([800] 822-7967), or the Division of Viral and Rickettsial Diseases, Center for Infectious Diseases, CDC ([404] 639-1050 during working hours, or [404] 639-2888 at other times).

4. Precautions and Contraindications:

Immunosuppression

Corticosteroids, other immunosuppressive agents, antimalarials, and immunosuppressive illnesses can interfere with the development of active immunity after vaccination. For persons with immunosuppression, preexposure prophylaxis should be administered with the awareness that the immune response might be inadequate (see Primary or Preexposure Vaccination). Patients who are immunosuppressed by disease or medications should postpone preexposure vaccinations and consider avoiding activities for which rabies preexposure prophylaxis is indicated. When this course is not possible, immunosuppressed persons who are at risk for rabies should be vaccinated by the IM route and their antibody titers checked. Failure to seroconvert after the third dose should be managed in consultation with appropriate public health officials (see Preexposure Vaccination and Serologic Testing). Immunosuppressive agents should not be administered during rabies PEP unless essential for the treatment of other conditions. When rabies PEP is administered to an immunosuppressed person, it is

especially important that a serum sample be tested for rabies antibody (by the RFFIT method) to ensure that an acceptable antibody response has developed.

Pregnancy

Because of the potential consequences of inadequately treated rabies exposure, and because there is no indication that fetal abnormalities have been associated with rabies vaccination, pregnancy is not considered a contraindication to rabies PEP. If the risk of exposure to rabies is substantial, preexposure prophylaxis might also be indicated during pregnancy.

Allergies

Persons who have a history of serious hypersensitivity to rabies vaccine should be revaccinated with caution (see Management of Adverse Reactions).

References:

[1] Human Rabies Prevention - United States, 1999, Recommendations of the Advisory Committee on Immunization Practices (ACIP), *MMWR*, January 8, 1999; 48(RR-1):1-23. http://www.cdc.gov/epo/mmwr/preview/mmwrhtml/00056176.htm or ftp://ftp.cdc.gov/pub/Publications/mmwr/RR/RR4801.pdf

[2] Jenkins SR et al, Compendium of Animal Rabies Prevention and Control, 2004., *JAVMA* 2004; 224(2):216-222. http://www.avma.org/pubhlth/default.asp

[3] Krebs JW, Wheeling JT, Childs JE, Rabies surveillance in the United States during 2002., *JAVMA* 2003; 223(12):1736-1748. http://www.electronicipc.com/JournalEZ/detail.cfm?code=04290022231204&CFID=385656&CFTOKEN=582651D3-397B-4F79-AA6B378E5E6975D0

[4] Poland GA et al, Determination of deltoid fat pad thickness. Implications for needle length in adult immunization., *JAMA* 1997 Jun 4; 277(21):1709-11.

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Division of Communicable Disease Control
Veterinary Public Health Section
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P.O. Box 997413
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Phone (916) 552-9740, Fax (916) 552-9725
http://www.dhs.ca.gov/ps/dcdc/disb/disbindex.htm

Part III.
California Department of Health Services
Compendium of U. S. Licensed Animal Rabies Vaccines - 2004, and Their Application in Animals Under the California Rabies Control Program

A) MONOVALENT – INACTIVATED

Product Name	Produced By	Marketed By	For Use In	Dosage/Route*	Age at Primary Vaccination*	Booster Recommendation
DEFENSOR 1	Pfizer, Incorporated License No. 189	Pfizer, Incorporated	**Dogs** Cats	**NOT APPROVED FOR USE IN CALIFORNIA** 1 ml SC	3 months	Annually
DEFENSOR 3	Pfizer, Incorporated License No. 189	Pfizer, Incorporated	**Dogs** Cats Sheep Cattle	1 ml IM or SC 1 ml SC 2 ml IM 2 ml IM	4 months 3 months 3 months 3 months	1 year later & triennially 1 year later & triennially Annually Annually
RABDOMUN 1	Pfizer, Incorporated License No. 189	Schering-Plough	**Dogs** Cats	**NOT APPROVED FOR USE IN CALIFORNIA** 1 ml SC	3 months	Annually
RABDOMUN	Pfizer, Incorporated License No. 189	Schering-Plough	**Dogs** Cats Sheep Cattle	1 ml IM or SC 1 ml SC 2 ml IM 2 ml IM	4 months 3 months 3 months 3 months	1 year later & triennially 1 year later & triennially Annually Annually
RABVAC 1	Fort Dodge Animal Health License No. 112	Fort Dodge Animal Health	**Dogs** Cats	**NOT APPROVED FOR USE IN CALIFORNIA** 1 ml IM or SC	3 months	Annually
RABVAC 3	Fort Dodge Animal Health License No. 112	Fort Dodge Animal Health	**Dogs** Cats Horses	1 ml IM or SC 1 ml IM or SC 2 ml IM	4 months 3 months 3 months	1 year later & triennially 1 year later & triennially Annually
RABVAC 3 TF	Fort Dodge Animal Health License No. 112	Fort Dodge Animal Health	**Dogs** Cats Horses	1 ml IM or SC 1 ml IM or SC 2 ml IM	4 months 3 months 3 months	1 year later & triennially 1 year later & triennially Annually
PRORAB-1	Intervet, Incorporated License No. 286	Intervet, Incorporated	**Dogs** Cats Ferrets Sheep	**NOT APPROVED FOR USE IN CALIFORNIA** 1 ml IM or SC 1 ml IM or SC 2 ml IM	3 months 3 months 3 months	Annually Annually Annually
PRORAB-3F	Intervet, Incorporated License No. 286	Intervet, Incorporated	Cats	1 ml IM or SC	3 months	1 year later & triennially
IMRAB 3	Merial, Incorporated License No. 298	Merial, Incorporated	**Dogs** Cats Sheep Cattle Horses Ferrets	1 ml IM or SC 1 ml IM or SC 2 ml IM or SC 2 ml IM or SC 2 ml IM or SC 1 ml SC	4 months 3 months 3 months 3 months 3 months 3 months	1 year later & triennially 1 year later & triennially 1 year later & triennially Annually Annually Annually
IMRAB 3 TF	Merial, Incorporated License No. 298	Merial, Incorporated	**Dogs** Cats Ferrets	1 ml IM or SC 1 ml IM or SC 1 ml SC	4 months 3 months 3 months	1 year later & triennially 1 year later & triennially Annually
IMRAB Large Animal	Merial, Incorporated License No. 298	Merial, Incorporated	Cattle Horses Sheep	2 ml IM or SC 2 ml IM or SC 2 ml IM or SC	3 months 3 months 3 months	Annually Annually 1 year later & triennially
IMRAB 1	Merial, Incorporated License No. 298	Merial, Incorporated	**Dogs** Cats	**NOT APPROVED FOR USE IN CALIFORNIA** 1 ml SC	3 months	Annually
B) MONOVALENT - RABIES GLYCOPROTEIN, LIVE CANARY POX VECTOR						
PUREVAX Feline Rabies	Merial, Incorporated License No. 298	Merial, Incorporated	Cats	1 ml SC	2 months	Annually

ROUTES AND SITES OF INOCULATION IN DOGS: California specifies sites and routes indicated to be effective in efficacy trials. Administration via other sites or routes may reduce effectiveness or be unsafe. Approved canine vaccines must be administered to dogs according to the manufacturer's recommendations either intramuscularly (IM) at one site in the thigh, or subcutaneously (SC) just behind the upper shoulder. For species other than dogs, refer to the product label.

Adapted from the Compendium of Animal Rabies Prevention and Control, 2004, National Association of State Public Health Veterinarians, Incorporated

- Continued -

Part III.
California Department of Health Services
Compendium of U. S. Licensed Animal Rabies Vaccines - 2004, and Their Application in Animals Under the California Rabies Control Program

C) COMBINATION - INACTIVATED RABIES

Product Name	Produced By	Marketed By	For Use In	Dosage/Route*	Age at Primary Vaccination*	Booster Recommendation
ECLIPSE 3 + FeLV/R	Fort Dodge Animal Health License No. 112	Schering-Plough	Cats	1 ml IM or SC	3 months	Annually
ECLIPSE 4 + FeLV/R	Fort Dodge Animal Health License No. 112	Schering-Plough	Cats	1 ml IM or SC	3 months	Annually
FEL-O-GUARD 3 + FeLV/R	Fort Dodge Animal Health License No. 112	Fort Dodge Animal Health	Cats	1 ml IM or SC	3 months	Annually
FEL-O-GUARD 4 + FeLV/R	Fort Dodge Animal Health License No. 112	Fort Dodge Animal Health	Cats	1 ml IM or SC	3 months	Annually
IMRAB 3 + FELINE 3	Merial, Incorporated License No. 298	Merial, Incorporated	Cats	1 ml SC	3 months	1 year later & triennially
IMRAB 3 + FELINE 4	Merial, Incorporated License No. 298	Merial, Incorporated	Cats	1 ml SC	3 months	1 year later & triennially
MYSTIQUE II POTOMAVAC +	Intervet, Incorporated License No. 286	Intervet, Incorporated	Horses	1 ml IM	3 months	Annually
EQUINE POTOMAVAC + IMRAB	Merial, Incorporated License No. 298	Merial, Incorporated	Horses	1 ml IM	3 months	Annually
D) COMBINATION - RABIES GLYCOPROTEIN, LIVE CANARY POX VECTOR						
PUREVAX FELINE 3/ RABIES	Merial, Incorporated License No. 298	Merial, Incorporated	Cats	1 ml SC	8 weeks	Annually
PUREVAX FELINE 4/ RABIES	Merial, Incorporated License No. 298	Merial, Incorporated	Cats	1 ml SC	8 weeks	Annually
PUREVAX FELINE 3/ RABIES+ LEUCAT	Merial, Incorporated License No. 298	Merial, Incorporated	Cats	1 ml SC	8 weeks	Annually
PUREVAX FELINE 4/ RABIES + LEUCAT	Merial, Incorporated License No. 298	Merial, Incorporated	Cats	1 ml SC	8 weeks	Annually

* Intramuscularly (IM) at one site in the thigh.
Subcutaneously (SC) just behind the upper shoulder.

* Minimum age (or older) and revaccinated one year later. A month = 28 days.