

# Vermont Rabies Control Resource Manual 2018



**Health Surveillance** 

HealthVermont.gov

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# Introduction

Vermont Rabies Control Resource Manual 2018 is a resource guide for veterinarians, wildlife officials, health care and public health professionals, and others to help prevent and control rabies in Vermont. It contains essential information such as: Vermont-specific rules and regulations on animal bite and treatment reporting and rabies vaccination; national guidelines for postexposure treatment, vaccination and animal quarantine; recommendations for schools on developing an animal policy; and forms and instructions for reporting and animal testing.

The table below outlines the contents of each of the five sections.

#### **Section 1. Rabies in Vermont**

Vermont Rabies Control Overview	An overview of rabies, procedures for when a human or pet is bitten by a potentially rabid animal, instructions for submitting specimens for rabies testing.
Vermont Rabies Epidemiology	Tables, charts, and a map showing the detection of rabies in Vermont by animal type, town, and year from 2005 to 2017.

#### **Section 2. Vermont-Specific Rules and Statutes**

Reportable and Communicable Diseases Rule	Rules to protect the public though early and prompt reporting of infectious diseases to the Health Department. From the Code of Vermont Rules [CVR 13-140-007].
20 VSA Chapter 193: Domestic Pet or Wolf- Hybrid Control	Vermont statute on licensing and rabies control in domestic pets and wolf-hybrids. From Vermont Statutes, Title 20: Internal Security and Public Safety, Chapter 193.
Animal Rabies Vaccination Rules	Rules on administration of rabies vaccination to domestic pets, wolf-hybrids and livestock.

#### **Section 3. National Guidelines**

Compendium of Animal Rabies Prevention and Control, 2016	Published by the National Association of State Public Health Veterinarians, the 2016 report recommends approaches to rabies prevention and control in animals.
Human Rabies	Published in the CDC's Morbidity and Mortality Weekly Report (2008), the report
Prevention – United	presents guidelines for rabies postexposure and pre-exposure prophylaxis in
States, 2008	humans.
Use of a Reduced (4-	
Dose) Vaccine Schedule	Published in the CDC's Morbidity and Mortality Weekly Report (2010), the report
for Postexposure	summarizes updates to the 2008 guidelines, including a reduced 4-dose rabies
Prophylaxis to Prevent	vaccine schedule.
Human Rabies, 2010	

#### **Section 4. Vermont Recommendations**

School Animal Policy	Provides guidance to schools on developing an animal policy to reduce the risk of
Guide	human exposure to rabies and other diseases from animals.

### **Section 5. Rabies Exposure Protocols**

Human Rabies Exposure Management by Animal Type	Recommendations for rabies postexposure management in humans by animal type (domestic pets, livestock, wild carnivores, rodents, etc.)
Management of Potential Human Exposures to Rabies	A flowchart used to determine course of action when a person is exposed to a potentially rabid animal.
Rabies Exposure Management for Bat- related Incidents	A flowchart used to determine human postexposure management for bat-related incidents.
Management of Potential Pet Exposures to Rabies	A flowchart used to determine course of action when a pet is exposed to a potentially rabid animal.

# **Section 6. Rabies Testing and Reporting Forms**

Rabies Specimen Lab Testing and Shipping Instructions	Instructions for preparing, packaging and shipping rabies specimens to the Vermont Department of Health Laboratory.
Request for Rabies Examination	After approval from Infectious Disease Epidemiology, submit this form with specimens to the Health Department Laboratory to request rabies testing.
Rabies Postexposure Prophylaxis Report Form	For health care professionals, after administering rabies postexposure prophylaxis, submit this form to the Health Department.
Town Health Officer Animal Bite Report Form	For health care professionals, veterinarians, and other adults, use this form to report an animal bite to the Town Health Officer.

For questions about this book, please call 802-863-7240 or e-mail <u>AHS.VDHPublicCommunication@vermont.gov</u>.

# **Section 1. Rabies in Vermont**

- A. Vermont Rabies Control Overview
- B. Vermont Rabies Epidemiology



### What's in this overview?

- Rabies disease and vaccination overview.
- Procedure when a human or pet is bitten by a potentially infected wild or domestic animal.
- Recommendations for capturing a bat if there has been a possibility of exposure.
- Instructions for **getting pre-approved specimens tested** for rabies at the Vermont Department of Health Laboratory.
- **Contact information** for the USDA Vermont Rabies Hotline, Vermont Department of Health Epidemiology Program, Vermont Department of Health Laboratory, and Vermont Fish and Wildlife Game Wardens.

## Rabies is a fatal viral disease most commonly found in wildlife.

In Vermont, rabies is most commonly found in racoons, foxes, bats, skunks and woodchucks, but domestic animal and human infection is possible. All species of mammals are susceptible to rabies infection. Though there has never been a documented human case of rabies in Vermont, between 1992 and 2017, 73 domestic animals tested positive for rabies – 29 cows, 25 cats, 9 horses, 5 dogs, 4 sheep and 1 pig – and hundreds of cases have been identified among wildlife.

The Vermont Department of Health is responsible for leading efforts to prevent rabies infections in humans and for the management of animals that may have exposed humans. Included in this role are:

- 1. Assessing human and domestic animal rabies exposures
- 2. Coordinating the management of wildlife that may have exposed humans or domestic animals
- 3. Coordinating the collection and submission of specimens for testing
- 4. Providing recommendations for pre- and post-exposure prophylaxis.
- 5. Performing rabies testing on animal specimens.

The USDA Vermont Rabies Hotline **(1-800-4-RABIES/802-223-8690)** offers general rabies and wildlife information to the public.

### Rabies is primarily transmitted through bites.

Rabies is a disease of the central nervous system. Rabid animals may show unusual aggression, extreme depression, or bizarre behavior, but you cannot tell whether an animal has rabies simply by looking at it. Animals are not infectious until the virus is present in their saliva, around the time of illness onset.

Rabies is mainly transmitted through bites when teeth penetrate the skin. Rare non-bite exposures can occur if wet infectious saliva or nervous tissue contacts a fresh open wound or mucous membranes of the eyes, nose or mouth. All salivary exposures by raccoons, skunks, foxes, coyotes, and other wild mammalian carnivores must be considered possible exposures to the rabies virus. Any animal not available for testing must be considered as potentially rabid. Indirect contact (petting or handling an animal, contact with blood, urine, feces or skunk spray) is not an exposure.

Promptly following the bite of a potentially rabid animal, the wound should be cleansed with soap and running water and irrigated with a virucidal agent such as a povidone-iodine. Tetanus prophylaxis and measures to control bacterial infection may be administered as indicated. The need for rabies postexposure prophylaxis (rPEP) should be assessed with a medical provider and initiated as soon as possible after exposure to wildlife unless the animal has been tested and shown not to be rabid. Initiation of rPEP is reportable to Vermont Department of Health by health care professionals (section 5.5.2 of the "Reportable and Communicable Diseases Rule" [CVR 13-140-007]). It is the responsibility of the medical provider and the patient to make decisions regarding the necessity of prophylaxis, but the Health Department can assist in rabies exposure risk assessments. If rPEP has been initiated and the animal tests negative for rabies, it may be discontinued.

# Contact a Town Health Officer when a human is bitten by a rabies vector animal.

Physicians, veterinarians, and adults shall report to the Town Health Officer the full name, age, and address of any person known to have been bitten by an animal of a species subject to rabies within 24 hours of actual or constructive notice (section 7.1.2 of the "Reportable and Communicable Diseases Rule" [CVR 13-140-007]). If a physician cannot reach a town official, they may call the Health Department and leave pertinent information (Name and phone number of victim, and the name, phone number, and address of animal owner).

The Town Health Officer shall cause an apparently healthy dog, cat, or ferret that bites a person to be confined and observed for 10 days, regardless of rabies vaccination status (section 7.2.2 of the "Reportable and Communicable Diseases Rule" [CVR 13-140-007]). It is at the discretion of the Town Health Officer as to where the confinement and observation will occur. The animal should not be vaccinated for rabies during confinement. During observation, any illness must be reported to the Town Health Officer and if the animal shows signs of rabies, the animal must be euthanized and sent to the Vermont Department of Health Laboratory for rabies testing. It is the responsibility of the Town Health Officer to check on the health of the animal at the end of 10 days and report to the bite victim. The town is responsible for any costs associated with the observation, euthanasia, or specimen transportation of any stray or feral animal that has bitten a person (section 3808 of Vermont Statutes Title 20, Chapter 193: Domestic Pet or Wolf-hybrid Control).

Whenever an animal, subject to rabies, is brought to a veterinarian to be destroyed, an attempt shall be made by the veterinarian to ascertain that the animal has not bitten any person within the previous 10 day period; before destroying the animal, he or she shall require the owner to sign a statement to this effect, and he or she shall not destroy any animal which has bitten a person within ten days. The

health officer must be notified by the veterinarian of any such biting incident (section 7.5 of the "Reportable and Communicable Diseases Rule" [CVR 13-140-007]).

If the animal is not immediately available for observation, then efforts should be made to find the animal. The Town Health Officer or Animal Control Officer can assist in this effort along with the individual who was bitten. Use of social media or community listservs can be helpful in trying to locate the animal. If the animal is not found, then the decision to start rPEP may be considered with a health care provider. The Health Department can assist in rabies exposure risk assessments for these situations. If the animal is found before treatment ends, and is healthy 10 days after the biting incident, then rPEP can be discontinued.

# Game Wardens can help capture a wild animal that may have exposed a human or domestic animal to rabies.

To prevent exposure to rabies, avoid wildlife and familiarize yourself with community members trained in animal control. If you find orphaned or sick wildlife, do not touch them.

Questions regarding potential human rabies exposures involving wild animals may be directed to the USDA Vermont Rabies Hotline or Vermont Department of Health Infectious Disease Epidemiology.

State Game Wardens may be called for assistance in situations in which a wild animal might have exposed a human or domestic animal to rabies. A Game Warden can assist in euthanizing, packaging, and transporting rabies-suspect animals for testing at the Vermont Department of Health Laboratory. Game Wardens may be contacted by calling the USDA Vermont Rabies Hotline or the nearest State Police dispatcher. In situations that require immediate intervention and a Game Warden is not available, complainants may seek assistance dispatching an animal from a Town Health Officer, Animal Control Officer or local police officer.

# Capture a bat if there has been a possible exposure.

Testing is recommended for any bat that has been in a room with an unattended child, a sleeping, intoxicated, or mentally impaired individual, unvaccinated pet, or that has had physical contact with a person. Game Wardens will assist in these situations by euthanizing the animal, packaging it, and sending or transporting it to the Vermont Department of Health Laboratory for testing, but will not be able to assist in the capture of a live bat. The Laboratory will not accept any live bats for testing.

How to capture a bat if there has been a possibility of exposure:

- Wear leather or thick gloves and avoid direct skin contact with the bat.
- Avoid damage to the bat's head.
- Confine the bat to one room. Turn on the lights if the room is dark.
- When the bat lands, approach it slowly, while wearing gloves, and place a small box or coffee can over the bat.
- Slide a piece of cardboard under the box or can, trapping the bat inside.
- Tape the cardboard to the container.

If there is no possibility that human or pet exposure has occurred, confine the bat to a room by closing all doors and windows leading out of the room except those to the outside. The bat will probably leave soon.

If a bat is unavailable for testing, then the need for rPEP must be assessed with a medical provider. rPEP should be considered when direct contact between a human and a bat has occurred, and rabies cannot be ruled out by testing the bat, unless the exposed person can be certain a bite, scratch, or mucous membrane exposure did not occur.

# Testing of small rodents and lagomorphs will be considered on a case-bycase basis.

Small rodents (squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, and mice) and lagomorphs (rabbits and hares) are almost never found to be infected with rabies and have never been known to transmit rabies to humans. Testing of these animals will be considered on a case-by-case basis in consultation with the Health Department. Bites from these animals almost never require rPEP.

## Keep up-to-date with rabies vaccinations for pets and livestock.

Adherence to a regular rabies vaccine schedule is critical to protect animals against recognized and unrecognized rabies exposures. Any animal bitten or scratched by a wild animal not available for testing must be regarded as having been exposed to rabies (section 7.2.1 of the "Reportable and Communicable Diseases Rule" [CVR 13-140-007]).

If there is concern that a domestic animal was exposed to a wild animal, owners should consult with their veterinarian. Dogs, cats, ferrets, and livestock with documentation of current or previous (dogs and cats only) rabies vaccination that are exposed to a rabid animal must be revaccinated immediately and kept under the owner's control and observed for 45 days (section 7.2.1.1 of the "Reportable and Communicable Diseases Rule" [CVR 13-140-007]). Ferrets and livestock with expired vaccinations will be evaluated case by case.

Dogs, cats, ferrets, and livestock without documentation of current or previous (dogs and cats only) rabies vaccination that are exposed to a rabid animal must be euthanized or vaccinated immediately and placed in strict isolation for four (dogs and cats) or six (ferrets and livestock) months. If vaccination is delayed, the quarantine period in dogs and cats may be extended to six months, considering the severity of exposure and length of delay of vaccination. Other animals exposed to rabies shall be evaluated case by case (section 7.2.1.2 of the "Reportable and Communicable Diseases Rule" [CVR 13-140-007]).

A booster vaccination should be considered for a currently vaccinated domestic pet with wounds of unknown origin, whereas an unvaccinated domestic pet should be immediately vaccinated and kept under the owner's control and observation for four (dogs and cats) or six (ferrets) months. Veterinarians should record all rabies conversations with owners in the animal's veterinary record.

# All specimens must be pre-approved for rabies testing.

All specimens must be pre-approved for rabies testing at Vermont Department of Health Laboratory by calling the Department of Health Epidemiology at 1-800-640-4374 (in Vermont) or 802-863-7240 or the USDA Vermont Rabies Hotline at 1-800-4-RABIES to assess need for testing, notify the Laboratory, and track the specimen. Only human exposure cases require testing on weekends and holidays; others will be tested during regular business hours.

Veterinarians should send only the head of a domestic pet. Brainstem and cerebellum is necessary for ruling out rabies in cows and horses and may be collected via the foramen magnum. The entire brain or head is required for small livestock. Wildlife specimens that fit into a rabies box can be shipped intact. See instructions for preparing, packaging, and shipping rabies specimens for more details.

The Laboratory offers two rabies submission kits. The small animal kit (kit 12) is intended for smaller animals such as bats and rodents, or for livestock brain tissue. The large animal kit (kit 10) is intended for entire animal bodies or large animal heads. Rabies submission kits can be obtained from the Laboratory or Health Department District Offices. Many Game Wardens, State Police stations, and veterinary clinics have rabies kits on hand.

If there is not an official rabies submission kit available, specimens can be packed in double plastic bags with cold packs (never ice cubes) and placed in a cardboard box, preferably insulated, with a Request for Rabies Examination form (Micro 201) for each specimen placed in an envelope and taped to the outside of the box. It is essential that the outside of the box be clearly marked with "Rabies Specimen," along with the address of the Laboratory:

Vermont Department of Health Lab – Rabies Lab 359 South Park Drive Colchester, VT 05446

Rabies specimens should not be shipped by U.S. mail.

## **Contact Information**

Vermont USDA Rabies Hotline: 1-800-4-RABIES (1-800-472-2437)

Vermont Department of Health Epidemiology: 1-800-640-4374 (VT only), 802-863-7240

Vermont Department of Health Laboratory: 1-800-660-9997 (VT only), 802-338-4724

Vermont Fish & Wildlife Game Warden: Call USDA Rabies Hotline or State Police dispatch

For the most up-to-date version of this resource manual and more information, visit the <u>Vermont Department of Health</u> rabies webpage.

Revised July 2018

Species	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total	%
Raccoon	16	42	103	41	31	18	13	31	18	28	11	21	21	393	51
Skunk	6	24	49	25	22	27	9	26	20	17	6	10	5	246	32
Bat	9	1	3	3	2	0	2	6	3	3	6	9	8	55	7
Gray fox	1	0	0	0	2	6	0	0	3	3	0	2	4	21	3
Bovine	0	4	1	1	7	0	0	1	2	0	0	1	0	17	2
Red fox	0	1	3	3	0	1	0	0	0	0	0	3	2	13	2
Cat	0	0	3	0	0	0	0	3	1	1	2	1	0	11	1
Woodchuck	0	1	1	1	0	1	3	0	0	1	0	0	1	9	1
Bobcat	0	0	1	0	0	1	0	0	1	2	0	0	0	5	1
Horse	0	0	1	0	1	0	0	0	1	0	0	0	0	3	0
Sheep	0	0	1	0	0	0	0	1	0	0	0	1	0	3	0
Dog	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0
Otter	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0
TOTAL	32	73	166	75	65	54	27	68	50	55	25	48	41	779	100

#### Table 1. Rabies by animal type and year — Vermont, 2005–2017





Source: Vermont Department of Health Laboratory

Animal	Total	Total	%
Animai	Positive	Tested	Positive
Raccoon	393	2693	14.6
Skunk	246	1258	19.6
Bat	55	1129	4.9
Gray fox	21	138	15.2
Bovine	17	160	10.6
Red fox	13	181	7.2
Cat	11	743	1.5
Woodchuck	9	186	4.8
Bobcat	5	70	7.1
Horse	3	31	9.7
Sheep	3	45	6.7
Dog	1	262	0.4
Otter	1	2	50.0
Total	778	7281	10.7

# Table 2. Rabies by animal type — Vermont,2005–2017

# Map. Rabies by town/county — Vermont, 2005–2017



# Table 3: Rabies by test reason — Vermont, 2005–2017

Reason for Test	Total Positive	Total Tested	% Positive
Surveillance	377	3829	9.8
Pet/domestic animal contact	206	609	33.8
Human exposure	141	2372	5.9
Other	36	247	14.6
Diagnostic	15	183	8.2
All reasons	775	7240	10.7

# Figure 2. Rabies testing by month — Vermont, 2005–2017



Source: Vermont Department of Health Laboratory

# **Section 2. Vermont-Specific Rules and Statutes**

- A. Reportable and Communicable Diseases Rule
- B. 20 VSA Chapter 193: Domestic Pet or Wolf-Hybrid Control
- C. Animal Rabies Vaccination Rules

### Chapter 4 – Health Surveillance and Infectious Disease Subchapter 1

#### **Reportable and Communicable Diseases Rule**

- **1.0** Authority These regulations are pursuant to 18 V.S.A. §1001, as amended, and by 18 V.S.A. §102, as amended, by 3 V.S.A. §3003, by 20 V.S.A. §3801, and by 13 V.S.A. § 3504(h).
- **2.0 Purpose** The purpose of these regulations is to protect the public health through the control of communicable diseases and other diseases dangerous to the public health. These regulations require the early and prompt reporting of diseases which have been identified as dangerous to the public health, so that the Department of Health may take any necessary action to protect the public from such diseases.

#### 3.0 Definitions

- **3.1** "Commissioner" means the Commissioner of Health.
- **3.2 "Communicable disease" or "communicable syndrome"** means an illness due to the infectious agent or its toxic products which is transmitted directly or indirectly to a person from an infected person or animal, host, or vector, or through the inanimate environment.
- **3.3 "Department"** means the Vermont Department of Health
- **3.4 "Subject species"** means any mammal species which may carry and potentially serve as a reservoir species for rabies including but not limited to raccoons, foxes, bats, skunks, woodchucks, and domestic animals.

#### 4.0 Confidentiality Requirements

- **4.1** Any person or entity required to report under this rule must have written policies and procedures in place that ensure the confidentiality of the records. Such policies and procedures must, at a minimum, include the following:
  - **4.1.1** Identification of those positions/individuals who are authorized to have access to confidential disease-reporting information and the limits placed upon their access;
  - **4.1.2** A mechanism to assure that the confidentiality policies and procedures are understood by affected staff;
  - **4.1.3** Process for training staff in the confidential handling of records;

- **4.1.4** A quality assurance plan to monitor compliance and to institute corrective action when necessary;
- **4.1.5** Process for the confidential handling of all electronically-stored records;
- **4.1.6** Process for authorizing the release of confidential records; and
- **4.1.7** Provision for annual review and revision of confidentiality policies and procedures.
- 4.2 In relation to the reporting of HIV and AIDS, the Department shall maintain:
  - **4.2.1** Procedures for ensuring the physical security of reports including procedures for personnel training and responsibilities for handling physical reports and data;
  - **4.2.2** Computer security procedures;
  - **4.2.3** Communication procedures;
  - **4.2.4** Procedures for the legal release of data; and
  - **4.2.5** Procedures to ensure that a disclosure of information from the confidential public health record is only made following notice to the individual subject of the public health record or the individual's legal representative and pursuant to a written authorization voluntary executed by the individual or the individual's representative (such notice and authorization is required prior to all disclosures, including disclosures to other states, the federal government, and other programs, departments, or agencies of state government).

#### 5.0 Communicable Disease Reports

- **5.1** Organizations and person required to report: The following organizations and persons who know or suspect that a person is sick or has died of a disease dangerous to the public health are required to report to the Department of Health within 24 hours of the time when they become aware of the disease (immediate reporting is essential for those diseases or laboratory reports indicated by a "\*"). Nonmedical community-based organizations are exempt from these requirements.
  - **5.1.1** Infection preventionists
  - **5.1.2** Health care providers
  - **5.1.3** Laboratory directors
  - **5.1.4** Nurse practitioners
  - **5.1.5** Nurses
  - **5.1.6** Physician assistants

- **5.1.7** Physicians
- **5.1.8** School health officials
- 5.1.9 Administrators of long-term care and assisted living facilities
- **5.2** Nature of the report: The report of communicable diseases and other diseases dangerous to the public health and rare infectious diseases, as listed in 5.5, shall include the following information as it relates to the affected person:
  - name of person date of birth age sex address telephone number name of health care provider/physician address of health care provider/physician name of disease being reported date of onset of the disease any other pertinent information.
- **5.3** The report should be made by telephone, or in writing, or electronically to the Department of Health, Epidemiology Program. HIV and AIDS reports shall be made on the Adult HIV/AIDS Confidential Case Report Form or the Pediatric HIV/AIDS Confidential Case Report Form as appropriate.
- **5.4** Laboratories must report in accordance with section 5.6.
- **5.5** Diseases, syndromes, and treatments required to be reported.
  - **5.5.1** Reportable Diseases and Syndromes (to include any rare infectious disease or one dangerous to public health) Any unexpected pattern of cases, suspected cases, deaths or increased incidence of any other illness of major public health concern, because of the severity of illness or potential for epidemic spread, which may indicate a newly recognized infectious agent, an outbreak, epidemic, related public health hazard or act of bioterrorism, must be reported. Such reports may be made by sharing medical encounter information with the Department of Health so that the Department can determine if there is sufficient probability that a case or an outbreak warrants further public health response (immediate reporting is essential for those diseases or laboratory reports indicated by a "\*").
    - Anaplasmosis AIDS Anthrax\* Arboviral illness Babesiosis Blood lead levels Botulism\*

**Brucellosis** Campylobacteriosis Chlamydia trachomatis infection Cholera Creutzfeldt-Jakob disease/transmissible spongiform encephalopathies Cryptosporidiosis Cyclosporiasis Dengue Diphtheria\* Eastern Equine Encephalitis illness Ehrlichiosis Encephalitis Gonorrhea Guillain Barre Syndrome Haemophilus influenzae disease, invasive Hantavirus disease Hemolytic uremic syndrome (HUS) Hepatitis A Hepatitis B Hepatitis B, positive surface antigen in a pregnant woman Hepatitis C Hepatitis E Human immunodeficiency virus (HIV) Influenza: Report only - Individual cases of influenza due to a novel strain of Influenza A\* - Pediatric influenza-related deaths - Institutional outbreaks Legionellosis Leptospirosis Listeriosis Lyme Disease Malaria Measles (Rubeola)\* Meningitis, bacterial Meningococcal disease\* Middle East Respiratory Syndrome (MERS) Mumps Pertussis (Whooping cough) Plague\* Poliovirus infection, including poliomyelitis\* Psittacosis **O** Fever Rabies, human\* and animal cases Reve syndrome Spotted Fever Rickettsiosis

Rubella (German Measles) Rubella, congenital rubella syndrome Salmonellosis Severe Acute Respiratory Syndrome (SARS)\* Shigatoxin-producing E.coli (STEC) Shigellosis Smallpox\* Streptococcal disease, Group A, invasive Streptococcal disease, Group B invasive (infants less than one month of age) Streptococcus pneumoniae disease, invasive **Syphilis** Tetanus Toxic Shock Syndrome Trichinosis Tuberculosis Tularemia\* Typhoid Fever Varicella (Chicken pox only) Viral hemorrhagic fever\* Vibriosis West Nile virus illness Yellow Fever Yersiniosis

- **5.5.2** Human rabies post exposure treatment (HRPET) is reportable irrespective of evidence of rabies. Identifying information as indicated in 5.2 must be provided to the Department of Health.
- **5.6** Reportable Laboratory Findings
  - **5.6.1** Positive, presumptive or confirmed, isolation or detection of the following organisms or positive, presumptive or confirmed, serological results for the following organisms OR results from specific laboratory tests as indicated below (to include any rare infectious disease or one dangerous to public health) (immediate reporting is essential for those diseases or laboratory reports indicated by a "\*"):

Anaplasma phagocytophilum Arboviruses Babesia microti Bacillus anthracis\* Bordetella pertussis

Borrelia burgdorferi Brucella species Burkholderia mallei Burkholderia pseudomallei *Campylobacter* species Carbapenem-resistant Enterobacteriaceae (CRE), including susceptibility results CD4+ T-lymphocyte counts of less than 200 cells/uL or a CD4+ percentage of less than 14 Chlamydia psittaci Chlamydia trachomatis Clostridium botulinum\* Clostridium tetani Corynebacterium diphtheriae\* Coxiella burnetii Creutzfeldt-Jakob disease/transmissible spongiform encephalopathies Cryptosporidium species Cyclospora cayetanensis Dengue virus Eastern Equine Encephalitis virus Ehrlichia species Haemophilus influenzae, isolated from a normally sterile site Hantavirus Hepatitis A virus (anti-HAV IgM) Hepatitis B virus (HBsAg, anti-HBcIgM, HBeAg, HBV DNA) Hepatitis C virus (HCV) Hepatitis E virus (IgM anti-HEV) Human immunodeficiency virus (HIV): Includes the following: - HIV viral load measurement (including non-detectable results) Influenza virus: Report only – Positive PCR Legionella species

Leptospira species Listeria monocytogenes Measles virus\* MERS CoV Mumps virus Mycobacterium tuberculosis complex Neisseria gonorrhoeae Neisseria meningitidis, isolated from a normally sterile site\* *Plasmodium* species Poliovirus\* **Rabies virus** Rickettsia Rubella virus Salmonella species SARS-CoV/SARS - associated virus\* Shigella species. Shigatoxin-producing E.coli (STEC) Smallpox (yariola)\* Staphylococcus aureus, vancomycin resistant (VRSA) and vancomycin intermediate (VISA), including susceptibility results *Streptococcus*, Group A, isolated from a normally sterile site Streptococcus, Group B, isolated from a normally sterile site (infants less than one month of age) Streptococcus pneumoniae, isolated from a normally sterile site, including susceptibility results Treponema pallidum Trichinella spiralis Francisella tularensis\*

Varicella virus

Vibrio species

Viral hemorrhagic fever (filoviruses [e.g. Ebola, Marburg] and arenaviruses [e.g. Lassa, Machupo])\*

West Nile virus Yellow fever virus Yersinia enterocolitica Yersinia pestis\*

- 5.6.2 In addition, the following laboratory tests must be reported: Blood lead (all results, including undetectable) CSF cultures (all positive findings)
  - Nontreponemal tests for syphilis (all positive findings)
- **5.6.3** Laboratory reporting shall include:
  - name of patient

date of birth

age

sex

address of patient

telephone number of patient

name of health care provider/physician

address of health care provider/physician

telephone number of provider/physician

positive test results

specimen type, e.g., serum, swab, etc.

specimen source, e.g., cervix, throat, etc.

- **5.6.4** Laboratories are required to provide a written or electronic report irrespective of the required reporting of other parties under 5.1. If no positive reportable laboratory findings have been made during a given week then a written report of "No reportable findings" shall be made.
- **5.6.5** For laboratories with validated electronic laboratory reporting, a report of "No reportable findings" is not required.
- **5.6.6** Specimens or isolates of the following organisms shall be sent to the Vermont Department of Health Laboratory for further analysis or typing:

Burkholderia mallei Burkholderia pseudomallei Campylobacter species Carbapenem-resistant Enterobacteriaceae Coxiella burnetti

Neisseria meningitidis, isolated from a normally sterile site

Listeria monocytogenes

Salmonella species.

Shigella species.

Shigatoxin-producing E. coli (STEC) (including O157:H7)

Mycobacterium tuberculosis

VRSA (vancomycin-resistant *Staphylococcus aureus*)

VISA (vancomycin-intermediate *Staphylococcus aureus*)

Vibrio species

**5.6.7** The Department of Health Laboratory will provide transport containers and instruction on how to submit specimens or isolates.

#### 6.0 Prophylaxis for Eyes of Newborn

- 6.1 Duties of Health Care Providers
  - **6.1.1** Prophylaxis for conjunctivitis of the newborn (ophthalmia neonatorum) shall be administered to all infants immediately after birth by the medical provider attending the birth.

#### 7.0 Rabies Control

- 7.1 Reporting of Animal Bites:
  - 7.1.1 Physician Reporting
  - **7.1.2** Physicians shall report to the local health officer the full name, age and address of any person known to have been bitten by an animal of a species subject to rabies within 24 hours of actual or constructive notice.
  - 7.1.3 Minors and Adults; No Attending Physician
    - 7.1.3.1 Minors: If no physician is in attendance and the person bitten is under 18 years of age, the parent or guardian shall to make such report within 24 hours of actual or constructive notice to the local town health officer.
    - 7.1.3.2 Adults: If no physician is in attendance and the person bitten is an adult, the person shall report, or cause to be reported, such information to the local town health officer.
- 7.2 Control Methods in Domestic and Confined Animals.
  - **7.2.1** Post exposure management. Any animal bitten or scratched by a wild mammal not available for testing shall be regarded as having been exposed to rabies.

- 7.2.1.1 Dogs, Cats and Ferrets. When an unvaccinated dog<del>s</del>, cat<del>s</del> or ferrets is exposed to a rabid animal the Department may order that the exposed animal be euthanized immediately or be placed in strict isolation for 6 months and vaccinated 1 month before being released. Dogs, cats and ferrets that are currently vaccinated shall be revaccinated immediately, kept under the owner's control, and observed for 45 days. Animals with expired vaccinations need to be evaluated on a case by case basis.
- 7.2.1.2 Other Animals. Other animals exposed to rabies should be evaluated on a case by case basis.
- 7.2.2 Management of Animals that Bite Humans.
  - 7.2.2.1 The local health officer shall cause an apparently healthy dog, cat or ferret that bites a person to be confined and observed for 10 days.
  - 7.2.2.2 A rabies vaccine should not be administered during the observation period and such animals must be evaluated by a veterinarian at the first sign of illness during confinement. Any illness in the animal must be reported immediately to the local health officer.
  - 7.2.2.3 If clinical signs consistent with rabies develop, the animal must be euthanized immediately its head removed, and the head shipped under refrigeration for examination by the state Health Department laboratory.
  - 7.2.2.4 Other animals, which may have bitten and exposed a person to rabies, shall be reported within 24 hours to the local health officer. Prior vaccinations of an animal may not preclude the necessity for euthanasia and testing if the period of virus shedding is unknown for that species. Management of animals other than dogs, cats or ferrets depends on the species, the circumstances of the bite, and the epidemiology of rabies in the area, and the biting animal's history, current health status, and potential for exposure to rabies.
- **7.3** Removal: A confined animal being observed for signs of rabies shall not be removed from one health district into another prior to the conclusion of the prescribed isolation period except with the permission of the local health officer from whose district such animal is to be removed and the permission of the health officer to whose jurisdiction such animal is to be transferred.
  - **7.3.1** The former shall give permission only after securing the consent of the local health officer to whose jurisdiction the animal is to be transferred, except that if removal is to be to another state, he or she shall give permission only after securing the consent of the commissioner of health of the state of Vermont.

- **7.3.2** Such removal shall be private conveyance, in charge of a responsible person and conducted in such manner as to prevent the escape of the animal or its coming in contact with other animals or persons.
- **7.4** Laboratory Specimens: Whenever any animal that has or is suspected of having rabies dies or is killed it shall be the duty of the local health officer to cause the head of such animal to be removed and sent immediately, properly packed, with a complete history of the case to a laboratory approved for this purpose by the state commissioner of health. The local health officer shall notify the health department of the specimen's intended arrival.
- **7.5** Destruction of Animals, Subject to Rabies; Precautions: Whenever an animal, subject to rabies, is brought to a veterinarian to be destroyed, an attempt shall be made by the veterinarian to ascertain that the animal has not bitten any person within the previous ten day period; before destroying the animal, he or she shall require the owner to sign a statement to this effect, and he or she shall not destroy any animal which has bitten a person within ten days. The health officer must be notified by the veterinarian of any such biting incident.

#### 8.0 Pharmacist Reporting

- 8.1 Pharmacists are required to report any recognized unusual or increased prescription requests, unusual types of prescriptions, or unusual trends in pharmacy visits that may result from bioterrorist acts, epidemic or pandemic disease, or novel and highly fatal infectious agents or biological toxins, and might pose a substantial risk of significant number of human fatalities or incidents of permanent or long-term disability within 24 hours of when they become aware of such an event.
- **8.2** Prescriptions Required to be Reported
  - **8.2.1** Reportable Prescription Requests includes any unusual request of a prescription specific to a disease that is relatively uncommon and may be the result of bioterrorism.

Botulinum antitoxin (botulinum)

Unusual antitoxins and antidotes

**8.2.2** Unusual Increase in Prescriptions includes any unusual increase in the number of prescriptions or over-the-counter sales of medications or drug classes listed below or that treat a disease that is relatively uncommon and may be the result of bioterrorism.

Anti-pyretics (prescription and/or over-the-counter)

Anti-diarrheal (prescription and/or over-the-counter)

Decongestants and anti-tussive medications used to treat respiratory or influenza-like illness (prescription and/or over-thecounter) Analgesics (prescription and/or over-the-counter)

Anticonvulsants

Antibiotics (for example, streptomycin, doxycycline, ciprofloxacin)

Antivirals

- **8.2.3** Unusual Number of Requests for Information: Includes over-the-counter pharmaceuticals to treat fever, respiratory and gastrointestinal complaints or other symptoms that may result from bioterrorism.
- **8.3** Nature of the Report: The report should be made by telephone, in writing, by fax or electronically (when available by email or internet) to the Department of Health within 24 hours.
  - **8.3.1** Reportable Prescription Requests: The pharmacy report of an unusual prescription request or any prescription that treats a disease that is relatively uncommon and may be the result of bioterrorism shall include as much of the following information as is available:

Name of patient

Date of birth [or age if date of birth not available]

Sex

Race

Address of patient (include city and county)

Name of health care provider/physician

Address of health care provider/physician

Name of unusual prescriptions

Date prescription was written

Date prescription was filled

Name of pharmacist

Address of pharmacist

Date of report

Any other pertinent information

**8.3.2** Unusual Increase in Prescriptions or Unusual Number of Requests for Information: The pharmacy report of an increase in the number of prescription requests or over-the-counter sales for certain classes of pharmaceuticals OR an unusual number of requests for information shall include as much of the following information as is available:

Name of prescription, over-the-counter medication, or drug class

Approximate date the increase began

Magnitude of increase (e.g. 20 prescription requests for a drug in 1 day – usually receive 1-2 requests per day)

Name of pharmacist

Address of pharmacist

Date of report

Any other pertinent information

**8.4** Communication: The Department of Health will immediately notify the Department of Public Safety by the most expeditious method possible if information received in accordance with these rules appears to present a threat to the public safety.

#### 9.0 Animal Disease Surveillance

- **9.1** Veterinarians and veterinary diagnostic laboratory directors shall report to the Division of Health Surveillance, Department of Health, within 24 hours of the time when they become aware of the following:
  - **9.1.1** Clinical or laboratory diagnosis or suspicion of the following communicable diseases or any other rare infectious disease in animals that might pose a risk of significant number of human and animal fatalities or incidents or permanent or long-term disability shall be reported.

Anthrax

Avian Chlamydiosis (Psittacosis, Ornithosis)

Botulism (Clostridium botulinum toxin)

Brucellosis (*Brucella* species) (confirmed cases only, as determined by the Agency of Agriculture Food and Markets)

*Clostridium perfringens* epsilon toxin (laboratory confirmed epsilon toxin only)

Glanders (Burkholderia mallei)

Hantavirus

Melioidosis (Burkholderia pseudomallei)

Nipah (Nipah virus)

Plague (Yersinia pestis)

Q Fever (*Coxiella burnetti*)

Ricin toxin (from *Ricinis communis* (castor beans))

Staphylococcal enterotoxins

Tularemia (Francisella tularensis)

Typhus fever (Rickettsia prowazekii)

Viral Encephalitis (alphaviruses [e.g., Venezuelan equine encephalitis, eastern equine encephalitis, western equine encephalitis])

Viral hemorrhagic fevers (filoviruses [e.g., Ebola, Marburg] and arenaviruses [e.g., Lassa, Machupo])

- **9.1.2** Unusual cases or clusters of animal illnesses or deaths that pose a threat to human health.
- **9.1.3** Any evidence or suspicion of terrorism, including intentional or threatened use of viruses, bacteria, fungi, toxins, chemicals, or radiologic material to produce malfunction, illness or deaths in animals and/or humans shall be reported.
- **9.2** Veterinarians shall act on behalf of livestock owners and persons having care of animals who have reported illness consistent with such diseases.
- 9.3 Nature of the Report

The report should be made by telephone, in writing, by fax or electronically (when available by email or internet) to the Department of Health within 24 hours.

**9.3.1** 1) Clinical report: The report of a clinical diagnosis or suspicion of the above named diseases or any unusual cluster of animal illnesses or deaths shall include as much of the following information as is available:

Location or suspected location of the animal

Name of any known owner

Address of any known owner

Name of reporting individual

Address of reporting individual

Name of disease or suspected disease being reported

Type of animal(s) affected

Number of animals affected

Date of confirmation of disease or onset of clinical signs

**9.3.2** 2) Laboratory report: The report of positive, presumptive or confirmed, isolation or detection OR positive, presumptive or confirmed, serological results shall include as much of the following information as is available:

Name of any known owner

Address of any known owner

Name of person who submitted specimen

Address of person who submitted specimen

Name of test

Result of test

Date submitted

Date of positive test result

Specimen type (e.g. swab)

Specimen source (e.g. skin, mouth)

**9.3.3** Laboratories are required to provide a written report even if the reportable disease has been reported by others.

### **The Vermont Statutes Online**

#### **Title 20: Internal Security And Public Safety**

#### **Chapter 193: Domestic Pet Or Wolf-hybrid Control**

#### Subchapter 1: General Provisions

#### § 3541. Definitions

As used in this chapter:

- (1) "Secretary" where no other department is referenced means the Secretary of Agriculture, Food and Markets, and includes his or her designee.
- (2) "Domestic animal" means those animals defined by 6 V.S.A. § 1151(2).
- (3) "Domestic pet" or "pet" means any domestic dogs, domestic cats, and ferrets. The term shall also include such other domestic animals as the Secretary shall establish by rule, provided that the Secretary finds that the animal has the potential to become an imminent danger to public health or welfare if not subjected to the provisions of this chapter.
- (4) "Ferret" means only the European ferret (Mustela putorious furo).
- (5) "Legislative body" means the legislative body of a town, city, or incorporated village.
- (6) "Owner" means any person who owns a domestic pet or wolf-hybrid and includes any person who has actual or constructive possession of the pet or wolf-hybrid. The term also includes those persons who provide feed or shelter to a domestic pet or wolf-hybrid.
- (7) "Respondent" means a person alleged to have violated any provision of this chapter.
- (8) "Wolf-hybrid" means an animal that is the progeny or descendant of a domestic dog (Canis familiaris) and a wolf (Canis lupus or Canis rufus). "Wolf-hybrid" also means an animal that is advertised, registered, licensed, or otherwise described or represented as a wolf-hybrid by its owner or an animal that exhibits primary physical and behavioral wolf characteristics. The Commissioner of Fish and Wildlife shall adopt a rule describing primary physical and behavioral wolf characteristics.
- (9) "Working farm dog" means a dog that is bred or trained to herd or protect livestock or poultry or to protect crops and that is used for those purposes and that is registered as a working farm dog pursuant to subsection 3581(a) of this title.
- (10) "Pet dealer" means any person who sells or exchanges or who offers to sell or exchange cats, dogs, or wolf-hybrids, or any combination thereof, from three or more litters of cats, dogs, or wolf-hybrids in any 12-month period. This

definition shall not apply to pet shops, animal shelters, or rescue organizations as those terms are defined in section 3901 of this title.

#### § 3541a. Feral animals; responsibility

It is not the intent of the General Assembly to require a person to be responsible under this chapter for a feral animal that takes up residence in a building other than the person's home, even if the person occasionally provides feed to the animal.

#### §§ 3542-3544. Repealed.

#### § 3545. Right to kill domestic pets or wolf-hybrids generally

- (a) A person may kill a domestic pet or wolf-hybrid that suddenly assaults him or her or when necessary to discontinue an attack upon the person or another person provided that the attack or assault does not occur while the domestic pet or wolf-hybrid is restrained, within an enclosure containing the domestic pet or wolf-hybrid, or on the premises of the owner.
- (b) A domestic pet or wolf-hybrid found wounding, killing or worrying another domestic pet or wolf-hybrid, a domestic animal or fowl may be killed when the attendant circumstances are such that the killing is reasonably necessary to prevent injury to the animal or fowl which is the subject of the attack.

#### § 3546. Investigation of vicious domestic pets or wolf-hybrids; order

- (a) When a domestic pet or wolf-hybrid has bitten a person while the domestic pet or wolf-hybrid is off the premises of the owner or keeper, and the person bitten requires medical attention for the attack, such person may file a written complaint with the legislative body of the municipality. The complaint shall contain the time, date and place where the attack occurred, the name and address of the victim or victims, and any other facts that may assist the legislative body in conducting its investigation required by subsection (b) of this section.
- (b) The legislative body, within seven days from receipt of the complaint, shall investigate the charges and hold a hearing on the matter. If the owner of the domestic pet or wolf-hybrid which is the subject of the complaint can be ascertained with due diligence, said owner shall be provided with a written notice of the time, date and place of hearing and the facts of the complaint.
- (c) If the domestic pet or wolf-hybrid is found to have bitten the victim without provocation, the municipal officials shall make such order for the protection of persons as the facts and circumstances of the case may require, including, without limitation, that the domestic pet or wolf-hybrid is disposed of in a humane way, muzzled, chained, or confined. The order shall be sent by certified mail, return receipt requested. A person who, after receiving notice, fails to comply with the terms of the order shall be subject to the penalties provided in section 3550 of this chapter.
- (d) The procedures provided in this section shall apply if the domestic pet or wolf-hybrid is not a rabies suspect. If a member of the legislative body or a municipal official designated by the legislative body determines that the animal is a rabies suspect, the

provisions of subchapter 5 of this chapter and the rules of the department of health shall apply.

(e) The procedures provided in this section shall not apply if the voters of a municipality, at a special or annual meeting duly warned for the purpose, have authorized the legislative body of the municipality to regulate domestic pets or wolf-hybrids by ordinances that are inconsistent with this section, in which case those ordinances shall apply.

#### § 3547. Repealed.

#### § 3548. Application to unorganized towns and gores; supervisors

The provisions of subchapters 1, 2, 4 and 5 of this chapter shall apply to unorganized towns and gores, and the duties imposed upon municipal clerks by this chapter shall, in unorganized towns and gores, be performed by the supervisors thereof.

#### § 3549. Domestic pets or wolf-hybrids; regulation by towns

The legislative body of a city or town by ordinance may regulate the licensing, keeping, leashing, muzzling, restraint, impoundment, and destruction of domestic pets or wolf-hybrids and their running at large, except that a legislative body of a city or town shall not prohibit or regulate the barking or running at large of a working farm dog when it is on the property being farmed by the person who registered the working farm dog, pursuant to subsection 3581(a) of this title, in the following circumstances:

- (1) if the working farm dog is barking in order to herd or protect livestock or poultry or to protect crops; or
- (2) if the working farm dog is running at large in order to herd or protect livestock or poultry or to protect crops.

#### § 3550. Penalties; enforcement; municipal legislative body; Secretary

- (a) A municipal legislative body or an officer designated by the Secretary may impose a civil penalty of up to \$500.00 per violation in accordance with the provisions of this section.
- (b) A municipal legislative body may impose penalties for violation of any provisions of subchapter 1 or 2, refusal to obtain a pet dealer permit under subchapter 3, or a refusal to comply with an order issued by a municipal officer under subchapter 5 of this chapter.
- (c) An officer designated by the Secretary may impose penalties for violation of a rule adopted by a State agency under subchapter 5 of this chapter, violation of a quarantine order issued under subchapter 5 of this chapter, or refusal to comply with an order issued by a State officer under subchapter 5 of this chapter.
- (d) In determining the amount of the civil penalty to be ordered, the legislative body or officer shall consider the following:
  - (1) the degree of actual or potential impact on public health, safety, and welfare resulting from the violation;
  - (2) whether the respondent has cured the violation;

- (3) the presence of mitigating circumstances;
- (4) whether the respondent knew or had reason to know the violation existed;
- (5) the respondent's record of compliance;
- (6) the deterrent effect of the penalty;
- (7) the costs of enforcement; and
- (8) the length of time the violation has existed.
- (e) When the legislative body or officer has reasonable grounds to believe that a person has violated a provision of this chapter under its purview, the legislative body or officer may issue a notice of the alleged violation, which shall be delivered to the respondent in person or mailed to the respondent by registered mail. The notice of violation shall include:
  - (1) a civil penalty of up to \$500.00;
  - (2) a brief description of the alleged violation and identification of the law alleged to have been violated;
  - (3) a statement that the respondent has a right to a hearing before the legislative body or a hearing officer designated by the Secretary at no cost to the respondent, a description of the procedures for requesting a hearing, and a statement that failure to request a hearing within 21 days of the date of mailing of the notice shall result in a final decision with no right of appeal; and
  - (4) if applicable, a directive that the respondent take actions necessary to achieve compliance with the law.
- (f) A person who receives a notice of violation shall be offered an opportunity for a hearing before the legislative body or hearing officer, provided that the request for hearing is made in writing to the clerk of the municipality or the Secretary no later than 21 days after the date of mailing of the notice of violation. If the respondent does not request a hearing in a timely fashion, the decision shall be final and the penalty shall be payable within 35 days following mailing of the notice of violation. If the respondent does make a timely request for a hearing, the legislative body or hearing officer shall hold a hearing within 14 days of receipt of the request. After the hearing, the legislative body or hearing officer may affirm, reduce, or eliminate the penalty. The decision shall be delivered or mailed to the respondent in the same manner as the notice of violation and shall be effective five days following mailing of the decision or immediately following delivery of the decision.
- (g) Imposition of a penalty under this subchapter precludes imposition of any other administrative or civil penalty under any other provision of law for the same violation.
- (h) The civil penalty shall be paid to the enforcing agency or enforcing legislative body. If the respondent fails to pay the penalty within the time prescribed, the legislative body or Secretary may bring a collection action, including a small claims action, in the Civil Division of the Superior Court.
- (i) A respondent aggrieved by a decision made following a hearing before the legislative body or hearing officer may appeal within 30 days of receipt of the decision to the Civil Division of the Superior Court, which shall consider the matter de novo.
- (j) On application of a municipality or the Secretary, the Civil Division of the Superior Court shall have jurisdiction to enjoin the violation of any provision of this chapter.

The Court may also authorize the seizure and disposition of domestic pets or wolfhybrids when owners refuse to have the pets or wolf-hybrids inoculated or licensed, or when the Court determines that there is a threat to the public welfare.

#### § 3551. Search warrants

An officer who has attempted to seize a domestic pet or wolf-hybrid under sections 3546, 3549, 3624, 3745, 3806, or 3807 of this chapter and has not been permitted to search for or take the animal, may apply to a judicial officer authorized to issue search warrants for a warrant to search the properties of the owner of the animal or any other property if the officer has reasonable cause to believe that the animal may be on it. If the judicial officer is satisfied that there is a reasonable cause to believe that the animal is on a property, the judicial officer shall issue a search warrant authorizing a law enforcement officer of the state of Vermont to search the property and premises for the animal within a specified period of time not to exceed 10 days and to seize the animal. The warrant shall be served between the hours of 6:00 A.M. and 10:00 P.M. unless the warrant directs that it may be served at any time. The judicial officer may, by appropriate provision in the warrant, and for reasonable cause shown, authorize its execution at other times. The warrant shall designate the court to which it shall be returned.

#### Subchapter 2: Licenses

#### § 3581. General requirements

- (a) A person who is the owner of a dog or wolf-hybrid more than six months old shall annually on or before April 1 cause it to be registered, numbered, described, and licensed on a form approved by the Secretary for one year from that day in the office of the clerk of the municipality wherein the dog or wolf-hybrid is kept. A person who owns a working farm dog and who intends to use that dog on a farm pursuant to the exemptions in section 3549 of this title shall cause the working farm dog to be registered as a working farm dog and shall, in addition to all other fees required by this section, pay \$5.00 for a working farm dog license. The owner of a dog or wolfhybrid shall cause it to wear a collar, and attach thereto a license tag issued by the municipal clerk. Dog or wolf-hybrid owners shall pay for the license \$4.00 for each neutered dog or wolf-hybrid, and \$8.00 for each unneutered dog or wolf-hybrid. If the license fee for any dog or wolf-hybrid is not paid by April 1, its owner or keeper may thereafter procure a license for that license year by paying a fee of 50 percent in excess of that otherwise required.
- (b) Before a person shall be entitled to obtain a license for a neutered dog or wolf-hybrid, he or she shall exhibit to the clerk a certificate signed by a duly licensed veterinarian showing that the dog or wolf-hybrid has been sterilized.

(c)

(1) A mandatory license fee surcharge of \$4.00 per license shall be collected by each city, town, or village for the purpose of funding the dog, cat, and wolf-

hybrid spaying and neutering program established in chapter 193, subchapter 6 of this title.

- (2) An optional license fee surcharge of up to \$10.00 per license is to be implemented by the legislative body of a city, town, or village that has established an animal and rabies control program for the sole purpose of funding the rabies control program.
- (3) The license fee surcharges in this subsection shall not be considered part of the license fee for purposes of calculating a penalty for late payment.
- (d) Before obtaining a license for a dog or wolf-hybrid six months of age or older, a person shall deliver to the municipal clerk a certificate or a certified copy thereof issued by a duly licensed veterinarian, stating that the dog or wolf-hybrid has received a current preexposure rabies vaccination with a vaccine approved by the Secretary, and the person shall certify that the dog or wolf-hybrid described in the certificate or copy is the dog or wolf-hybrid to be licensed. The municipal clerk shall keep the certificates or copies thereof on file. The Secretary shall prescribe the size and format of rabies certificates. The owner of any such dog or wolf-hybrid shall maintain a copy of the rabies vaccination form and provide it to State or municipal officials upon request.
- (e) For the purposes of licensing a dog or wolf-hybrid, a current vaccination against rabies means that:
  - (1) All dog and wolf-hybrid vaccinations recognized by State and local authorities shall be administered by a licensed veterinarian or under the supervision of a licensed veterinarian.
  - (2) All dogs and wolf-hybrids over three months of age shall be vaccinated against rabies. The initial vaccination shall be valid for 12 months. Within nine to 12 months of the initial vaccination, the animal must receive a booster vaccination.
  - (3) All subsequent vaccinations following the initial vaccination shall be valid for 36 months.
  - (4) All vaccinations, including the initial vaccination, shall be with a U.S. Department of Agriculture-approved three-year rabies vaccine product.
- (f) In addition to the license fees assessed in subsections (a) and (c) of this section and section 3583 of this title, municipal clerks shall assess a \$1.00 fee for each license sold. The clerks shall forward the fees collected under this subsection to the State Treasurer on or before the 15th day of May, September, and January of each year, together with an accounting of the licenses sold. The funds collected under this subsection are to be used for rabies control programs. For this purpose, on or before the 30th days of May, September, and January, the State Treasurer shall disburse the funds collected under this subsection as follows:
  - (1) Forty-five percent to the Fish and Wildlife Fund.
  - (2) Forty-five percent to the Commissioner of Health.
  - (3) Ten percent to the Secretary of Agriculture, Food and Markets.

#### § 3581a. Immunization

- (a) An owner of a domestic pet or wolf-hybrid shall have that animal inoculated against rabies by a licensed veterinarian in accordance with section 3581 of this title, if applicable, and with rules adopted by the secretary.
- (b) No rabies vaccine may be used for domestic pets unless it is first approved by the secretary.
- (c) Until the secretary approves a rabies vaccine for use on wolf-hybrids, these animals shall be vaccinated with a vaccine approved by the secretary for domestic dogs and a veterinarian inoculating a wolf-hybrid in accordance with this section shall not be liable for the failure of the rabies vaccine to protect the animal from rabies nor for any adverse reaction that may be attributable to the vaccination.
- (d) A person may use an approved vaccine to inoculate a feral feline that takes up residence in a building other than the person's home and need not use the services of a licensed veterinarian for this purpose.
- (e) The secretary of the agency of agriculture, food and markets and the department of health shall provide notices to veterinarians designed to help them to inform people about the provisions of this section regarding cats, wolf-hybrids and other domestic pets.

#### § 3582. Dogs or wolf-hybrids obtained after April 1

A person who becomes the owner after April 1 of a dog or wolf-hybrid six months old which has not been licensed, or a person who owns, keeps or harbors a dog or wolfhybrid in which becomes six months old after April 1 shall within 30 days apply for and obtain a license for the dog or wolf-hybrid the same manner as the annual license is obtained. If an application under this section is made after October 1, the fee for the license shall be one-half the amount otherwise required. If the license fee is not paid within 30 days, the owner may thereafter procure a license for that license year by paying a license fee of 50 percent in excess of that otherwise required.

#### § 3582a. Repealed.

#### § 3583. Domestic pets and wolf-hybrids kept for breeding purposes

- (a) The owner or keeper of domestic pets and wolf-hybrids kept for breeding purposes may take out annually, on or before April 1, a special license for the domestic pets or wolf-hybrids, provided:
  - (1) He or she keeps the domestic pets or wolf-hybrids within a proper enclosure. A proper enclosure is a locked fence or structure of sufficient height and sufficient depth into the ground to prevent the entry of young children and to prevent the animal from escaping. A proper enclosure also provides humane shelter for the animal.
  - (2) The domestic pets or wolf-hybrids at all times have a current vaccination against rabies.

- (3) When the number of domestic pets or wolf-hybrids so kept does not exceed ten, the fee shall be \$30.00 and for each additional domestic pet or wolf-hybrid so kept, an annual fee of \$3.00.
- (b) Domestic pets and wolf-hybrids covered by the special license hereunder shall be exempt from other license fees, and all licenses under this section are exempt from the surcharge enacted under subsection (c) of section 3581 of this title.
- (c) If the license fee is not paid by April 1, the owner or keeper may thereafter procure a license for that license year by paying a fee of 50 percent in excess of that otherwise required. These license fees are in addition to any fees required for the operation of a kennel under subchapter 3 of this chapter.

#### §§ 3584-3586. Repealed.

#### § 3587. Dogs brought into state

Without obtaining a Vermont license, a person may bring or cause to be brought into the state for a period not exceeding 90 days, one or more licensed dog or dogs bearing the identification of the owner, provided that the owner possesses a certificate signed by a licensed veterinarian or a state official of any other state that the dog has received a rabies vaccination that is current for the 90 days following entry into the state.

#### § 3588. Issuance of licenses; record of licenses

Municipal clerks shall issue licenses and receive the money therefor, and pay the same into the municipal treasury, within 60 days of the receipt thereof, retaining to their own use \$2.00 for each license or permit, and shall return therewith a sworn statement of the amount of moneys thus received and paid over by them.

#### § 3589. Record of licenses

Municipal clerks shall also keep a record of licenses issued by them, with the names of the owners or keepers of the dogs or wolf-hybrids licensed and the names, registered numbers and descriptions of such dogs or wolf-hybrids.

#### § 3590. List of dogs and wolf-hybrids not licensed

- (a) The legislative body shall annually designate one or more persons to maintain a list of unlicensed, inoculated and licensed dogs and wolf-hybrids owned or kept in their municipality and to submit the list to the municipal clerk.
- (b) On receiving a list of dogs and wolf-hybrids from persons authorized by the legislative body, the municipal clerk shall notify the owners or keepers of all dogs and wolf-hybrids named on the list that have not already been licensed or inoculated, and after May 30 shall furnish to the legislative body a list of dogs and wolf-hybrids not licensed or inoculated as required by law. Owners shall also be notified that unlicensed or uninoculated dogs or wolf-hybrids may be destroyed.

#### § 3591. Transfer of license
A license from a municipal clerk shall be valid in any part of the state and may be transferred with the dog or wolf-hybrid licensed, provided such license is recorded by the clerk of the municipality where such dog or wolf-hybrid is kept.

#### § 3592. Repealed.

#### § 3621. Issuance of warrant to impound; complaint

- (a)
- (1) The legislative body of a municipality may at any time issue a warrant to one or more police officers, constables, pound keepers, or appointed animal control officers, directing them to proceed forthwith to impound all dogs or wolf-hybrids within the town or city not licensed according to the provisions of this subchapter, except as exempted by section 3587 of this title, and to enter a complaint against the owners or keepers thereof.
- (2) A dog or wolf-hybrid impounded by a municipality under this section may be transferred to an animal shelter or rescue organization for the purpose of finding an adoptive home for the dog or wolf-hybrid. If the dog or wolf-hybrid cannot be placed in an adoptive home or transferred to a humane society or rescue organization within ten days, or a greater number of days established by the municipality, the dog or wolf-hybrid may be destroyed in a humane way. The municipality shall not be liable for expenses associated with keeping the dog or wolf-hybrid at the animal shelter or rescue organization beyond the established number of days.
- (b) A municipality may waive the license fee for a dog or wolf-hybrid impounded pursuant to subsection (a) of this section for the current year upon a showing of current vaccinations and financial hardship. In the event of waiver due to financial hardship, the State shall not receive its portion of a dog license fee.

#### § 3622. Form of warrant

Such warrant shall be in the following form:

State of Vermont:	)
	)
	)
County, ss.	)
То	, constable or police officer of the town or city of

By the authority of the State of Vermont, you are hereby commanded forthwith to impound all dogs and wolf-hybrids not duly licensed according to law, except as exempted by 20 V.S.A. § 3587; and you are further required to make and return complaint against the owner or keeper of

any such dog or wolf-hybrid. A dog or wolf-hybrid that is impounded may be transferred to an animal shelter or rescue organization for the purpose of finding an adoptive home for the dog or wolf-hybrid. If the dog or wolf-hybrid cannot be placed in an adoptive home or transferred to a humane society or rescue organization within ten days, or a greater number of days established by the municipality, the dog or wolf-hybrid may be destroyed in a humane way.

Hereof fail not, and due return make of this warrant, with your doings thereon, within 90 days from the date hereof, stating the number of dogs or wolf-hybrids destroyed and the names of the owners or keepers thereof, and whether all unlicensed dogs or wolf-hybrids in such town (or city) have been destroyed, and the names of persons against whom complaints have been made under the provisions of 20 V.S.A. chapter 193, subchapters 1, 2, and 4, and whether complaints have been made and returned against all persons who have failed to comply with the provisions of such subchapter. Given under our (my) hands at \_\_\_\_\_\_ aforesaid, this \_\_\_\_\_\_ day of \_\_\_\_\_\_, 20 \_\_\_\_\_.

Legislative Body

#### § 3623. Constable to make complaints

A constable to whom such warrant has been issued shall make complaints therein required to be made to the town grand jurors.

#### § 3624. Who may destroy; fees

A police officer or constable shall humanely destroy or cause to be destroyed dogs or wolf-hybrids whenever a warrant has been issued authorizing such actions, except as exempted by section 3587 of this title. Any action must be taken within 90 days of the issuance of the warrant. The officer shall incinerate, bury or cause to be buried or otherwise properly dispose of their remains.

Any officers, other than those employed under regular pay, shall receive compensation for each dog or wolf-hybrid so destroyed as authorized by the legislative body of their respective towns. Bills for any services shall be approved by the legislative body of the municipality in which the dogs or wolf-hybrids are destroyed, and paid from moneys received under the provisions of this subchapter.

#### § 3625. Return by officers

Each police officer or constable to whom such warrant is issued shall make the return therein directed to the authority issuing the warrant within 90 days from its date.

#### § 3626. Certificate to state's attorney

The selectmen or mayor shall annually, within ten days from July 25, transmit a certificate, subscribed and sworn to, of the fact of the issue of such warrant, and whether the same has been duly executed and returned agreeably to the provisions of this chapter, to the

state's attorneys of their respective counties, who shall prosecute town officers who fail to comply with the provisions of this subchapter.

§ 3627. Repealed.

#### Subchapter 3: Kennels

#### § 3681. Pet dealer permit

A pet dealer shall apply to the municipal clerk of the town or city in which the cats, dogs, or wolf-hybrids are kept for a pet dealer permit to be issued on forms prescribed by the Secretary and pay the clerk a fee of \$25.00 for the same. A pet dealer who acquires a pet dealer permit shall allow inspections of the pet dealer's premises pursuant to section 3682 of this title as a condition of receiving and retaining the permit. The provisions of subchapters 1, 2, and 4 of this chapter not inconsistent with this subchapter shall apply to the pet dealer permit, which shall be in addition to other permits required. A pet dealer permit shall expire on March 31 next after issuance and shall be displayed prominently on the premises on which the cats, dogs, or wolf-hybrids are kept. If the permit fee is not paid by April 1, the owner or keeper may thereafter procure a permit for that license year by paying a fee of 50 percent in excess of that otherwise required. Municipal clerks shall maintain a record of the type of animals being kept by the permit holder. Upon issuance of the pet dealer permit, the municipal clerk shall provide the pet dealer with a copy of Part 3 (Standards) of the Animal Welfare Regulations adopted by the Agency of Agriculture, Food and Markets relating to cats, dogs, and wolf-hybrids. The municipal clerk shall also provide the pet dealer with contact information for the Animal Health Section within the Division of Food Safety and Consumer Protection of the Agency of Agriculture, Food and Markets and with information from the Department of Taxes on sales tax obligations for the sale of pets.

#### § 3682. Inspection of premises

- (a) The pet dealer's premises may be inspected upon the issuance of the pet dealer permit or at any time the pet dealer permit is in effect. Inspections may be conducted by a municipal animal control officer, a law enforcement officer as that term is defined in 23 V.S.A. § 4(11), or a representative of the Agency of Agriculture, Food and Markets. The inspector may, at his or her discretion and with the approval of the municipality, be accompanied by a veterinarian or an officer or agent of a humane society incorporated in Vermont. This section shall not create an obligation on the part of any municipal legislative body to conduct inspections.
- (b) Inspections shall be scheduled in advance with the pet dealer or pet dealer's agent. Inspections shall be conducted to facilitate compliance with the applicable standards in Part 3 (Standards) of the Animal Welfare Regulations adopted by the Agency of Agriculture, Food and Markets relating to cats, dogs, and wolf-hybrids. The person or persons authorized to inspect the pet dealer's premises shall be accompanied by the

pet dealer or pet dealer's agent. If the pet dealer's premises are also used for human habitation, the inspection may occur only in those areas of the premises used for animal housing, animal care, birthing, and storage of food and bedding. Photographs or videos of the pet dealer's premises or property shall not be taken during an inspection and while on the pet dealer's premises without the written consent of the permit holder. Repeated failure to consent to an inspection may result in a revocation of the pet dealer permit.

- (c) If an inspector, during the course of an inspection under this section, has reason to believe that a criminal animal welfare violation exists on the pet dealer's premises, nothing in this chapter shall preclude a criminal investigation into the suspected violation or shall preclude seeking the remedies available under 13 V.S.A. chapter 8. Assessment of an administrative penalty under this chapter shall not prevent assessment of a criminal penalty under 13 V.S.A. chapter 8.
- (d) The inspector shall record the results of each inspection in a log and sign and date each entry. The entries shall be submitted to the municipality, which shall maintain records of all pet dealer inspections. A copy of the inspection results shall be provided to the permit holder.

#### § 3683. Quarantine of premises

In the event such officer, representative or agent and veterinarian shall find that domestic pets or wolf-hybrids are kept under unsanitary or inhumane conditions, that there is communicable disease among them, or that the condition of the domestic pets or wolf-hybrids is such as to jeopardize or endanger the health or safety of persons, they shall quarantine said premises by an order in writing delivered to the holder of the permit, which quarantine shall remain in effect until the conditions affording a basis for such quarantine order have been remedied.

#### § 3684. Offenses; bill of costs in prosecution

The person operating a kennel who is found to have neglected to remedy conditions specified in said quarantine order, other than the prevalence of contagious disease, within ten days after receiving notice of such order, or who sells, gives away or otherwise removes a domestic pet or wolf-hybrid under quarantine or affected with a contagious disease, shall be subject to the penalty provided in 13 V.S.A. § 353(a)(1). Necessary fees and expenses of a veterinarian designated by such officer or agent shall be included in the bill of costs in a prosecution made hereunder and shall be taxed to the respondent.

#### Subchapter 4: Damages By Dogs

§§ 3741-3747. Repealed.

#### Subchapter 5: Control Of Rabies

#### § 3801. Rabies control authority

- (a) In the event of an outbreak of rabies, the secretary of agriculture, food and markets, the commissioner of fish and wildlife, and the commissioner of health shall work together to assist the affected towns. In addition to the responsibilities provided by this chapter, the agency of agriculture, food and markets shall generally be responsible for management of rabies in livestock, education of veterinarians and livestock owners concerning rabies and vaccination recommendations for livestock. The department of fish and wildlife shall generally be responsible for management of the sporting community, municipal officials and the general public about rabies in wildlife. The department of health shall generally be responsible for the prevention of rabies in humans, management of rabies in animals that may have exposed humans, and assisting with diagnosis of rabies in animals that may have exposed humans and supervision of health officials' education.
- (b) In addition to any other applicable authority, the agency of agriculture, food and markets, the department of health, and the department of fish and wildlife, may individually, or jointly, adopt rules to control the spread of rabies within a specific region, or within the state as a whole. The secretary of agriculture, food and markets is authorized to adopt rules necessary to control the spread of rabies in domestic animals, domestic pets and wolf-hybrids, including mandating the vaccination of specific species of animals, the conditions under which rabies inoculation clinics may be operated and establishing quarantines for domestic animals. The commissioner of fish and wildlife is authorized to adopt rules necessary to control the spread of rabies in wildlife, including mandating the vaccination of specific species of wild animals, translocation of wild animals and the destruction of wild animals through the use of registered pesticides, trapping or other means as may be necessary. The commissioner of health is authorized to adopt rules requiring the reporting of incidents of animals biting humans, the confinement, quarantine, observation and disposition of animals that are suspected of exposing humans to rabies, and the disposition of animals bitten by animals suspected of carrying rabies and other rules as necessary to protect the general public from rabies.
- (c) The agency of agriculture, food and markets, the department of health, and the department of fish and wildlife, may cooperate with other federal, state and local officials in controlling the spread of rabies within the state and within the region.

#### § 3802. Quarantine

With the approval of the governor, a town, county or the entire state may be placed under quarantine for such time as may be considered necessary by the commissioner of health, or the secretary of agriculture, food and markets.

#### § 3803. Notice

When a quarantine is established as provided in section 3802 of this title notice of such quarantine shall be sent to the chairman of boards of selectmen, mayors, health officers and to the town clerk of each municipality in the quarantined area. Notice of such quarantine shall be printed in one or more newspapers circulating in the quarantined area.

#### §§ 3804, 3805. Repealed.

#### § 3806. Confining or impounding a domestic pet or wolf-hybrid

- (a) Any person authorized to enforce state livestock disease control, health, wildlife, or criminal laws and any person authorized to enforce local ordinances may confine, or impound any domestic pet or wolf-hybrid when:
  - (1) It is suspected of having been exposed to rabies.
  - (2) It is believed to have been attacked by another animal which may be rabid.
  - (3) It has been attacked by a wild animal.
  - (4) It has been running at large in violation of any of the provisions of this subchapter.
  - (5) It has an unknown rabies vaccination history.
- (b) In the event that a domestic pet or wolf-hybrid is confined or impounded under this section, the owner, if known, shall be notified within 24 hours. Notification may be accomplished by in-person communication, by telephone call, or by written statement sent to the last known address of the owner. If the owner's address is not known, notification may be posted in the municipal clerk's office and other usual places for public notice for a one-week period.
- (c) Any domestic pet or wolf-hybrid which is considered a rabies suspect shall be managed in accordance with the rules of the department of health. Rules adopted by the department of health in accordance with this chapter shall provide for management of domestic pets or wolf-hybrids for whom there is no approved rabies vaccine.

#### § 3807. Killing a domestic pet or wolf-hybrid

(a) When the legislative body, a municipal officer designated by the legislative body, the commissioner of the department of fish and wildlife, the commissioner of the department of health, or the secretary of the agency of agriculture, food and markets reasonably suspects that a domestic pet or wolf-hybrid impounded under section 3806 of this title has been exposed to rabies, has been attacked by a rabid animal or has been running at large in violation of any of the provisions of this subchapter the official shall order the domestic pet or wolf-hybrid to be killed. However, if the official finds that it is not reasonable to suspect that a domestic pet or wolf-hybrid

impounded under section 3806 of this title is rabid or has been exposed to rabies, the official may deliver the domestic pet or wolf-hybrid to the owner. When it is impractical to confine or impound a domestic pet or wolf-hybrid pursuant to section 3806 of this title, or when the owner of a domestic pet or wolf-hybrid confined or impounded cannot be ascertained, the officials may immediately order the domestic pet or wolf-hybrid to be killed.

- (b) In the event that a domestic pet is suspected of exposing a human, pet, wolf-hybrid, or domestic animal to rabies, it shall be managed in accordance with the provisions of this subchapter and the rules of the department of health.
- (c) Since there is no approved preexposure rabies vaccine for wolf-hybrids, until the commissioner finds and approves a rabies vaccine, any wolf-hybrid which bites or otherwise exposes a human, pet, or domestic animal to rabies shall immediately be destroyed and its head shall be sent to the state department of health for the purpose of testing its brain tissue for the presence of the disease. If an alternative means of testing is provided by rule of the department of health, that procedure may be substituted for the procedure described in this subsection. The legislative body of the municipality or a municipal officer designated by the legislative body shall be responsible for ensuring the provisions of this subsection are carried out.

#### § 3808. Fees for killing domestic pets or wolf-hybrids

Officers shall be entitled to the same fees for killing domestic pets or wolf-hybrids under the provisions of this subchapter as are provided in section 3624 of this title. The owner of an impounded domestic pet or wolf-hybrid or the town, in case the owner of the domestic pet or wolf-hybrid cannot be identified, shall be liable for all such fees.

#### § 3809. Killing a domestic pet or wolf-hybrid which attacks a person or domestic animal

Nothing in this subchapter shall be construed as preventing any person from killing a suspected rabid domestic pet or wolf-hybrid which attacks a person, another domestic pet or wolf-hybrid or domestic animal. A person so killing such domestic pet or wolf-hybrid shall not be held liable for damages for such killing.

#### § 3810. Repealed.

#### § 3811. Carcass disposal

In order to protect the public health, the legislative body of a municipality or a municipal officer designated by the legislative body may dispose of the carcass of any animal suspected of having been exposed to rabies through incineration. Disposal of animal carcasses in the manner provided by this section shall not be subject to the provisions of chapter 23 of Title 10 and the rules promulgated thereunder.

#### § 3812. Immunity from liability for volunteers

Any person who as a volunteer conducts or assists at a nonprofit public clinic for inoculating domestic pets, wolf-hybrids, and domestic animals against rabies shall not be liable to any other person for injuries resulting from the loss of animals, animal bites and from the inoculation process.

#### § 3813. Vaccination administration

- (a) The commissioner may purchase rabies vaccine for distribution at reduced cost to the public through rabies clinics.
- (b) The commissioner shall ensure that reduced cost rabies clinics take place in all geographic areas of the state and shall cooperate with the veterinary profession to make certain that all owners of domestic pets and wolf-hybrids have access to reasonably priced rabies vaccines.

Veterinarians shall provide an owner of a domestic pet or wolf-hybrid with a completed rabies vaccination form and tag for each animal which has been inoculated against rabies.

### Subchapter 6: Dog, Cat, And Wolf-hybrid Spaying And Neutering Program And Fund

#### § 3814. Findings

The general assembly finds:

- (1) The supply of dogs, cats, and wolf-hybrids in Vermont is a major concern.
- (2) There are insufficient resources in this state to care for or provide homes for these animals.
- (3) Many of these animals are ultimately euthanized or become victims of accidents, starvation, or disease.
- (4) Pet owners who have limited economic resources have great difficulty affording the cost of professional spaying and neutering services.

#### § 3815. Dog, cat, and wolf-hybrid spaying and neutering program

- (a) The agency of human services shall administer a dog, cat, and wolf-hybrid spaying and neutering program providing reduced-cost spaying and neutering services and presurgical immunization for dogs, cats, and wolf-hybrids owned or cared for by low income individuals. The agency shall implement the program through an agreement with a qualified organization consistent with the applicable administrative rules.
- (b) The program shall reimburse veterinarians who voluntarily consent to spay or neuter dogs, cats, and wolf-hybrids under the auspices of the program. The reimbursement shall be less any co-payment by the owner of a dog, cat, or wolf-hybrid for the cost of each spaying or neutering procedure.

(c) The secretary of human services, in consultation with the chair of the Vermont Board of Veterinary Medicine, may adopt and amend rules pursuant to chapter 25 of Title 3 to enable the agency to carry out the purposes of this act.

#### § 3816. Animal spaying and neutering fund; creation

- (a) There is created, pursuant to subchapter 5 of chapter 7 of Title 32, in the agency of human services the dog, cat, and wolf-hybrid spaying and neutering special fund to finance the costs of the dog, cat, and wolf-hybrid spaying and neutering program established in section 3815 of this title.
- (b) Revenue for the fund shall be derived from:
  - (1) The surcharge payment paid to a municipality pursuant to subdivision 3581(c)(1) of this title.
  - (2) Gifts from private donors.
  - (3) Any appropriation which the general assembly makes to the fund.
- (c) Interest earned on the fund shall be retained in the fund.
- (d) The agency of human services shall use the revenue in the fund created in subsection(a) of this section for administering the dog, cat, and wolf-hybrid spaying and neutering program.

#### § 3817. Rules adoption authority

The agency of agriculture, food and markets may adopt rules to implement this subchapter.

#### FINAL RULES

#### VACCINATION OF DOMESTIC PETS, WOLD/HYBRIDS AND LIVESTOCK AGAINST RABIES; RABIES VACCINATION CLINICS

#### **RABIES VACCINATION IN GENERAL**

#### 1. <u>DEFINITIONS:</u>

- a. "Commissioner" where no other department is referenced means the Commissioner of the Department of Agriculture, Food and Markets, and includes his or her designee.
- b. "Domestic Pet" or "Pets" means any domestic dogs, domestic cats and ferrets and such other domestic animals as the commissioner shall establish by rule, provided that the commissioner finds that the animals has the potential to become an imminent danger to public health or welfare if not subjected to the provisions of Title 20, Chapter 193, "Domestic Pet or Wolf-hybrid control."
- c. "Ferret" means only the European ferret (Mustela putorious furo).
- d. "For-profit clinics: means any rabies vaccination clinic conducted by a veterinarian, or organization that does not qualify as a non-profit public rabies clinic.
- e. "Livestock" means those domestic animals defined in 6 V.S.A. §1151(2), including but not limited to cattle, sheep, goats, equines, fallow and red deer, American bison, swine, camelids.
- f. "Non-profit public rabies clinic" or "non-profit clinic" means a clinic conducted for the public by a non-profit organization or municipality. Income from operation of the clinic minus reasonable expenses, shall be used for rabies management. However, if the clinic is staffed by volunteers provided by a nonprofit organization, the income from operation of the clinic, minus reasonable expenses, may be used to support the activities of that organization. Reasonable expenses of a non-profit public clinic may include the cost of: rabies vaccine; rabies certificates and tags; supplies needed to administer the vaccine; rental of facility to hold the clinic; advertising; and stipend paid to volunteers. The total stipend paid shall not exceed \$2.00 per rabies vaccination for the first 100 rabies vaccinations and \$1.00 per rabies vaccination thereafter.
- g. "Volunteer", a volunteer for purposes of the immunity from liability set forth in 20 V.S.A. §3812, means a lay person or veterinarian who works at a non-profit rabies vaccination clinic and received no compensation for his or her services or time, other than the stipend authorized by these rules.

h. "Wold-hybrid" means an animal which is the progeny or descendant of a domestic dog (Canis familiaris) and a wolf (Canis lupus or Canis rufus). "Wolf-hybrid" also means an animal which is advertised, registered, licensed or otherwise described or represented as a wolf-hybrid by its owner or an animal which exhibits primary physical and behavioral wolf characteristics, as defined by the Commissioner of the Department of Fish and Wildlife.

#### 2. <u>ADMINISTRATION AND USE OF RABIES VACCINATIONS:</u>

- a. The Commissioner shall maintain a list of rabies vaccines approved for domestic pets, livestock and when and if a vaccine becomes available, for wolf/hybrids, as required by 20 V.S.A. §3581a (b), (c) and §(a). No vaccine shall be used unless its use is first approved by the Commissioner.
- b. The following persons may administer rabies vaccinations:
  - (1) To domestic pets and wold-hybirds:

Rabies vaccinations must be performed by a licensed veterinarian or under the direct supervision of a licensed veterinarian, which shall mean that the veterinarian has examined the animal, has authorized its immediate vaccination against rabies, and is on the premises at the time the animal is vaccinated. The person who administers the rabies vaccine must be employed in, or working at, the same veterinary practice as the supervising licensed veterinarian. All rabies certificates must be signed by the licensed veterinarian.

(2) To feral cats:

A person may use an approved vaccine to inoculate a feral feline that takes up residence in a building other than the person's home. A licensed veterinarian is not required.

- (3) To livestock:
  - a. A person may administer an approved rabies vaccine for the species of livestock to be inoculated. The following should be considered:
    - 1. When a licensed veterinarian individually identifies the livestock and uses an approved rabies vaccine for the species, the livestock will be considered officially vaccinated by public health officials and others who require proof of vaccinations.

- 2. When rabies vaccine is administered by a person not licensed as a veterinarian, the livestock may not be considered vaccinated by public health officials and others who require proof of vaccination.
- A licensed veterinarian may recommend a rabies vaccine for use in livestock for which there is no approved vaccine commercially available. Any person may administer the rabies vaccine to livestock in accordance with the veterinarian's recommendation. Livestock vaccinated according to the veterinarian's recommendation may not be considered vaccinated by public health officials and others who require proof of vaccination.
- C. Rabies vaccinations shall be administered as follows:
  - (1) To domestic pet: in accordance with the manufacturer's recommendation.
  - (2) To wolf/hybrids: rabies vaccine approved for dogs must be administered to wolf/hybrids in a similar manner as recommended by the manufacturer for the inoculation of dogs against rabies until a rabies vaccine is approved for wolf/hybrids.
  - (3) To feral cats: in accordance with the manufacturer's recommendations.
  - (4) To livestock: approved vaccines must be administered in accordance with the manufacturer's recommendations. A licensed veterinarian may recommend the administration of rabies vaccine to livestock for which there is no approved rabies vaccine commercially available, including the dosage and the route of administration.
    - D. Rabies vaccination must be administered to domestic pets and wolf/hybrids prior to the age of 4 months unless in the judgement of the veterinarian the animals's medical condition would prevent the development of adequate immunity to rabies. Animals so exempted must be inoculated against rabies as soon as their medical condition permits.

#### 3. <u>RABIES VACCINATED CLINICS</u>

a. The rules for administration and use of rabies vaccine shall apply to rabies vaccines administered at any non-profit clinics and for-profit clinics. In the case of a non-profit clinic, if the vaccine is administered by other that a veterinarian, that person must be employed by or work at a veterinary practice. A licensed veterinarian shall be on site at all times any clinic is in operation.

- b. Records;
  - 1. Rabies vaccination certificates signed by a licensed veterinarians and rabies tags shall be provided for all domestic pets and wolf-hybrids vaccinated at rabies vaccination clinics.
  - 2. Copies of all the rabies vaccination certificates issued at the clinic will be provided to the municipal clerk of the municipality where the clinic is conducted. The clerk shall maintain these records for a minimum of three years or allow a veterinarian to maintain the records under the clerk's supervision

#### 4. <u>ENFORCEMENT</u>

A civil penalty up to \$500.00 per violation of these rules may be imposed by an officer designated by the Commissioner in accordance with 20 V.S.A. §3550.

# **Section 3. National Guidelines**

- A. Compendium of Animal Rabies Prevention and Control, 2016
- B. Human Rabies Prevention—United States, 2008
- C. Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies, 2010

### **Public Veterinary Medicine: Public Health**

# Compendium of Animal Rabies Prevention and Control, 2016

National Association of State Public Health Veterinarians Compendium of Animal Rabies Prevention and Control Committee

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Endorsed by the AVMA, American Public Health Association, Association of Public Health Laboratories, Council of State and Territorial Epidemiologists, and National Animal Care and Control Association.

This article has not undergone peer review.

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Rabies is a fatal viral zoonosis and serious public health problem.<sup>1</sup> All mammals are believed to be susceptible to the disease, and for the purposes of this document, use of the term animal refers to mammals. The disease is an acute, progressive encephalitis caused by viruses in the genus *Lyssavirus*.<sup>2</sup> Rabies virus is the most important lyssavirus globally. In the United States, multiple rabies virus variants are maintained in wild mammalian reservoir populations such as raccoons, skunks, foxes, and bats. Although the United States has been declared free from transmission of canine rabies virus variants, there is always a risk of reintroduction of these variants.<sup>3-7</sup>

The rabies virus is usually transmitted from animal to animal through bites. The incubation period is highly variable. In domestic animals, it is generally 3 to 12 weeks, but can range from several days to months, rarely exceeding 6 months.<sup>8</sup> Rabies is communicable during the period of salivary shedding of rabies virus. Experimental and historic evidence documents that dogs, cats, and ferrets shed the virus for a few days prior to the onset of clinical signs and during illness. Clinical signs of rabies are variable and include inappetance, dysphagia, cranial nerve deficits, abnormal behavior, ataxia, paralysis, altered vocalization, and seizures. Progression to death is rapid. There are currently no known effective rabies antiviral drugs.

The recommendations in this compendium serve as a basis for animal rabies prevention and control programs throughout the United States and facilitate standardization of procedures among jurisdictions, thereby contributing to an effective national rabies control program. The compendium is reviewed and revised as necessary, with the most current version replacing all previous versions. These recommendations do not supersede state and local laws or requirements. Principles of rabies prevention and control are detailed in Part I, and recommendations for parenteral vaccination procedures are presented in Part II. All animal rabies vaccines licensed by the USDA and marketed in the United States are listed and described in Appendix 1, and contact information for manufacturers of these vaccines is provided in Appendix 2.

Modifications of note in this updated version of the compendium, compared with the previous version,<sup>9</sup> include clarification of language, explicit encouragement of an interdisciplinary approach to rabies control, a recommendation to collect and report at the national level additional data elements on rabid domestic animals, changes to the recommended management of dogs and cats exposed to rabies that are either unvaccinated or overdue for booster vaccination, reduction of the recommended 6-month quarantine period for certain species, and updates to the list of marketed animal rabies vaccines.

#### Part I. Rabies Prevention and Control

# A. Principles of rabies prevention and control

**1. Case definition.** An animal is determined to be rabid after diagnosis by a qualified laboratory as specified (*see* Part I.A. 10. Rabies diagnosis).The national case definition for animal rabies requires laboratory confirmation on the basis of either a positive result for the direct fluorescent antibody test (preferably performed on CNS tissue) or isolation of rabies virus in cell culture or a laboratory animal.<sup>10</sup>

**2. Rabies virus exposure.** Rabies is transmitted when the virus is introduced into bite wounds, into open cuts in skin, or onto mucous membranes from saliva or other potentially infectious material such as neural tissue.<sup>11</sup> Questions regarding possible exposures should be directed promptly to state or local public health authorities.

3. Interdisciplinary approach. Clear and consistent communication and coordination among relevant animal and human health partners across and within all jurisdictions (including international, national, state, and local) is necessary to most effectively prevent and control rabies. As is the case for the prevention of many zoonotic and emerging infections, rabies prevention requires the cooperation of animal control, law enforcement, and natural resource personnel; veterinarians; diagnosticians; public health professionals; physicians; animal and pet owners; and others. An integrated program must include provisions to promptly respond to situations; humanely restrain, capture, and euthanize animals; administer quarantine, confinement, and observation periods; and prepare samples for submission to a testing laboratory.

4. Awareness and education. Essential components of rabies prevention and control include ongoing public education, responsible pet ownership, routine veterinary care and vaccination, and professional continuing education. Most animal and human exposures to rabies can be prevented by raising awareness concerning rabies transmission routes, the importance of avoiding contact with wildlife, and the need for appropriate veterinary care. Prompt recognition and reporting of possible exposures to medical and veterinary professionals and local public health authorities are critical.

5. Human rabies prevention. Rabies in humans can be prevented by eliminating exposures to rabid animals or by providing exposed persons prompt postexposure prophylaxis consisting of local treatment of wounds in combination with appropriate administration of human rabies immune globulin and vaccine. An exposure assessment should occur before rabies postexposure prophylaxis is initiated and should include discussion between medical providers and public health officials. The rationale for recommending preexposure prophylaxis and details of both preexposure and postexposure prophylaxis administration can be found in the current recommendations of the Advisory Committee on Immunization Practices.<sup>11,12</sup>These recommendations, along with information concerning the current local and regional epidemiology of animal rabies and the availability of human rabies biologics, are available from state health departments.

6. Domestic animal vaccination. Multiple vaccines are licensed for use in domestic animal species. Vaccines available include inactivated and modified-live virus vectored products, products for IM and SC administration, products with durations of immunity for periods of 1 to 3 years, and products with various minimum ages of vaccination. Recommended vaccination procedures are specified in Part II of this compendium; animal rabies vaccines licensed by the USDA and marketed in the United States are specified in Appendix 1. Local governments should initiate and maintain effective programs to ensure vaccination of all dogs, cats, and ferrets and to remove stray and unwanted animals. Such procedures have reduced laboratory-confirmed cases of rabies among dogs in the United States from 6,949 cases in 1947 to 89 cases in 2013.<sup>3</sup> Because more rabies cases are reported annually involving cats (247 in 2013) than dogs, vaccination of cats should be required.<sup>3</sup> Animal shelters and animal control authorities should establish policies to ensure that adopted animals are vaccinated against rabies.

An important tool to optimize public and animal health and enhance domestic animal rabies control is routine or emergency implementation of low-cost or free clinics for rabies vaccination. To facilitate implementation, jurisdictions should work with veterinary medical licensing boards, veterinary associations, the local veterinary community, animal control officials, and animal welfare organizations.

**7. Rabies in vaccinated animals.** Rabies is rare in vaccinated animals.<sup>13-15</sup> If rabies is suspected in a vaccinated animal, it should be reported to public health officials, the vaccine manufacturer, and the USDA APHIS Center for Veterinary Biologics

(www.aphis.usda.gov; search for "adverse event reporting"). The laboratory diagnosis should be confirmed and the virus variant characterized by the CDC's rabies reference laboratory. A thorough epidemiologic investigation including documentation of the animal's vaccination history and potential rabies exposures should be conducted.

8. Rabies in wildlife. It is difficult to control rabies among wildlife reservoir species.<sup>16</sup> Vaccination of free-ranging wildlife or point infection control is useful in some situations,<sup>17</sup> but the success of such procedures depends on the circumstances surrounding each rabies outbreak (See Part I. C. Prevention and control methods related to wildlife). Because of the risk of rabies in wild animals (especially raccoons, skunks, coyotes, foxes, and bats), the AVMA, American Public Health Association, Council of State and Territorial Epidemiologists, National Animal Care and Control Association, and National Association of State Public Health Veterinarians strongly recommend the enactment and enforcement of state laws prohibiting the importation, distribution, translocation, and private ownership of wild animals.

9. Rabies surveillance. Laboratory-based rabies surveillance and variant typing are essential components of rabies prevention and control programs. A comprehensive surveillance program should not be limited to testing only those animals that have potentially exposed people or domestic animals to rabies. Accurate and timely information and reporting are necessary to guide decisions regarding postexposure prophylaxis in potentially exposed humans, determine appropriate management of potentially exposed animals, aid in the discovery of emerging variants, describe the epidemiology of the disease, and assess the effectiveness of vaccination programs for domestic animals and wildlife. Every animal submitted for rabies testing should be reported to the CDC to evaluate surveillance trends. Public health authorities should implement electronic laboratory reporting and notification systems.<sup>18</sup> Information reported on every animal submitted for rabies testing should include species, point location, vaccination status, rabies virus variant (if rabid), and human or domestic animal exposures. To enhance the ability to make evidencebased recommendations from national surveillance data, additional data should be collected and reported on all rabid domestic animals. In this regard, essential data elements include age, sex, neuter status, ownership status, quarantine dates (if any), date of onset of any clinical signs, and complete vaccination history. Rabid animals with a history of importation into the United States within the past 60 days are immediately notifiable by state health departments to the CDC; for all indigenous cases, standard notification protocols should be followed.<sup>19</sup>

#### 10. Rabies diagnosis.

a) The direct fluorescent antibody test is the gold standard for rabies diagnosis. The test should be performed in accordance with the established national standardized protocol (www.cdc.gov/rabies/pdf/rabiesdfaspv2. pdf) by a qualified laboratory that has been designated by the local or state health department.<sup>20,21</sup> Animals submitted for rabies testing should be euthanized<sup>22,23</sup> in such a way as to maintain the integrity of the brain so that the laboratory can recognize anatomic structures. Except in the case of very small animals, such as bats, only the head or entire brain (including brainstem) should be submitted to the laboratory. To facilitate prompt laboratory testing, submitted specimens should be stored and shipped under refrigeration without delay. The need to thaw frozen specimens will delay testing. Chemical fixation of tissues should be avoided to prevent significant testing delays and because such fixation might preclude reliable testing. Questions about testing of fixed tissues should be directed to the local rabies laboratory or public health department.

b) Rabies testing should be available outside of normal business hours at the discretion of public health officials to expedite exposure management decisions.<sup>20</sup> When confirmatory testing is needed by state health departments (eg, in the event of inconclusive results, unusual species, or mass exposures), the CDC rabies laboratory can provide additional testing and results within 24 hours of sample receipt.<sup>24</sup>

c) Professional associations such as the Association of Public Health Laboratories should advocate for, distribute, and promote the development of guidelines for routinely assessing testing practices within rabies laboratories to ensure maintenance of quality and safety.

d) A direct rapid immunohistochemical test (referred to as dRIT) is being used by trained field personnel in surveillance programs for specimens not involved in human or domestic animal exposures.<sup>25-28</sup> All positive direct rapid immunohistochemical test results need to be confirmed by means of direct fluorescent antibody testing at a qualified laboratory.

e) Currently, there are no commercially available, USDA-licensed rapid test kits for rabies diagnosis. Unlicensed tests should not be used owing to the following concerns: sensitivity and specificity of these tests are not known, the tests have not been validated against current standard methods, the excretion of virus in the saliva is intermittent and the amount varies over time, any unlicensed test result would need to be confirmed by validated methods such as direct fluorescent antibody testing on brain tissue, and the interpretation of results from unlicensed tests may place exposed animals and persons at risk.

**11. Rabies serology**. Some jurisdictions require evidence of vaccination and rabies virus antibodies for animal importation purposes. Rabies virus antibody titers are indicative of a response to vaccine or infection. Titers do not directly correlate with protection because other immunologic factors also play a role in preventing rabies and our abilities to measure and interpret those other factors are not well-developed. Therefore, evidence of circulating rabies virus antibodies in animals should not be used as a substitute for current vaccination in managing rabies exposures or determining the need for booster vaccination.<sup>29-32</sup>

12. Rabies research. Information derived from well-designed studies is essential for the development of evidence-based recommendations. Data are needed in several areas, including viral shedding periods for domestic livestock and lagomorphs, potential shedding of virus in milk, the earliest age at which rabies vaccination is effective, protective effect of maternal antibody, duration of immunity, postexposure prophylaxis protocols for domestic animals, models for treatment of clinical rabies, extralabel vaccine use in domestic animals and wildlife rabies reservoir species, host-pathogen adaptations and dynamics, and the ecology of wildlife rabies reservoir species, especially in relation to the use of oral rabies vaccines.

# **B.** Prevention and control methods in domestic and confined animals

1. Preexposure vaccination and management. Adherence to a regular rabies vaccination schedule is critical to protect animals against recognized and unrecognized rabies exposures. Parenteral animal rabies vaccines should be administered only by or under the direct supervision of a licensed veterinarian on premises. Rabies vaccines may be administered under the supervision of a licensed veterinarian to animals held in animal shelters before release.<sup>33,34</sup> The veterinarian signing a rabies vaccination certificate must ensure that the person who administered the vaccine is identified on the certificate and has been appropriately trained in vaccine storage, handling, and administration and in the management of adverse events. This ensures that a qualified and responsible person can be held accountable for properly vaccinating the animal.

Within 28 days after initial vaccination, a peak rabies virus antibody titer is expected, and the animal can be considered immunized.<sup>31,35-37</sup> Regardless of the age of the animal at initial vaccination, a booster vaccination should be administered 1 year later (*see* Part II and Appendix 1). An animal is currently vaccinated and is consid-

ered immunized immediately after any booster vaccination.<sup>38,39</sup>

a) Booster vaccination. Following the initial vaccination, booster vaccinations should be given in a manner consistent with the manufacturer's label. If a previously vaccinated animal is overdue for any booster vaccination, including the first booster vaccination due 1 vear after initial vaccination, it should be given a booster vaccination. Immediately after this booster vaccination, the animal is considered currently vaccinated and should be placed on a booster vaccination schedule consistent with the label of the vaccine used. There are no laboratory or epidemiological data to support the annual or biennial administration of 3-year vaccines after completion of the initial vaccine series (ie, the initial vaccination and 1-year booster vaccination).

b) Dogs, cats, and ferrets. All dogs, cats, and ferrets should be vaccinated against rabies and revaccinated in accordance with recommendations in this compendium (Appendix 1).

c) Livestock. All horses should be vaccinated against rabies.<sup>40</sup> Livestock, including species for which licensed vaccines are not available, that have frequent contact with humans (eg, in petting zoos, fairs, and other public exhibitions) should be vaccinated against rabies.<sup>41,42</sup> Consideration should also be given to vaccinating livestock that are particularly valuable.

d) Captive wild animals and wild animal hybrids (the offspring of wild animals crossbred to domestic animals).

(1) Wild animals and wild animal hybrids should not be kept as pets.<sup>43,44</sup> No parenteral rabies vaccines are licensed for use in wild animals or wild animal hybrids.<sup>45</sup>

(2) Animals that are farmed (eg, for food, fur, or fiber) or maintained in exhibits or zoological parks and that are not completely excluded from all contact with rabies vectors can become infected.<sup>46</sup> Moreover, wild animals might be incubating rabies when initially captured. Therefore, wild-caught animals susceptible to rabies should be quarantined for a minimum of 6 months.

(3) Employees who work with animals in exhibits or zoological parks should receive preexposure rabies vaccination. The use of preexposure or postexposure rabies vaccination for handlers who work with animals at such facilities might reduce the need for euthanasia of captive animals that expose handlers. Carnivores and bats should be housed in a manner that precludes direct contact with the public.<sup>41,42</sup> Consideration may be given to vaccinating animals that are particularly valuable (*see* Part II. D. Vaccination of wild-life and wild animal hybrids).

**2. Stray animals**. Stray dogs, cats, and ferrets should be removed from the community, and mechanisms should be put in place to facilitate voluntary surrender of animals to prevent abandonment. Local health departments and animal control officials can enforce the removal of strays more effectively if owned animals are required to have identification and be confined or kept on leash. Strays should be impounded for at least 3 business days to determine whether human exposure has occurred and to give owners sufficient time to reclaim animals.

Stray and feral cats serve as a significant source of rabies exposure risk.<sup>47</sup> If communities allow maintenance of feral cat colonies despite this risk, they should safeguard the health of the cats and the communities in which they reside by requiring that cats receive initial rabies vaccinations and appropriately scheduled booster vaccinations.

#### 3. Importation and interstate movement of animals.

a) Areas with dog-to-dog rabies transmission. Canine rabies virus variants have been eliminated from the United States<sup>3,7</sup>; however, rabid dogs and a rabid cat have been introduced into the continental United States from areas with dog-to-dog rabies transmission.<sup>4–6,48,49</sup> The movement of dogs for the purposes of adoption or sale from areas with dog-to-dog rabies transmission increases the risk of introducing canine-transmitted rabies to areas where it does not currently exist, and this practice should be prohibited.

b) International importation. Current federal regulations are insufficient to prevent the introduction of rabid animals into the United States and must be strengthened and appropriately enforced.<sup>4-6,48,49</sup> The CDC and USDA APHIS have regulatory authority over the importation of dogs and cats into the United States.<sup>6</sup> Importers of dogs must comply with rabies vaccination requirements.<sup>50,51</sup> These regulations require that dogs from rabiesendemic countries be currently vaccinated against rabies prior to importation. The appropriate health official of the state of destination should be notified by the appropriate federal authorities within 72 hours of the arrival of any unvaccinated imported dog required to be placed in confinement (as defined by the CDC<sup>52</sup>) under these regulations. Failure of the owner to comply with these confinement requirements should be promptly reported to the CDC's Division of Global Migration and Quarantine (CDCAnimalImports@cdc.gov).

All imported dogs and cats are also subject to state and local laws governing rabies and

should be currently vaccinated against rabies with USDA-licensed products in accordance with this compendium. Failure of the owner to comply with state or local requirements should be referred to the appropriate state or local official.

c) Interstate movement (including commonwealths and territories). Before interstate movement occurs, dogs, cats, ferrets, and horses should be currently vaccinated against rabies in accordance with this compendium.Animals in transit should be accompanied by a current, valid rabies vaccination certificate such as Form 51 from the National Association of State Public Health Veterinarians.<sup>53</sup> When an interstate health certificate or certificate of veterinary inspection is required, it should contain the same rabies vaccination information as Form 51.

**4.** Adjunct procedures. Methods or procedures that enhance rabies control include the following<sup>54</sup>:

a) Identification. Dogs, cats, and ferrets should be identified (eg, metal or plastic tags or microchips) to allow for verification of rabies vaccination status.

b) Licensure. Registration or licensure of all dogs, cats, and ferrets is an integral component of an effective rabies control program.A fee is frequently charged for such licensure, and revenues collected are used to maintain rabies or animal control activities. Evidence of current vaccination should be an essential prerequisite to licensure.

c) Canvassing. House-to-house canvassing by animal control officials facilitates enforcement of vaccination and licensure requirements.

d) Citations. Citations are legal summonses issued to owners for violations, including the failure to vaccinate or license their animals. The authority for officers to issue citations should be an integral part of animal control programs.

e) Animal control. All local jurisdictions should incorporate training and continuing education of personnel regarding stray-animal control, leash laws, animal bite prevention, and rabies prevention and control into their programs.

f) Public education. All local jurisdictions should incorporate education covering responsible pet ownership, bite prevention, and appropriate veterinary care into their programs.

**5. Postexposure management.** This section refers to any animal exposed (*see* Part I.A. 2. Rabies virus exposure) to a confirmed or suspected rabid animal. Wild mammalian carnivores, skunks, and bats that are not available or suitable for testing should be regarded as rabid. The rationale for

observation, confinement, or strict quarantine periods of exposed animals despite previous vaccination is based in part on the potential for overwhelming viral challenge, incomplete vaccine efficacy, improper vaccine administration, variable host immunocompetence, and immune-mediated death (ie, early death phenomenon).<sup>13,55-57</sup>

a) Dogs, cats, and ferrets. Any illness in an exposed animal should be reported immediately to the local health department. If signs suggestive of rabies develop (eg, paralysis or seizures), the animal should be euthanized, and the head or entire brain (including brainstem) should be submitted for testing (*see* Part I.A. 10. Rabies diagnosis).

(1) Dogs, cats, and ferrets that are current on rabies vaccination should immediately receive veterinary medical care for assessment, wound cleansing, and booster vaccination. The animal should be kept under the owner's control and observed for 45 days.

(2) Dogs, cats, and ferrets that have never been vaccinated should be euthanized immediately. There are currently no USDA-licensed biologics for postexposure prophylaxis of previously unvaccinated domestic animals, and there is evidence that the use of vaccine alone will not reliably prevent the disease in these animals.<sup>58</sup> If the owner is unwilling to have the animal euthanized, the animal should be placed in strict guarantine for 4 (dogs and cats) or 6 (ferrets) months. Strict quarantine in this context refers to confinement in an enclosure that precludes direct contact with people and other animals. A rabies vaccine should be administered at the time of entry into quarantine to bring the animal up to current rabies vaccination status. Administration of vaccine should be done as soon as possible. It is recommended that the period from exposure to vaccination not exceed 96 hours.<sup>59,60</sup> If vaccination is delayed, public health officials may consider increasing the quarantine period for dogs and cats from 4 to 6 months, taking into consideration factors such as the severity of exposure, the length of delay in vaccination, current health status, and local rabies epidemiology.

(3) Dogs and cats that are overdue for a booster vaccination and that have appropriate documentation of having received a USDA-licensed rabies vaccine at least once previously should immediately receive veterinary medical care for assessment, wound cleansing, and booster vaccination. The animal should be kept under the owner's control and observed for 45 days.<sup>39</sup> If booster vaccination is delayed, public health officials may consider increasing the observation period for the animal, taking into consideration factors such as the severity of exposure, the length of delay in booster vaccination, current health status, and local rabies epidemiology.

(4) Dogs and cats that are overdue for a booster vaccination and without appropriate documentation of having received a USDA-licensed rabies vaccine at least once previously should immediately receive veterinary medical care for assessment, wound cleansing, and consultation with local public health authorities.

(a) The animal can be treated as unvaccinated, immediately given a booster vaccination, and placed in strict quarantine (*see* Part I. B. 5. a) (2)).

(b) Alternatively, prior to booster vaccination, the attending veterinarian may request guidance from the local public health authorities in the possible use of prospective serologic monitoring. Such monitoring would entail collecting paired blood samples to document prior vaccination by providing evidence of an anamnestic response to booster vaccination. If an adequate anamnestic response is documented, the animal can be considered to be overdue for booster vaccination (see Part I. B. 5. a) (3)) and observed for 45 days.<sup>39</sup> If there is inadequate evidence of an anamnestic response, the animal is considered to have never been vaccinated and should be placed in strict quarantine (see Part I. B. 5. a) (2)).

(5) Ferrets that are overdue for a booster vaccination should be evaluated on a case-by-case basis, taking into consideration factors such as the severity of exposure, time elapsed since last vaccination, number of previous vaccinations, current health status, and local rabies epidemiology, to determine need for euthanasia or immediate booster vaccination followed by observation or strict quarantine.

b) Livestock. All species of livestock are susceptible to rabies; cattle and horses are the most frequently reported infected species.<sup>3</sup> Any illness in an exposed animal should be reported immediately to the local health department and animal health officials. If signs suggestive of rabies develop, the animal should be euthanized, and the head or entire brain (including brainstem) should be submitted for testing (*see* Part I.A. 10. Rabies diagnosis).

(1) Livestock that have never been vaccinated should be euthanized immediately. Animals that are not euthanized should be confined and observed on a case-by-case basis for 6 months.

(2) Livestock that are current on rabies vaccination with a USDA-licensed vaccine approved for that species should be given a booster vaccination immediately and observed for 45 days.

(3) Livestock overdue for a booster vaccination should be evaluated on a case-by-case basis, taking into consideration factors such as severity of exposure, time elapsed since last vaccination, number of previous vaccinations, current health status, and local rabies epidemiology, to determine need for euthanasia or immediate booster vaccination followed by observation or strict quarantine.

(4) Multiple rabid animals in a herd and herbivore-to-herbivore transmission of rabies are uncommon.<sup>61</sup> Therefore, restricting the rest of the herd if a single animal has been exposed to or infected with rabies is usually not necessary.

(5) Rabies virus is widely distributed in the tissues of rabid animals.<sup>62-64</sup>Tissues and products from a rabid animal should not be used for human or animal consumption<sup>65,66</sup> or transplantation.<sup>67</sup> However, pasteurization and cooking will inactivate rabies virus.<sup>68</sup>Therefore, inadvertently drinking pasteurized milk or eating thoroughly cooked animal products does not constitute a rabies exposure.

(6) Handling and consumption of uncooked tissues from exposed animals might carry a risk for rabies transmission.<sup>69</sup> Persons handling exposed animals, carcasses, and tissues should use appropriate barrier precautions.<sup>69,70</sup> State and local public health authorities, state meat inspectors, and the USDA Food Safety and Inspection Service should be notified if exposures occur in animals intended for commercial use. Animals should not be presented for slaughter in a USDA-regulated establishment if such animals originate from a quarantine area and have not been approved for release by the proper authority. If an exposed animal is to be custom slaughtered or home slaughtered for consumption, it should be slaughtered immediately after exposure, and all tissues should be cooked thoroughly.

c) Other animals. Other mammals exposed to a rabid animal should be euthanized

immediately. Animals maintained in USDAlicensed research facilities or accredited zoological parks should be evaluated on a case-bycase basis in consultation with public health authorities. Management options may include quarantine, observation, or administration of rabies biologics.

#### 6. Management of animals that bite humans.

a) Dogs, cats, and ferrets. Rabies virus is excreted in the saliva of infected dogs, cats, and ferrets during illness and for only a few days before the onset of clinical signs or death.71-73 Regardless of rabies vaccination status, a healthy dog, cat, or ferret that exposes a person should be confined and observed daily for 10 days from the time of the exposure<sup>74</sup>; administration of rabies vaccine to the animal is not recommended during the observation period to avoid confusing signs of rabies with rare adverse vaccine reactions.<sup>15</sup> Any illness in the animal should be reported immediately to the local health department. Such animals should be evaluated by a veterinarian at the first sign of illness during confinement. If signs suggestive of rabies develop, the animal should be euthanized, and the head or entire brain (including brainstem) should be submitted for testing (see Part I.A. 10. Rabies diagnosis). Any stray or unwanted dog, cat, or ferret that exposes a person may be euthanized immediately, and the head or entire brain (including brainstem) should be submitted for testing (see Part I.A. 10. Rabies diagnosis).

b) Other animals. Other animals that might have exposed a person to rabies should be reported immediately to the local health department. Management of animals other than dogs, cats, and ferrets depends on the species, the circumstances of the exposure, the epidemiology of rabies in the area, the exposing animal's history and current health status, and the animal's potential for exposure to rabies. The shedding period for rabies virus is undetermined for most species. Previous vaccination of these animals might not preclude the necessity for euthanasia and testing.

**7. Outbreak prevention and control**. The emergence of new rabies virus variants or the introduction of nonindigenous viruses poses a significant risk to humans, domestic animals, and wildlife.<sup>75-82</sup> A rapid and comprehensive response involves coordination of multiple agencies (*see* Part I. A. 3. Interdisciplinary approach) to accomplish the following outcomes<sup>83</sup>:

- Characterize the virus at the national reference laboratory.
- Identify and control the source of the introduction.

- Enhance laboratory-based surveillance in wild and domestic animals.
- Increase animal rabies vaccination rates.
- Restrict the movement of animals.
- Evaluate the need for wildlife intervention activities (eg, point infection control, trap-vaccinate-release programs, and oral rabies vaccination programs).
- Provide public and professional outreach and education.

**8. Disaster response**. Animals might be displaced during and after man-made or natural disasters and require emergency sheltering.<sup>84-86</sup> Animal rabies vaccination and exposure histories are often not available for displaced animals, and disaster response can create situations where animal caretakers might lack appropriate training or preexposure vaccination. In such situations, it is critical to implement and coordinate rabies prevention and control measures to reduce the risk of rabies transmission and the need for human postexposure prophylaxis. Such measures include the following actions:

- Coordinate relief efforts of individuals and organizations with the local emergency operations center before deployment.
- Examine each animal at a triage site for possible bite injuries or signs of rabies.
- Isolate animals exhibiting signs of rabies pending evaluation by a veterinarian.
- Ensure that all animals have a unique identifier.
- Administer a rabies vaccine to all dogs, cats, and ferrets unless reliable proof of current vaccination exists.
- Adopt minimum standards for animal caretakers as feasible, including use of personal protective equipment, completion of the preexposure rabies vaccination series prior to deployment, and provision of appropriate training.<sup>87</sup>
- Maintain documentation of animal disposition and location (eg, returned to owner, died or euthanized, adopted, or relocated to another shelter with address of new location).
- Provide facilities to confine and observe animals involved in exposures (*see* Part I. B. 6. Management of animals that bite humans).
- Report human exposures to appropriate public health authorities (*see* Part I. A. 2. Rabies virus exposure).

# **C. Prevention and control methods related to wildlife**

The public should be warned not to handle or feed wild mammals. Wild mammals and wild animal hybrids that expose persons, pets, or livestock should be considered for euthanasia and rabies testing. A person exposed by any wild mammal should immediately wash the wound thoroughly and report the incident to a health-care provider who, in consultation with public health authorities, can evaluate the need for postexposure prophylaxis.<sup>11,12</sup> Translocating infected wildlife has contributed to the spread of rabies,<sup>75-80,88</sup> and animals that appear healthy can still be rabid. Therefore, translocation (ie, moving live animals from their point of capture and releasing them) of known rabies reservoir species should be prohibited.<sup>89</sup> Whereas state-regulated wildlife rehabilitators and nuisance-wildlife control operators should play a role in a comprehensive rabies control program, minimum standards for these persons who handle wild mammals should include rabies preexposure vaccination, specific rabies prevention and control training, and ongoing continuing education.

1. Carnivores. The use of oral rabies vaccines for mass vaccination of free-ranging wildlife should be considered in selected situations, with the approval of appropriate state and local agencies.<sup>16,90</sup> There have been documented successes using oral rabies vaccines to control rabies in wildlife in North America.90-93 The currently licensed vaccinia-vectored oral rabies vaccine is labeled for use in raccoons and covotes. Research to improve existing oral rabies vaccine and baits and to develop and test novel products to determine safety and efficacy must be encouraged. The distribution of oral rabies vaccines should be based on scientific assessments of the target species and followed by timely and appropriate analysis of surveillance data, with results provided to all stakeholders. In addition, parenteral vaccination (trap-vaccinate-release) of wildlife rabies reservoir species may be integrated into coordinated oral rabies vaccine programs to enhance their effectiveness. Continuous and persistent programs for trapping or poisoning wildlife are not effective in reducing populations of wildlife rabies reservoir species on a statewide basis. However, limited population control in high-contact areas (eg, picnic grounds, camps, and suburban areas) might be indicated for the removal of selected highrisk species of wildlife. State agriculture, public health, and wildlife agencies should be consulted for planning, coordination, and evaluation of vaccination or point infection control programs.<sup>16</sup>

**2. Bats.** From the 1950s to today, indigenous rabid bats have been reported from every state except Hawaii and have caused rabies in at least 54 humans in the United States.<sup>94–103</sup> Bats should be excluded, using appropriate methods, from houses, public buildings, and adjacent structures to prevent direct association with humans.<sup>104,105</sup> Such structures should then be made bat-proof by sealing entrances used by bats. Controlling rabies in bats through programs designed to reduce bat populations is neither feasible nor desirable.

#### Part II. Recommendations for Parenteral Rabies Vaccination Procedures

#### A. Vaccine administration

All animal rabies vaccines should be restricted to use by or under the direct supervision of a veterinarian,<sup>106</sup> except as recommended otherwise (*see* Part I. B. 1. Preexposure vaccination and management).

#### **B. Vaccine selection**

All vaccines licensed by the USDA and marketed in the United States at the time of publication of this compendium are listed (Appendix 1). Newly approved vaccines and changes in label specifications made subsequent to publication should be considered as part of this list. Any of the listed vaccines can be used for revaccination, even if the product is not the same as the one previously administered. Vaccines used in state and local rabies control programs should have at least a 3-year duration of immunity. This constitutes the most effective method of increasing the proportion of immunized dogs and cats in any population.<sup>107</sup>

#### **C.Adverse events**

Currently, no epidemiological association exists between any particular licensed vaccine product and adverse events.<sup>15,34,108-110</sup> Although rare, adverse events such as vomiting, injection site swelling, lethargy, hypersensitivity, and the occurrence of rabies despite previous vaccination of an animal have been reported. Adverse events should be reported to the vaccine manufacturer and to USDA APHIS's Center for Veterinary Biologics (www.aphis.usda.gov; search for "adverse event reporting"). Although ill animals may not have a full immunologic response to vaccination, there is no evidence to suggest that adverse events are more likely to occur with rabies vaccination of ill than healthy animals. A veterinarian choosing to temporarily delay vaccinating an animal with an acute illness or condition should ensure that the animal is vaccinated as soon as possible. Animals with a previous history of anaphylaxis can be medically managed and observed after vaccination.<sup>56</sup> Severe adverse events related to rabies vaccination are extremely rare in animals. Decisions concerning rabies vaccination of animals with well-documented severe adverse events to rabies vaccine must be made within the context of a valid veterinarian-client-patient relationship. Due consideration should be given to the attendant risks and benefits of not vaccinating, including regulatory noncompliance. Animals not currently vaccinated that experience a rabies exposure are at greater risk for infection and death and also put their owners and the community at risk.

#### **D. Vaccination of wildlife** and wild animal hybrids

The safety and efficacy of parenteral rabies vaccines in wildlife and wild animal hybrids have not been established, and no rabies vaccines are currently licensed for use in these animals. Thus, any use of rabies vaccines in these animals is considered extralabel use. Zoos or research institutions may establish vaccination programs in an attempt to protect valuable animals, but these should not replace appropriate public health activities that protect humans (*see* Part I. B. 1. d) (3)).

## E. Accidental human exposure to rabies vaccines

Human exposure to parenteral animal rabies vaccines listed in Appendix 1 does not constitute a risk for rabies virus infection. Human exposure to vacciniavectored oral rabies vaccines should be reported to state health officials.<sup>111,112</sup>

#### F. Rabies certificates

All agencies and veterinarians should use Form 51, the rabies vaccination certificate recommended by the National Association of State Public Health Veterinarians,<sup>53</sup> or should use an equivalent. The form must be completed in full and signed by the administering or supervising veterinarian. Computer-generated forms containing the same information are also acceptable.

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Appendix 1

2016.
States,
United
the
ц.
marketed
and
licensed
vaccines
Rabies

Product name	Produced by	Marketed by	For use in	Dose	Age at primary vaccination*	<b>B</b> ooster vaccination	Route of inoculation
Monovalent (inactivated) RABVAC I RABVAC 3	Boehringer Ingelheim Vetmedica Inc License No. 124 Boehringer Ingelheim Vetmedica Inc License No. 124	Boehringer Ingelheim Vetmedica Inc Boehringer Ingelheim Vetmedica Inc	Dogs and cats Dogs and cats	말 다 3	3 mo 3 mo	Annually I year later and triennially	IM or SC IM or SC M
EQUI-RAB with Havlogen DEFENSOR 1	Merck Animal Health License No. 165A Zoetis License No. 190	Merck Animal Health Zoetis	Horses Dogs		4 mo 3 mo 1 mo	Annualy Annualy	M or SC
DEFENSOR 3	Zoetis License No. 190	Zoetis	Cats Dogs Cats Sheen and carrie		3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	Annually I year later and triennially I year later and triennially Annually	SC SC Mor SC
NOBIVAC: I-Rabies	Zoetis License No. 190	Merck Animal Health	Dogs		3 mo	Annually	IM or SC
NOBIVAC: 3-Rabies and 3-Rabies CA	Zoetis License No. 190	Merck Animal Health	Cats Dogs Cats Sheep and cattle		3 3 3 3 1 0 3 3 0 0 8 0	Amuany I year later and triennially I year later and triennially Amually	Mor SC
IMRAB I IMRAB I TF IMRAR 3	Merial Inc License No. 298 Merial Inc License No. 298 Marial Inc I irense No. 298	Merial Inc Merial Inc Merial Inc	Does and cats		3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	Annually Annually I vear later and rriennially	SC SC SC
			Sheep Cattle and horses	2 mL	3 mo 9 mo	I year later and triennially Annually	IM or SC
IMRAB 3 TF	Merial Inc License No. 298	Merial Inc	Ferrets Dogs and cats Ferrets		3 mo 3 mo 3 mo	Annualy I year later and triennially Annually	SC IM or SC SC
IMRAB Large Animal	Merial Inc License No. 298	Merial Inc	Dons and cats Cattle and horses Sheep	2 mL 2 mL	3 mo 3 mo 3 mo	l year later and triennially Annually I year later and triennially	IX or SC IX or SC IX or SC
Monovalent (rabies glycoprotein; live canary pox vector) PUREVAX Feline Rabies PUREVAX Feline Rabies 3YR	Merial Inc License No. 298 Merial Inc License No. 298	Merial Inc Merial Inc	Cats Cats	ר שר 	3 mo 3 mo	Annually I year later and triennially	S S
Combination (inactivated) Equine POTOMAVAC + IMRAB	Merial Inc License No. 298	Merial Inc	Horses	l mL	3 mo	Annually	Σ
Combination (rabies glycoprotein; live canary pox vector) PUREVAX Feline 3/Rabies	Merial Inc License No. 298	Merial Inc	Cats	л Ц Ш	8 %k	Every 3 to 4 wk until 3 mo and annually	SC
PUREVAX Feline 4/Rabies	Merial Inc License No. 298	Merial Inc	Cats	ا سلا ا	3 то 8 wk 3 то	3 to 4 wk later and annually Every 3 to 4 wk until 3 mo and annually 3 to 4 wk later and annually	s so S
Oral (rabies gyvcoprotein; live vaccinia vector)† RABORAL V.RG	Merial Inc License No. 298	Merial Inc	Raccoons and coyotes	AN	NA	As determined by local authorities	Oral

### Appendix 2

Rabies vaccine manufacturer contact information

Manufacturer	Phone No.	URL
Boehringer Ingelheim Vetmedica Inc	800-638-2226	www.bi-vetmedica.com
Merck Animal Health Inc	800-521-5767	www.merck-animal-health-usa.com
Merial Inc	888-637-4251	us.merial.com
Zoetis	800-366-5288	www.zoetis.com



**Recommendations and Reports** 

May 23, 2008 / Vol. 57 / No. RR-3

## Human Rabies Prevention — United States, 2008

# Recommendations of the Advisory Committee on Immunization Practices

**INSIDE:** Continuing Education Examination

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#### **Disclosure of Relationship**

CDC, our planners, and our presenters wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters with the exception of Praveen Dhankhar, who wishes to disclose that he is currently an employee of Merck Research Labs, Merck and Co. and Harry F. Hull, who wishes to disclose that he is President of a consulting firm unrelated to this continuing education activity.

Presentations will not include any discussion of the unlabeled use of a product or a product under investigational use.

### Human Rabies Prevention — United States, 2008 Recommendations of the Advisory Committee on Immunization Practices

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#### Summary

These recommendations of the Advisory Committee on Immunization Practices (ACIP) update the previous recommendations on human rabies prevention (CDC. Human rabies prevention—United States, 1999: recommendations of the Advisory Committee on Immunization Practices. MMWR 1999;48 [No. RR-1]) and reflect the status of rabies and antirabies biologics in the United States. This statement 1) provides updated information on human and animal rabies epidemiology; 2) summarizes the evidence regarding the effectiveness/efficacy, immunogenicity, and safety of rabies biologics; 3) presents new information on the cost-effectiveness of rabies postexposure prophylaxis; 4) presents recommendations for rabies postexposure and pre-exposure prophylaxis; and 5) presents information regarding treatment considerations for human rabies patients.

These recommendations involve no substantial changes to the recommended approach for rabies postexposure or pre-exposure prophylaxis. ACIP recommends that prophylaxis for the prevention of rabies in humans exposed to rabies virus should include prompt and thorough wound cleansing followed by passive rabies immunization with human rabies immune globulin (HRIG) and vaccination with a cell culture rabies vaccine. For persons who have never been vaccinated against rabies, postexposure antirabies vaccination should always include administration of both passive antibody (HRIG) and vaccine (human diploid cell vaccine [HDCV] or purified chick embryo cell vaccine [PCECV]). Persons who have ever previously received complete vaccination regimens (pre-exposure or postexposure) with a cell culture vaccine or persons who have been vaccinated with other types of vaccines and have previously had a documented rabies virus neutralizing antibody titer should receive only 2 doses of vaccine: one on day 0 (as soon as the exposure is recognized and administration of vaccine can be arranged) and the second on day 3. HRIG is administered only once (i.e., at the beginning of antirabies prophylaxis) to previously unvaccinated persons to provide immediate, passive, rabies virus neutralizing antibody coverage until the patient responds to HDCV or PCECV by actively producing antibodies. A regimen of 5 1-mL doses of HDCV or PCECV should be administered intramuscularly to previously unvaccinated persons. The first dose of the 5-dose course should be administered as soon as possible after exposure (day 0). Additional doses should then be administered on days 3, 7, 14, and 28 after the first vaccination. Rabies pre-exposure vaccination should include three 1.0-mL injections of HDCV or PCECV administered intramuscularly (one injection per day on days 0, 7, and 21 or 28).

Modifications were made to the language of the guidelines to clarify the recommendations and better specify the situations in which rabies post- and pre-exposure prophylaxis should be administered. No new rabies biologics are presented, and no changes

were made to the vaccination schedules. However, rabies vaccine adsorbed (RVA, Bioport Corporation) is no longer available for rabies postexposure or pre-exposure prophylaxis, and intradermal pre-exposure prophylaxis is no longer recommended because it is not available in the United States.

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#### Introduction

Rabies is a zoonotic disease caused by RNA viruses in the Family *Rhabdoviridae*, Genus *Lyssavirus* (1-4). Virus is typically present in the saliva of clinically ill mammals and is transmitted through a bite. After entering the central nervous system of the next host, the virus causes an acute, progressive encephalomyelitis that is almost always fatal. The incubation period in humans is usually several weeks to months, but ranges from days to years.

As a result of improved canine vaccination programs and stray animal control, a marked decrease in domestic animal rabies cases in the United States occurred after World War II. This decline led to a substantial decrease in indigenously acquired rabies among humans (5). In 1946, a total of 8,384 indigenous rabies cases were reported among dogs and 33 cases in humans. In 2006, a total of 79 cases of rabies were reported in domestic dogs, none of which was attributed to enzootic dog-to-dog transmission, and three cases were reported in humans (6). The infectious sources of the 79 cases in dogs were wildlife reservoirs or dogs that were translocated from localities where canine rabies virus variants still circulate. None of the 2006 human rabies cases was acquired from indigenous domestic animals (6). Thus, the likelihood of human exposure to a rabid domestic animal in the United States has decreased substantially. However, one of the three human rabies cases diagnosed in 2006 was associated with a dog bite that occurred in the Philippines, where canine rabies is enzootic. The risk for reintroduction from abroad remains (7). International travelers to areas where canine rabies remains enzootic are at risk for exposure to rabies from domestic and feral dogs.

Unlike the situation in developing countries, wild animals are the most important potential source of infection for both humans and domestic animals in the United States. Most reported cases of rabies occur among carnivores, primarily raccoons, skunks, and foxes and various species of bats. Rabies among insectivorous bats occurs throughout the continental United States. Hawaii remains consistently rabiesfree. For the past several decades, the majority of naturally acquired, indigenous human rabies cases in the United States have resulted from variants of rabies viruses associated with insectivorous bats (5). The lone human case reported in the United States during 2005 and two of the three human rabies cases in 2006 were attributed to bat exposures (6,8). During 2004, two of the eight human rabies cases resulted from bat exposures. One of these rabies patients recovered and remains the only rabies patient to have survived without the administration of rabies vaccination (9). Rabies was not immediately recognized as the cause of death in the other 2004 patient, and organs and a vascular graft from this patient were transplanted into four persons, resulting in clinical rabies and death in all of the recipients (*10*).

Approximately 16,000–39,000 persons come in contact with potentially rabid animals and receive rabies postexposure prophylaxis each year (11). To appropriately manage potential human exposures to rabies, the risk for infection must be accurately assessed. Administration of rabies postexposure prophylaxis is a medical urgency, not a medical emergency, but decisions must not be delayed. Prophylaxis is occasionally complicated by adverse reactions, but these reactions are rarely severe (12–16).

For these recommendations, data on the safety and efficacy of active and passive rabies vaccination were derived from both human and animal studies. Because controlled human trials cannot be performed, studies describing extensive field experience and immunogenicity studies from certain areas of the world were reviewed. These studies indicated that postexposure prophylaxis combining wound treatment, local infiltration of rabies immune globulin (RIG), and vaccination is uniformly effective when appropriately administered (17-22). However, rabies has occasionally developed among humans when key elements of the rabies postexposure prophylaxis regimens were omitted or incorrectly administered. Timely and appropriate human pre-exposure and postexposure prophylaxis will prevent human rabies; however, the number of persons receiving prophylaxis can be reduced if other basic public health and veterinary programs are working to prevent and control rabies. Practical and accurate health education about rabies, domestic animal vaccination and responsible pet care, modern stray animal control, and prompt diagnosis can minimize unnecessary animal exposures, alleviate inherent natural risks after exposure, and prevent many circumstances that result in the need for rabies prophylaxis.

#### **Methods**

The Advisory Committee on Immunization Practices (ACIP) Rabies Workgroup first met in July 2005 to review previous ACIP recommendations on the prevention of human rabies (published in 1999) and to outline a plan for updating and revising the recommendations to provide clearer, more specific guidance for the administration of rabies preexposure and postexposure prophylaxis. The workgroup held monthly teleconferences to discuss their review of published and unpublished data on rabies and related biologic products. Data on the effectiveness, efficacy, immunogenicity, and safety of rabies biologics in both human and animal studies were reviewed using a systematic, evidence-based approach.

Randomized trials or well-conducted cohort studies with untreated comparison groups would provide the best evidence of the direct effectiveness of rabies pre-exposure and postexposure prophylaxis to prevent rabies-associated death. However, because of the almost universal fatality among untreated persons infected with rabies virus, no such controlled studies exist. However, studies describing final health outcomes among persons exposed to the rabies virus do exist, including studies using formulations of rabies biologics, timing of vaccine doses, and routes of administration that are not recommended for use in the United States. These and other studies were identified by reviewing the PubMed database and relevant bibliographies and by consulting subjectmatter experts. The literature review did not identify any studies of the direct effectiveness of rabies pre-exposure vaccination in preventing human rabies cases. Such studies would be difficult to conduct because rabies pre-exposure vaccination is intended to simplify the postexposure prophylaxis that is required after a recognized rabies exposure. Rabies preexposure vaccination also might afford immunity against an unrecognized rabies exposure, an outcome that would be difficult to measure in controlled studies. However, rabies cases have occurred among those who received rabies pre-exposure prophylaxis and did not receive rabies postexposure prophylaxis (23), indicating that pre-exposure prophylaxis in humans is not universally effective without postexposure prophylaxis. Because of the paucity of formal studies on the effectiveness of rabies pre-exposure vaccination in humans, the literature was searched for studies that reported clinical outcomes among animals that received pre-exposure rabies prophylaxis with cell culture rabies vaccine and were subsequently challenged with rabies virus. Evaluation of the effectiveness of antirabies biologics in experimental animal models has been essential to developing successful rabies prevention approaches for exposed humans. Animal studies investigating the effectiveness of both pre-exposure and posteexposure rabies prophylaxis were reviewed and were used to make inferences about the direct effectiveness of licensed rabies biologics in preventing human rabies.

Data regarding the immunogenicity of rabies biologics also were reviewed. Assessing protective immunity against rabies is complex. Virus neutralizing antibodies are believed to have a primary role in preventing rabies virus infection. However, antibody titers alone do not always directly correlate with absolute protection because of other important immunologic factors. Nonetheless, the ability of a vaccine to elicit rabies virus neutralizing antibodies in animals and humans and the demonstration of protection in animals is generally viewed as a reasonable surrogate of protection for inferential extension to humans (24). Although a definitive "protective" titer cannot be described for all hosts under all exposure scenarios, two working definitions of adequate rabies virus neutralizing antibody reference values have been developed to define an appropriate, intact adaptive host response to vaccination. The literature review included studies in humans that measured rabies virus neutralizing antibody in response to rabies postexposure prophylaxis consisting of human rabies immune globulin (HRIG) and 5 intramuscular (IM) doses of cell culture rabies vaccine and the recommended pre-exposure prophylaxis regimen of 3 IM doses of cell culture vaccine. The outcomes of interest for these studies were antibody titers of 0.5 IU/mL (used by the World Health Organization [WHO] as an indicator of an adequate adaptive immune response) (25) or complete virus neutralization at a 1:5 serum dilution by the rapid fluorescent focus inhibition test (RFFIT) (used by ACIP as an indicator of an adequate adaptive immune response) (26). The literature also was searched for evidence regarding the safety of the licensed rabies biologics available for use in the United States in both pre-exposure and postexposure situations.

ACIP's charter requires the committee to consider the costs and benefits of potential recommendations when they are deliberating recommendations for vaccine use in the United States. Few studies exist on the cost-effectiveness of rabies prophylaxis in various potential exposure scenarios. A challenge in conducting such studies is the lack of data on the probability of rabies transmission under different exposure scenarios, except when the involved animal tests positive for rabies. To provide information on the cost-effectiveness of rabies postexposure prophylaxis, a new analysis was conducted to estimate the cost-effectiveness of rabies postexposure prophylaxis in various potential exposure scenarios. A Delphi methodology was used to estimate the risk for transmission of rabies to a human in each of the scenarios, and this information was used in the cost-effectiveness calculations.

The rabies workgroup reviewed the previous ACIP recommendations on the prevention of human rabies and deliberated on the available evidence. When definitive research evidence was lacking, the recommendations incorporated expert opinion of the workgroup members. The workgroup sought input from members of the National Association of State Public Health Veterinarians, the Council of State and Territorial Epidemiologists (CSTE), and state and local public health officials. The proposed revised recommendations and a draft statement were presented to ACIP in October 2006. After deliberations, the recommendations were unanimously approved with minor modifications. Further modifications to the draft statement were made following the CDC and external review process to update and clarify wording in the document.

#### **Rabies Biologics**

Three cell culture rabies vaccines are licensed in the United States: human diploid cell vaccine (HDCV, Imovax<sup>®</sup> Rabies, sanofi pasteur), purified chick embryo cell vaccine (PCECV, RabAvert<sup>®</sup>, Novartis Vaccines and Diagnostics), and rabies vaccine adsorbed (RVA, Bioport Corporation). Only HDCV and PCECV are available for use in the United States (Table 1). For each of the available vaccines, the potency of 1 dose is greater than or equal to the WHO-recommended standard of 2.5 international units (IU) per 1.0 mL of vaccine (27). A full 1.0-mL IM dose is used for both pre-exposure and postexposure prophylaxis regimens. Rabies vaccines induce an active immune response that includes the production of virus neutralizing antibodies. The active antibody response requires approximately 7-10 days to develop, and detectable rabies virus neutralizing antibodies generally persist for several years. A vaccination series is initiated and completed usually with one vaccine product. No clinical trials were identified that document a change in efficacy or the frequency of adverse reactions when the series is initiated with one vaccine product and completed with another.

The passive administration of RIG is intended to provide an immediate supply of virus neutralizing antibodies to bridge the gap until the production of active immunity in response to vaccine administration. Use of RIG provides a rapid, passive immunity that persists for a short time (half-life of approximately 21 days) (28). Two antirabies immune globulin (IgG) formulations prepared from hyperimmunized human donors are licensed and available for use in the United States: HyperRab<sup>TM</sup> S/D (Talecris Biotherapeutics) and Imogam<sup>®</sup> Rabies-HT (sanofi pasteur). In all postexposure prophylaxis regimens, except for persons previously vaccinated, HRIG should be administered concurrently with the first dose of vaccine.

#### Vaccines Licensed for Use in the United States

#### **Human Diploid Cell Vaccine**

HDCV is prepared from the Pitman-Moore strain of rabies virus grown on MRC-5 human diploid cell culture, concentrated by ultrafiltration, and inactivated with beta-propiolactone (22). HDCV is formulated for IM administration in a single-dose vial containing lyophilized vaccine that is reconstituted in the vial with the accompanying sterile diluent to a final volume of 1.0 mL just before administration. One dose of reconstituted vaccine contains <150  $\mu$ g neomycin sulfate, <100 mg albumin, and 20  $\mu$ g of phenol red indicator. It contains no preservative or stabilizer.

#### **Purified Chick Embryo Cell Vaccine**

PCECV became available in the United States in 1997. The vaccine is prepared from the fixed rabies virus strain Flury LEP grown in primary cultures of chicken fibroblasts (29). The virus is inactivated with betapropiolactone and further processed by zonal centrifugation in a sucrose density gradient. It is formulated for IM administration in a single-dose vial containing lyophilized vaccine that is reconstituted in the vial with the accompanying sterile diluent to a final volume of 1.0 mL just before administration. One dose of reconsti-

Human rabies vaccine	Product name	Manufacturer	Dose	Route	Indications
Human diploid cell vaccine	lmovax® Rabies*	sanofi Pasteur Phone: 800-822-2463 Website: http://www.vaccineplace.com/products/	1 mL	Intramuscular	Pre-exposure or postexposure <sup>†</sup>
Purified chick embryo cell vaccine	RabAvert®	Novartis Vaccines and Diagnostics Phone: 800-244-7668 Website: http://www.rabavert.com	1 mL	Intramuscular	Pre-exposure or postexposure <sup>†</sup>
Rabies immune globulin	Imogam® Rabies-HT	sanofi pasteur Phone: 800-822-2463 Website: http://www.vaccineplace.com/products/	20 IU/kg	Local <sup>§</sup>	Postexposure only
	HyperRab <sup>TM</sup> S/D	Talecris Biotherapeutics Bayer Biological Products Phone: 800-243-4153 Website: http://www.talecris-pi.info	20 IU/kg	Local <sup>§</sup>	Posteexposure only

TABLE 1. Currently available rabies biologics — United States, 2008

\* Imovax rabies I.D., administered intradermally, is no longer available in the United States.

<sup>†</sup> For postexposure prophylaxis, the vaccine is administered on days 0, 3, 7, 14 and 28 in patients who have not been previously vaccinated and on days 0 and 3 in patients who have been previously vaccinated. For pre-exposure prophylaxis, the vaccine is administered on days 0, 7 and 21 or 28.

§As much of the product as is anatomically feasible should be infiltrated into and around the wound. Any remaining product should be administered intramuscularly in the deltoid or quadriceps (at a location other than that used for vaccine inoculation to minimize potential interference). tuted vaccine contains <12 mg polygeline, <0.3 mg human serum albumin, 1 mg potassium glutamate, and 0.3 mg sodium EDTA. No preservatives are added.

# Rabies Immune Globulins Licensed for Use in the United States

The two HRIG products, HyperRab<sup>™</sup> S/D and Imogam<sup>®</sup> Rabies-HT, are IgG preparations concentrated by cold ethanol fractionation from plasma of hyperimmunized human donors. The HyperRab  $^{\text{TM}}$  S/D is formulated through the treatment of the immune globulin fraction with 0.3% tri-n-butyl phosphate (a solvent to inactivate potential adventitious viruses) and 0.2% sodium cholate (a detergent to inactivate potential adventitious viruses) and the application of heat (30°C [86°F] for 6 hours). After ultrafiltration, the final product is a 15%–18% protein solution in glycine. The Imogam<sup>®</sup> Rabies-HT is prepared from the cold ethanol fraction of pooled venous plasma of donors, stabilized with glycine, and subjected to a heat-treatment process (58°C-60°C [136°F-140°F] for 10 hours) to inactivate potential adventitious viruses, with the final formulation consisting of 10%-18% protein. Both HRIGs are standardized at an average potency value of 150 IU per mL, and supplied in 2-mL (300 IU) vials for pediatric use and 10-mL (1,500 IU) vials for adult use. The recommended dose is 20 IU/kg (0.133 mL/kg) body weight. Both HRIG preparations are considered equally efficacious when used as described in these recommendations.

These products are made from the plasma of hyperimmunized human donors that, in theory, might contain infectious agents. Nevertheless, the risk that such products will transmit an infectious agent has been reduced substantially by screening plasma donors for previous exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses. No transmission of adventitious agents has been documented after administration of HRIGs licensed in the United States.

# Effectiveness and Immunogenicity of Rabies Biologics

#### Effectiveness of Rabies Postexposure Prophylaxis: Human Studies

A literature search identified 11 studies regarding the direct effectiveness of varying regimens of rabies postexposure prophylaxis in preventing rabies-associated deaths (18,30-39). An additional eight studies were identified from reviews of bibliographies or consultations with subject matter experts (19,40-46).

Three large retrospective cohort studies were identified that describe differences in rabies mortality between rabies-exposed persons (persons who were exposed to proven or suspected rabid animals) who were vaccinated with older formulations of rabies vaccine compared with similarly exposed persons who were not administered prophylaxis (41,44,46). In one 1923 study of 2,174 persons bitten by "presumably rabid" dogs in India, 2.9% of persons vaccinated with 1% Semple nerve tissue rabies vaccine (NTV) subcutaneously for 14 days died from rabies compared with 6.2% of unvaccinated persons (41). Another study of persons bitten by assumed infective rabid animals (i.e., one or more other persons bitten by the same animal died from rabies) during 1946-1951 indicated that 8.3% of persons "completely treated" with 5% Semple rabies vaccine, 23.1% of "incompletely treated", and 43.2% of unvaccinated persons died from rabies (46). A third study in Thailand in 1987 documented no deaths among 723 persons bitten by dogs (661 of these persons were bitten by confirmed rabid dogs) who received one of three rabies vaccines: Semple vaccine (n = 427), HDCV (n = 257), or duck embryo vaccine (n = 39) (44). However, 45% (nine of 20) of unvaccinated persons who were bitten by confirmed rabid dogs died from rabies. All of the persons who died were severely bitten on the face, neck, or arms. All unvaccinated persons who survived after having been bitten by confirmed rabid dogs were bitten either on the legs or feet. Although these studies describe outcomes of persons receiving older formulations of rabies vaccines that are not used in the United States, they demonstrate that a majority of persons bitten by known rabid dogs did not acquire rabies and provide historical evidence of a substantial protective effect of rabies vaccination after rabies exposure.

The effectiveness of cell culture rabies vaccine plus rabies IgG in preventing human deaths after rabies exposure has been demonstrated in certain studies (18,19,30-32,39,45). One prospective study described 10 children (aged <12 years) and 32 adults who had been administered HRIG (Hyperrab<sup>®</sup>, Cutter Laboratories, Berkeley, CA, USA) and 5 IM doses of HDCV (L'Institut Merieux, Lyons, France) after exposure to suspected or confirmed rabid animals (brain-tissue positive by fluorescent antibody testing) (30). All exposed persons remained rabies-free during 5 years of observation. Another study investigated outcomes for 90 persons with high-risk exposures (bites or direct exposure to saliva from animals shown to be rabid by fluorescent antibody tests or bites from wild carnivores or bats that were not available for testing) who were treated with HRIG and 5 IM doses of HDCV (Wyeth Laboratories, Radnor, PA) (18). All patients, including 21 who were bitten by proven rabid animals (brain tissue fluorescent antibody positive), were rabies-free after 10-18 months of follow-up. A third study documented 45 persons severely bitten by confirmed rabid animals (brain tissue fluorescent antibody positive) who were administered RIG of mule origin and 5 IM doses of HDCV (L'Institut Merieux) (19). No rabies-related deaths were documented 6-12 months after exposure. A fourth study indicated no human rabies cases in 12 months of follow-up among 45 patients receiving HRIG (Berirab<sup>®</sup>) and 6 IM doses of PCECV (Behringwerke Research Laboratories, Marburg, West Germany) after contact with proven rabid animals (brain tissue fluorescent antibody positive) (32). Other studies examining outcomes for persons with varying degrees of exposure to confirmed rabid animals who were administered 6 doses of PCECV IM with or without HRIG also reported no rabies deaths in 12-15 months of follow-up (39,45). Several studies also have demonstrated the effectiveness of intradermal (ID) administration of cell culture rabies vaccine with or without RIG (of human or equine origin) in preventing rabies among exposed humans (33-35,37).

Two studies demonstrated the role of RIG administration in conjunction with vaccine in rabies postexposure prophylaxis (42,43). The first described quantitative serologic outcomes in 29 persons severely bitten by a rabid wolf and demonstrated the importance of rabies antiserum administration in the establishment of an early, passive, rabies virus neutralizing antibody level in patients and protection against rabies (40,43). Among five patients treated with 2 doses of rabies antiserum and NTV for 21 days, all had detectable levels of rabies virus neutralizing antibody during the first 5 days and all survived. Among seven patients treated with 1 dose of antiserum in addition to NTV, all had detectable antibody during the first 5 days, but four of six had low antibody titers by day 21. One of the seven failed to develop more than a very low antibody level beyond day 7 and eventually died from rabies. Among the five persons treated with NTV without antiserum, none had detectable antibody levels before day 19, and three died from rabies. In the second study, none of 27 persons severely wounded by rabid animals in China who were treated with purified hamster kidney cell (PHKC) rabies vaccine plus horse-origin rabies immune serum died from rabies (42). In contrast, all three severely wounded persons treated with PHKC alone died.

#### Effectiveness of Rabies Postexposure Prophylaxis: Animal Studies

During the preceding four decades, results of experimental studies using various animal species have supported the use of cell culture-based vaccines for protection against rabies after infections. For example, a postexposure prophylaxis experiment conducted in 1971 in rhesus monkeys using an experimental purified, concentrated tissue-culture vaccine alone, or in combination with homologous antirabies serum, demonstrated that a single administration of tissue-culture vaccine after exposure to rabies virus provided substantial (seven of eight animals) protection against the development of rabies. In addition to demonstrating that homologous or heterologous antirabies serum alone resulted in poor protection from rabies (63%-88% mortality), the experimental data suggested that highly concentrated, purified tissue-culture vaccine might be effective for postexposure prophylaxis in humans (47). A study in 1981 documented limited protection against a lethal rabies virus challenge in goats who received ERA vaccine with or without antirabies goat serum (48). In cattle, another livestock species, the superiority of tissue culture vaccine over brain-origin vaccine was demonstrated (49). Similarly, in sheep, vaccine alone provided limited protection, but vaccine in combination with polyclonal IgG provided the best outcome (50). A 1989 evaluation of postexposure prophylaxis administered to dogs demonstrated similar findings. The combination of serum and vaccine provided nearly complete protection compared with animals receiving vaccine only and nontreated controls (51).

Previous animal postexposure research focused primarily on interventions against traditional rabies viruses. However, new causative agents of rabies continue to emerge, as demonstrated by the recent description of four novel lyssaviruses from bats in Eurasia, Aravan (ARAV), Khujand (KHUV), Irkut (IRKV), and West Caucasian bat virus (WCBV) (52,53). The combined effect of RIG and vaccine after exposure to these four new isolates was investigated in a Syrian hamster model, using commercially available human products or an experimental mAb (54). Conventional rabies postexposure prophylaxis provided little or no protection against all four new bat viruses. In general, protection was inversely related to the genetic distance between the new isolates and traditional rabies viruses, which demonstrated the usefulness of this animal model in estimating the potential impact of these new lyssaviruses on human and domestic animal health.

#### Immunogenicity of Rabies Postexposure Prophylaxis

To assess the ability of rabies postexposure prophylaxis to elicit rabies virus neutralizing antibodies in humans, studies were reviewed that documented antibody responses to rabies postexposure prophylaxis. Four studies of antibody responses to rabies postexposure prophylaxis with 5 IM doses of HDCV with or without HRIG were identified (*30,55–57*). Because no studies were identified that examined antibody responses to postexposure or simulated postexposure prophylaxis with 5 IM doses of the licensed PCECV vaccine (RabAvert<sup>®</sup>) plus HRIG, a study reporting antibody responses to 6 IM doses of another PCECV formulation (Rabipur®, Novartis Vaccines and Diagnostics) administered with or without HRIG was reviewed (36). In a randomized trial, all persons receiving HRIG and 5 IM doses of HDCV (Imovax<sup>®</sup> Rabies) developed rabies virus antibody titers ≥0.5 IU/mL lasting up to 42 days after prophylaxis initiation (56). In a 1999 case-series, among 40 persons with diverse histories of exposure to animals suspected of having rabies, all persons who received 5 IM doses of HDCV with or without HRIG seroconverted or had increases in baseline serum antibody titers after the fifth vaccine dose (geometric mean titer [GMT] = 6.22 IU/mL) (57). Furthermore, a significantly higher mean antibody titer was observed in the group that received HDCV and HRIG (GMT = 12.3 IU/mL; standard error [SE] = 2.9) than in the group that received HDCV alone (GMT = 8.5 IU/mL; SE = 1.6; p=0.0043). In a randomized, modified double-blind, multicenter, simulated postexposure trial, 242 healthy adult volunteers were administered HRIG (Imogam<sup>®</sup> Rabies-HT) and 5 IM doses of either HDCV (Imovax<sup>®</sup> Rabies) or a chromatographically purified Vero-cell rabies vaccine (CPRV) (55). All participants had rabies virus neutralizing antibody titers  $\geq$ 0.5 IU/mL by day 14 and maintained this level through day 42. Participants receiving HDCV had higher GMTs on days 14 and 42 than did participants receiving CPRV. In the prospective study comparing rabies neutralizing antibodies in the serum of children compared with adults following postexposure prophylaxis, all 25 adults and eight children tested on day 14 had rabies virus neutralizing antibody concentrations  $\geq 0.5$  IU/mL (30). In addition, no differences in antibody titer were observed between adults and children, and all persons remained alive during the 5 years of follow-up.

#### Effectiveness of Rabies Pre-Exposure Prophylaxis: Animal Studies

Because no studies exist on the effectiveness of rabies preexposure prophylaxis in preventing rabies deaths in humans, literature was reviewed on the effectiveness of pre-exposure vaccination in animal models. The effectiveness of rabies vaccine has been appreciated for most of the 20<sup>th</sup> century on the basis of animal experiments. Commercial rabies vaccines are licensed for certain domestic species, all of which entail the direct demonstration of efficacy after the administration of a single pre-exposure dose, and observed protection from rabies virus challenge for a minimum duration of 1–4 years after vaccination of captive animals. In addition, rabies preexposure vaccine research varies typically either by modification of standard regimens of vaccination or the relative antigenic value or potency of vaccine administration to animals. For example, at least five studies involved animals challenged with rabies viruses (challenge standard virus [CVS] or street rabies virus isolates) and other lyssaviruses (European bat lyssavirus [EBL] 1, EBL2, Australian bat lyssavirus [ABL], and WCBV, IRKV, ARAV, KHUV) after primary vaccination with PCECV (58) or HDCV (54,58-62). Two of seven studies reported seroconversion in mice and humans. Complete protection of animals from rabies virus infection was observed in all experiments that used PCECV or HDCV IM for primary vaccination except in one group that had been challenged by CVS through the intracranial route and experienced 5% mortality (59). Evaluation of crossprotection of HDCV against WCBV, ARAV, IRKV, KHUV, and ABL through IM challenge showed 44%, 55%, 67%, 89% and 79% survival, respectively (54). These studies demonstrated the usefulness of commercial human vaccines when administered to animals, with resulting protection dependent on the relative degree of phylogenetic relatedness between the rabies vaccine strain and the particular lyssavirus isolate.

#### Immunogenicity of Rabies Pre-Exposure Prophylaxis: Human Studies

Thirteen studies were identified that provide evidence of the effectiveness of pre-exposure rabies vaccination in eliciting an adaptive host immune response in humans. The outcomes of interest for these studies (29, 63-74) include the two working definitions of adequate rabies virus neutralizing antibody reference values that have been developed to define an appropriate, intact adaptive host response to vaccination: antibody titers of 0.5 IU/mL or complete virus neutralization at a 1:5 serum dilution by RFFIT (26).

Multiple studies comparing different pre-exposure prophylaxis regimens provide evidence that vaccination with 3 IM doses of cell culture rabies vaccine (the recommended preexposure regimen) result in neutralizing antibody titers ≥0.5 IU/mL by days 14 (70,71), 21 (63,74), 28 (64,69,72), or 49 (67,68,75) after primary vaccination. One study in 1987 documented antibody responses in 177 healthy student volunteers aged 18-24 years following primary vaccination with either PCECV (Behringwerke) or HDCV (Behringwerke) (71). On day 14 after vaccination (first dose administered on day 0), no significant difference in GMT was observed between participants who received 3 IM doses of PCECV on days 0, 7, and 21 (GMT = 5.9 IU/mL) compared with persons who received 3 IM doses of HDCV (GMT = 4.4 IU/mL). On day 42, the GMT of the HDCV group was significantly higher than that of the PCECV group (13.7 IU/mL versus 8.4 IU/mL; p<0.025). Another study documented similar antibody responses to primary vaccination with HDCV in healthy veterinary students (64). The GMT of persons
receiving 3 IM doses of HDCV on days 0, 7, and 28 was 10.2 IU/mL (range: 0.7-51.4) on day 28 and 37.7 IU/mL (range: 5.4-278.0) on day 42. Another study documented even higher GMTs among 78 volunteers in a randomized trial studying differences between primary vaccination with PCECV (Behringwerke) and HDCV (L'Institut Merieux) administered IM or ID on days 0, 7, and 28 (29). The day 28 GMT among persons receiving HDCV IM (GMT = 239 RFFIT titer/mL; range: 56-800) was significantly higher than the GMT among persons receiving PCECV IM (GMT = 138 RFFIT titer/mL; range: 45–280). On days 50 and 92, no significant difference in GMT was observed between the two groups in which vaccine was administered IM, and the GMTs of the IM groups were significantly higher than the ID groups. Another study also observed higher antibody titers on days 49 and 90 and 26 months after primary vaccination with HDCV (Imovax<sup>®</sup> Rabies) when the vaccine was administered IM compared with ID on days 0, 7, and 28 (68). A randomized trial was conducted to determine the equivalence and interchangeability of PCECV (RabAvert<sup>®</sup>) and HDCV (Imovax<sup>®</sup> Rabies) administered IM on days 0, 7, and 28 for rabies pre-exposure prophylaxis to 165 healthy, rabies vaccine naïve veterinary students (66). No significant difference in GMT was observed among the HDCV and PCECV groups on days 28 and 42.

Although the 3-dose rabies pre-exposure prophylaxis series has been the standard regimen recommended by WHO (17) and ACIP (26), a 2-dose pre-exposure series has been used previously in some countries (76). One study compared antibody responses in persons receiving 2 (days 0 and 28) versus 3 (days 0, 7, and 28) IM doses of either HDCV (Pasteur Merieux Connaught, Lyon, France) or purified Vero cell rabies vaccine (PVRV) (Pasteur Merieux Connaught) and indicated that the cohort seroconversion rate decreased more rapidly among persons receiving 2 doses compared with those receiving 3 doses (p<0.001), indicating superior longer term immunogenicity when 3 vaccine doses were administered (73).

In addition to the rapidity of the immune response resulting from rabies pre-exposure vaccination, another important consideration is the length of duration or persistence of the immune response. One study reported rapid declines in GMT at 4 months after initial vaccination among persons receiving 3-dose primary vaccination with HDCV (L'Institut Merieux) or PVRV (L'Institut Merieux) on days 0, 7, and 21 followed by stabilization of the antibody level through 21 months (*63*). Another study observed persistent GMTs among persons receiving 3-dose (days 0, 7, and 28) primary vaccination with PCECV (Behringwerke) and HDCV (L'Institut Merieux) IM on day 365 (PCECV GMT = 189 RFFIT titer/mL; range:

53-1400; HDCV GMT = 101 RFFIT titer/mL; range: 11-1400) and day 756 (PCECV GMT = 168 RFFIT titer/ mL; range: 50–3600; HDCV GMT = 92 RFFIT titer/mL; range: 11-480) after initial vaccination (29). On day 387 post vaccination, another study indicated that the GMT among persons receiving PCECV (RabAvert®) IM on days 0, 7, and 28 (GMT = 2.9 IU/mL) was significantly higher than the GMT in the HDCV (Imovax<sup>®</sup> Rabies) group (GMT = 1.5 IU/mL; p<0.05) (66). All persons vaccinated with PCECV had antibody titers >0.5 IU/mL on days 387, as did 95.7% of persons vaccinated with HDCV. Another study indicated that all persons receiving PCECV (Behringwerke) IM on days 0, 7, and 21 maintained antibody titers >0.5 IU/mL 2 years after primary vaccination (71). In summary, rabies virus neutralizing antibody titers >0.5 IU/mL were observed in all persons at 180 days and 96.8% at 365 days after initial vaccination (72), 94% of persons at 21 months after initial vaccination (63), and all persons tested at 26 months after primary vaccination (77).

An important use of rabies pre-exposure prophylaxis is to prime the immune response to enable a rapid anamnestic response to postexposure booster vaccination and simplify the postexposure prophylaxis requirements for previously vaccinated persons. One study observed antibody responses to 1or 2-dose (days 0 and 3) IM booster vaccinations with PCECV (RabAvert<sup>®</sup>) in persons who had received primary vaccination with either PCECV IM or HDCV IM 1 year earlier (66). All participants who had initially received PCECV primary vaccination and 66 of 69 (96%) who had initially received HDCV primary vaccination had titers >0.5 IU/mL before booster vaccination. No significant differences in GMT were observed between 1- and 2-dose booster groups on days 3 (2-dose GMT = 2.07 IU/mL; 1-dose GMT = 2.87 IU/ mL), seven (2-dose GMT = 51.67 IU/mL; 1-dose GMT = 51.23 IU/mL) and 365 (2-dose GMT = 30.60 IU/mL; 1-dose GMT = 26.10 IU/mL) (66). However, a significantly higher GMT was observed on day 21 for persons receiving 2-dose boosters (GMT = 151.63 IU/mL) compared with 1-dose boosters (GMT = 120.91 IU/mL). All persons tested at day 365 post-booster dose in both 1- and 2-dose booster groups had rabies virus neutralizing antibody titers >0.5 IU/mL regardless of whether PCECV or HDCV was used for primary vaccination. Another study documented rapid antibody responses to a single booster dose of HDCV (Imovax<sup>®</sup> Rabies) or CPRV (Pasteur Merieux Connaught), with all persons in both groups exhibiting antibody titers >0.5 IU/mL on days 7 and 14 post-booster dose (72).

### **Safety of Rabies Biologics**

Eight studies regarding the safety of rabies biologics used in postexposure or simulated postexposure settings (36,55-57,78-81) and eight studies of safety in pre-exposure settings were identified (63-65,68,71,72,82). Three identified studies investigated reports of adverse events in both postexposure and pre-exposure settings (14,83,84). Reviews of relevant bibliographies identified one additional study examining the safety of PCECV when used without HRIG for postexposure prophylaxis in children (85).

### HDCV

Studies of the use of HDCV reported local reactions (e.g., pain at the injection site, redness, swelling, and induration) among 60.0%–89.5% of recipients (63–65,68,72). Local reactions were more common than systemic reactions. Most local reactions were mild and resolved spontaneously within a few days. Local pain at the injection site was the most frequently reported adverse reaction occurring in 21%–77% of vaccinees (24,63,68,71,72,80). Mild systemic reactions (e.g., fever, headache, dizziness, and gastrointestinal symptoms) were reported in 6.8%–55.6% of recipients (63,64,68,72).

Systemic hypersensitivity reactions have been reported in up to 6% of persons receiving booster vaccination with HDCV following primary rabies prophylaxis, 3% occurring within 1 day of receiving boosters, and 3% occurring 6-14 days after boosters (82). In one study, hypersensitivity reactions (e.g., urticaria, pruritic rash, and angioedema) were reported in 5.6% (11 of 99) of schoolchildren aged 5-13 years following pre-exposure prophylaxis with IM HDCV (72). Angioedema was observed in 1.2% of these school children after booster doses of HDCV 1 year after primary vaccination with HDCV. In 46 months of surveillance for adverse events following HDCV administration during 1980–1984, CDC received reports of 108 systemic allergic reactions (ranging from hives to anaphylaxis) following HDCV (11 per 10,000 vaccinees) (14). These included nine cases of presumed Type I immediate hypersensitivity (one of 10,000), 87 cases of presumed Type III hypersensitivity (nine of 10,000), and 12 cases of hypersensitivity of indeterminate type. All nine of the presumed immediate hypersensitivity reactions occurred during either primary pre-exposure or postexposure vaccination. Most (93%) of the Type III hypersensitivity reactions were observed following booster vaccination. Systemic allergic reactions have been associated with the presence of betapropiolactone-altered human albumin in HDCV and the development of immunoglobulin E (IgE) antibodies to this

allergen (82,86). No deaths resulting from these reactions were reported.

In four studies investigating the safety of rabies postexposure prophylaxis with both HRIG and HDCV, no serious adverse events were observed (55-57,78). Local reactions were common, and pain at the injection site was reported by 7%-92%of participants (55-57). Studies of the frequency of systemic adverse reactions following rabies vaccination are limited by small sample sizes. Systemic adverse reactions were not observed in any of the participants in one study with a relatively small sample size (78). In two other studies in which adverse events were collected using patient self-monitoring forms and investigator interviews at each visit, systemic reactions were reported by 76%-100% of participants (55,56). However, none of these reported systemic adverse events was considered to be serious.

Rare, individual case reports of neurologic adverse events following rabies vaccination have been reported, but in none of the cases has causality been established. Four cases of neurologic illness resembling Guillain-Barré syndrome occurring after treatment with HDCV were identified (13,87–89). One case of acute neurologic syndrome involving seizure activity was reported following the administration of HDCV and HRIG (90). Other central and peripheral nervous system disorders have been temporally associated with HDCV vaccine (91).

### PCECV

In studies of PCECV use, local reactions (e.g., pain at the injection site, redness, swelling, and induration) were reported among 11%-57% of recipients (29,79,84). Local pain at the injection site, the most common local reaction, was reported in 2%-23% of vaccinees (29,71,79,81,83,85). Systemic reactions were less common and have been reported in 0-31% of vaccine recipients (79,83,84). One study investigated adverse events among 271 children in India who received rabies postexposure prophylaxis with PCECV IM without HRIG following bites from suspected or confirmed rabid dogs (85). Overall, 7% of the children experienced mild to moderate clinical reactions. The most frequently reported reaction was local pain after the first or second dose (4%). Another study documented clinical reactions in 29 persons administered 6 IM doses of PCECV with (n = four) or without HRIG following bites by suspected rabid stray dogs. No serious adverse events were observed during the course of or after prophylaxis (36). Another case report documented one case of neurologic illness resembling Guillain-Barré syndrome after vaccination with PCECV in India (92).

A retrospective review of adverse events following administration of PCECV was conducted using data from the United States Vaccine Adverse Events Reporting System (VAERS) (93). During 1997-2005, approximately 1.1 million doses of PCECV were distributed in the United States and 336 reports describing adverse events following PCECV administration were received by VAERS (30 events per 100,000 doses distributed and three serious events per 100,000 doses distributed). A total of 199 reported adverse events (4% serious [i.e., adverse events that involve hospitalization, lifethreatening illness, disability, or death]) occurred following administration of PCECV alone, and 137 (12% serious) occurred following PCECV administered concomitantly with another vaccine or following postexposure prophylaxis (PCECV co-administered with HRIG). Among the 312 nonserious adverse events, the most frequently reported were headache, fever, myalgia, nausea, and weakness. A limitation of VAERS is that causality between vaccine administration and reported adverse events cannot be established (94). No deaths or rabies cases were reported following administration of PCECV.

### HRIG

In a clinical trial involving 16 volunteers in each group, participants receiving HRIG plus placebo (administered to mimic vaccine) commonly reported local reactions (100% in conventionally produced HRIG group, 75% in heat-treated HRIG group), including pain/tenderness (100% conventional HRIG, 50% heat-treated HRIG), erythema (63% conventional, 25% heat-treated), and induration (50% conventional, 31% heat-treated) (56). Systemic reactions were reported in 75% of participants in the conventional HRIG group and 81% in the heat-treated group. Headache was the most commonly reported systemic reaction (50% conventional, 69% heat-treated). The majority of the reported local and systemic reactions were mild, and no significant differences were observed in the frequency of adverse events between treatment groups. No serious adverse events, including immediate hypersensitivity reactions or immune-complex-like disease, were reported.

### Cost-Effectiveness of Rabies Postexposure Prophylaxis

ACIP's charter requires the committee, when deliberating recommendations for vaccine use in the United States, to consider the cost and benefits of potential recommendations. Cost-effectiveness studies combine different types of data (e.g., epidemiologic, clinical, cost, and vaccine effectiveness), and the results from such studies allow public health officials, medical practitioners, and the public to make more informed decisions when evaluating the risk for disease against the cost of the vaccine, including vaccine-related side effects.

CDC analyzed the cost-effectiveness of rabies postexposure prophylaxis for each of eight contact (risk of transmission) scenarios, with the outcome being the net cost (in dollars) per life saved (in 2004 dollars). The perspective was societal, which means that all costs and all benefits were included, regardless of who pays and who benefits. For each risk-oftransmission scenario, three cost-effectiveness ratios were calculated: average, most, and least cost-effective. Average cost-effective ratios were calculated using median transmission risk values (Table 2) and average cost of postexposure prophylaxis. Most cost-effective ratios were calculated using greatest (largest) transmission risk values and least cost of postexposure prophylaxis. Least cost-effective ratios were calculated using lowest transmission risk and greatest cost of postexposure prophylaxis. The analysis assumed that the direct medical costs associated with postexposure prophylaxis included 1 dose of HRIG (\$326-\$1,434), 5 doses of HDCV (\$113-\$679 each), hospital charges (\$289-\$624), and physician charges (\$295-\$641) (95). Indirect costs included travel, lost wages, alternative medicine, and other costs (\$161-\$2,161) (96). A societal perspective requires the valuation of the loss of productivity to society caused by premature death. Therefore, human life lost was valued using the average present value, in 2004 dollars, of expected future lifetime earnings and housekeeping services (\$1,109,920) (97). All costs were adjusted to 2004 dollars using the medical care price index. The study also assumed that rabies postexposure prophylaxis, when administered according to these recommendations, was essentially 100% effective in preventing a clinical case of human rabies. The probabilities of rabies transmission to a human following possible contact with different species of potentially rabid animals was assessed by a panel of experts using the Delphi methodology, except for "animal tests positive for rabies" when probabilities were obtained from a previous study (98) (Table 2).

Under all three cost-effectiveness scenarios, the analysis determined that it is always cost saving to administer postexposure prophylaxis if a patient is bitten by a rabid animal that has tested positive for rabies or if a patient is bitten by a reservoir or vector species (e.g. skunk, raccoon, bat, or fox bite in the United States or dog bite in countries with dog variant rabies), even if the animal is not available for testing. For all other transmission risk situations, the average net cost effectiveness ratio was always a net cost per life saved (range: \$2.9 million per life saved following a bite from an untested cat to \$4 billion per life saved following a lick from an untested dog). The wide range of probabilities of risk for trans-

Contact scenario	Probability of rabies⁺ Median (minimum–maximum)	Baseline cost scenario <sup>s</sup> Average cost effectiveness (most cost-effective–least cost-effective)
Animal tests positive for rabies	(0.01–0.7)	Cost Saving
Skunk bite <sup>¶</sup>	0.05 (0.01–0.1)	Cost Saving
Possible bat bite <sup>¶</sup> **	0.001 (0.000001–0.01)	\$2.9 million (Cost saving–\$8.4 billion)
Dog bite <sup>¶</sup>	0.00001 (0.00001–0.001)	\$403 million (\$524,080–\$840 million)
Dog lick <sup>¶</sup>	0.000001 (0.000001–0.00001)	\$4 billion (\$162 million–\$8.4 billion)
Cat bite <sup>1</sup>	0.001 (0.00001–0.01)	\$2.9 million (Cost saving-\$840 million)
Cat lick <sup>¶</sup>	0.000001 (0.000001–0.0001)	\$4 billion (\$15 million–\$8.4 billion)
Contact with rabid human in clinical setting**	0.000001 (0.000001–0.00001)	\$4 billion (\$162 million–\$8.4 billion)

# TABLE 2. Cost-effectiveness ratios (cost/life saved) for rabies postexposure prophylaxis, by different scenarios of potential exposure\* — United States

\* Contact with a potentially rabid animal does not necessarily constitute an exposure. A bite exposure is defined as "any penetration of the skin by teeth." A nonbite exposure is defined as "contamination of open wounds, abrasions (including scratches) or mucous membranes with saliva or other potentially infectious material (e.g., neural tissue)."

<sup>†</sup> Probabilities of rabies transmission to a human were obtained from a panel of experts, except for "animal tests positive for rabies" when probabilities obtained from a previous study.

§ Estimates of the direct medical costs of rabies postexposure prophylaxis (PEP) were converted into 2004 dollars using the medical care price index. The cost-effectiveness of PEP under each contact scenario is calculated using the median probability of becoming clinically ill with rabies and the average cost of PEP. The most cost-effective ratio is calculated using the minimum cost of PEP and the maximum probability of becoming clinically ill with rabies. The least cost-effective ratio is calculated using the maximum cost of PEP and the minimum probability of becoming clinically ill with rabies.

<sup>¶</sup> Animals not available for testing. The skunk bite data are considered applicable to bites from other rabies reservoir species (e.g., bats, raccoons, and foxes in the United States and dog bites occurring in countries with dog variant rabies).

\*\* No recognized bite or saliva exposure.

mission for the bat bite scenario resulted in the widest range of cost-effectiveness ratios (Table 2). Until more precise estimates of risk for transmission are obtained, these estimates illustrate the difficulty clinicians and public health officials will continue to encounter in unequivocally determining the cost-effectiveness of providing PEP.

# **Rabies Postexposure Prophylaxis**

### **Rationale for Prophylaxis**

ACIP (26) and WHO (25) recommend that prophylaxis for the prevention of rabies in humans exposed to rabies virus should include prompt and thorough wound cleansing followed by passive vaccination with HRIG and vaccination with cell culture rabies vaccines. Administration of rabies postexposure prophylaxis is a medical urgency, not a medical emergency. Because rabies biologics are valuable resources that are periodically in short supply, a risk assessment weighing potential adverse consequences associated with administering postexposure prophylaxis along with their severity and likelihood versus the actual risk for the person acquiring rabies should be conducted in each situation involving a possible rabies exposure. Because the balance of benefit and harm will differ among exposed persons on the basis of the risk for infection, recommendations regarding rabies postexposure prophylaxis are dependent upon associated risks including 1) type of exposure, 2) epidemiology of animal rabies in the area where the contact occurred and species of animal involved, and 3) circumstances of the exposure incident. The reliability of this information should be assessed for each incident. The decision of whether to initiate rabies postexposure prophylaxis also depends on the availability of the exposing animal for observation or rabies testing (Table 3). Because the epidemiology and pathogenesis of rabies are complex, these recommendations cannot be specific for every possible circumstance. Clinicians should seek assistance from local or state public health officials for evaluating exposures or determining the need for postexposure management in situations that are not routine. State and local officials have access to CDC rabies experts for particularly rare situations or difficult decisions.

Animal type	Evaluation and disposition of animal	Postexposure prophylaxis recommendations
Dogs, cats, and ferrets	Healthy and available for 10 days observation	Persons should not begin prophylaxis unless animal develops clinical signs of rabies.*
	Rabid or suspected rabid	Immediately begin prophylaxis.
	Unknown (e.g., escaped)	Consult public health officials.
Skunks, raccoons, foxes, and most other carnivores; bats <sup>†</sup>	Regarded as rabid unless animal proven negative by laboratory tests§	Consider immediate prophylaxis.
Livestock, small rodents (rabbits and hares), large rodents (woodchucks and beavers), and other mammals	Consider individually	Consult public health officials. Bites from squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, other small rodents, rabbits, and hares almost never require antirabies postexposure prophylaxis.

#### TABLE 3. Rabies postexposure prophylaxis guide — United States, 2008

\* During the 10-day observation period, begin postexposure prophylaxis at the first sign of rabies in a dog, cat, or ferret that has bitten someone. If the animal exhibits clinical signs of rabies, it should be euthanized immediately and tested.

<sup>†</sup> Postexposure prophylaxis should be initiated as soon as possible following exposure to such wildlife unless the animal is available for testing and public health authorities are facilitating expeditious laboratory testing or it is already known that brain material from the animal has tested negative. Other factors that might influence the urgency of decision-making regarding initiation of postexposure prophylaxis before diagnostic results are known include the species of the animal, the general appearance and behavior of the animal, whether the encounter was provoked by the presence of a human, and the severity and location of bites. Discontinue vaccine if appropriate laboratory diagnostic test (i.e., the direct fluorescent antibody test) is negative.
§The animal should be euthanized and tested as soon as possible. Holding for observation is not recommended.

**Types of Exposure** 

When an exposure has occurred, the likelihood of rabies infection varies with the nature and extent of that exposure. Under most circumstances, two categories of exposure (bite and nonbite) should be considered. The most dangerous and common route of rabies exposure is from the bite of a rabid mammal. An exposure to rabies also might occur when the virus, from saliva or other potentially infectious material (e.g., neural tissue), is introduced into fresh, open cuts in skin or onto mucous membranes (nonbite exposure). Indirect contact and activities (e.g., petting or handling an animal, contact with blood, urine or feces, and contact of saliva with intact skin) do not constitute exposures; therefore, postexposure prophylaxis should not be administered in these situations. Exposures to bats deserve special assessment because bats can pose a greater risk for infecting humans under certain circumstances that might be considered inconsequential from a human perspective (i.e., a minor bite or lesion). Human-to-human transmission occurs almost exclusively as a result of organ or tissue transplantation. Clinicians should contact local or state public health officials for assistance in determining the likelihood of a rabies exposure in a specific situation.

**Bite exposures.** Any penetration of the skin by teeth constitutes a bite exposure. All bites, regardless of body site or evidence of gross trauma, represent a potential risk. The risk for transmission varies in part with the species of biting animal, the anatomic site of the bite, and the severity of the wound (98). Although risk for transmission might increase with wound severity, rabies transmission also occurs from bites by some animals (e.g., bats) that inflict rather minor injury compared with larger-bodied carnivores, resulting in lesions that are difficult to detect under certain circumstances (8,99–103).

Nonbite exposures. Nonbite exposures from animals very rarely cause rabies. However, occasional reports of nonbite transmission suggest that such exposures require assessment to determine if sufficient reasons exist to consider postexposure prophylaxis (104). The nonbite exposures of highest risk appear to be among surgical recipients of corneas, solid organs, and vascular tissue transplanted from patients who died of rabies and persons exposed to large amounts of aerosolized rabies virus. Two cases of rabies have been attributed to probable aerosol exposures in laboratories, and two cases of rabies have been attributed to possible airborne exposures in caves containing millions of free-tailed bats (Tadarida brasiliensis) in the Southwest. However, alternative infection routes can not be discounted (105-109). Similar airborne incidents have not occurred in approximately 25 years, probably because of elevated awareness of such risks resulting in increased use of appropriate preventive measures.

The contamination of open wounds or abrasions (including scratches) or mucous membranes with saliva or other potentially infectious material (e.g., neural tissue) from a rabid animal also constitutes a nonbite exposure. Rabies virus is inactivated by desiccation, ultraviolet irradiation, and other factors and does not persist in the environment. In general, if the suspect material is dry, the virus can be considered noninfectious. Nonbite exposures other than organ or tissue transplants have almost never been proven to cause rabies, and postexposure prophylaxis is not indicated unless the nonbite exposure met the definition of saliva or other potentially infectious material being introduced into fresh, open cuts in skin or onto mucous membranes.

**Bat Exposures.** The most common rabies virus variants responsible for human rabies in the United States are bat-related; therefore, any potential exposure to a bat requires a thorough evaluation. If possible, bats involved in potential human exposures should be safely collected and submitted for rabies diagnosis. Most submitted bats (approximately 94%) (*110*) will not be rabid and such timely diagnostic assessments rule out the need for large investments in risk assessments and unnecessary prophylaxis.

The risk for rabies resulting from an encounter with a bat might be difficult to determine because of the limited injury inflicted by a bat bite (compared with more obvious wounds caused by the bite of terrestrial carnivores), an inaccurate recall of a bat encounter that might have occurred several weeks or months earlier, and evidence that some bat-related rabies viruses might be more likely to result in infection after inoculation into superficial epidermal layers (111). For these reasons, any direct contact between a human and a bat should be evaluated for an exposure. If the person can be reasonably certain a bite, scratch, or mucous membrane exposure did not occur, or if the bat is available for testing and is negative for presence of rabies virus, postexposure prophylaxis is not necessary. Other situations that might qualify as exposures include finding a bat in the same room as a person who might be unaware that a bite or direct contact had occurred (e.g., a deeply 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). These situations should not be considered exposures if rabies is ruled out by diagnostic testing of the bat, or circumstances suggest it is unlikely that an exposure took place. Other household members who did not have direct contact with the bat or were awake and aware when in the same room as the bat should not be considered as having been exposed to rabies. Circumstances that make it less likely that an undetected exposure occurred include the observation of bats roosting or flying in a room open to the outdoors, the observation of bats outdoors or in a setting where bats might normally be present, or situations in which the use of protective covers (e.g., mosquito netting) would reasonably be expected to preclude unnoticed contact. Because of the complexity of some of these situations, consultation with state and local health departments should always be sought. If necessary, further guidance can be sought from CDC and experts in bat ecology.

During 1990–2007, a total of 34 naturally acquired batassociated human cases of rabies was reported in the United States. In six cases, a bite was reported; in two cases, contact with a bat and a probable bite were reported; in 15 cases, physical contact was reported (e.g., the removal of a bat from the home or workplace or the presence of a bat in the room where the person had been sleeping), but no bite was documented; and in 11 cases, no bat encounter was reported. In these cases, an unreported or undetected bat bite remains the most plausible hypothesis because the genetic sequences of the human rabies viruses closely matched those of specific species of bats. Clustering of human cases associated with bat exposures has never been reported in the United States (e.g., within the same household or among a group of campers where bats were observed during their activities) (8,101,110).

Human-to-Human Exposures. Human-to-human transmission can occur in the same way as animal-to-human transmission (i.e., the virus is introduced into fresh open cuts in skin or onto mucous membranes from saliva or other potentially infectious material such as neural tissue). Organ and tissue transplantation resulting in rabies transmission has occurred among 16 transplant recipients from corneas (n = eight), solid organs (n = seven), and vascular tissue (n = one). Each of the donors died of an illness compatible with or proven to be rabies (10,112-123). The 16 cases occurred in five countries: the United States (five cases: one corneal transplant transmission, three solid organ transmissions, and one vascular graft transmission), Germany (four cases), Thailand (two cases), India (two cases), Iran (two cases), and France (one case).

No documented laboratory-diagnosed cases of human-tohuman rabies transmission have been documented from a bite or nonbite exposure other than the transplant cases (124). At least two cases of human-to-human rabies transmission in Ethiopia have been suggested, but rabies as the cause of death was not confirmed by laboratory testing (125). The reported route of exposure in both cases was direct salivary contact from another human (i.e., a bite and a kiss). Routine delivery of health care to a patient with rabies is not an indication for postexposure prophylaxis unless the health-care worker is reasonably certain that he or she was bitten by the patient or that his or her mucous membranes or nonintact skin was exposed directly to potentially infectious saliva or neural tissue. Adherence to standard precautions for all hospitalized patients as outlined by the Hospital Infection Control Practices Advisory Committee will minimize the need for postexposure prophylaxis in such situations (126). Staff should wear gowns, goggles, masks, and gloves, particularly during intubation and suctioning (25).

### **Animal Rabies Epidemiology**

**Bats.** Rabid bats have been documented in the 49 continental states, and bats are increasingly implicated as important wildlife reservoirs for variants of rabies virus transmitted to humans (5,101,102,110). Transmission of rabies virus can occur from minor, seemingly underappreciated or unrecognized bites from bats (8,99–103). Laboratory data support a hypothesis that bat rabies virus variants associated with silver-haired bats (*Lasionycteris noctivagans*) and eastern pipistrelles (*Pipistrellus subflavus*) have biologic characteristics that might allow a higher likelihood of infection after superficial inoculation, such as into cells of epidermal origin (127). Human and domestic animal contact with bats should be minimized, and bats should never be handled by untrained and unvaccinated persons or be kept as pets (128).

Wild Terrestrial Carnivores. Raccoons, skunks, and foxes are the terrestrial carnivores most often infected with rabies in the United States (5). Suggestive clinical signs of rabies among wildlife cannot be interpreted reliably. All bites by such wildlife should be considered possible exposures to rabies virus. Postexposure prophylaxis should be initiated as soon as possible following exposure to such wildlife, unless the animal is available for diagnosis and public health authorities are facilitating expeditious laboratory testing, or if the brain tissue from the animal has already tested negative. Wild terrestrial carnivores that are available for diagnostic testing should be euthanized as soon as possible (without unnecessary damage to the head), and the brain should be submitted for rabies diagnosis (129,130). If the results of testing are negative by immunofluorescence, human rabies postexposure prophylaxis is not necessary. Other factors that might influence the urgency of decision-making regarding the initiation of postexposure prophylaxis before diagnostic results are known include the species of the animal, the general appearance and behavior of the animal, whether the encounter was provoked by the presence of a human, and the severity and location of bites.

**Other Wild Animals.** Rodents are not reservoirs of rabies virus. Small rodents (e.g., squirrels, chipmunks, rats, mice, hamsters, guinea pigs, and gerbils) and lagomorphs (including rabbits and hares) are rarely infected with rabies and have not been known to transmit rabies to humans (*131,132*). During 1990–1996, in areas of the country where raccoon rabies was enzootic, woodchucks accounted for 93% of the 371 cases of rabies among rodents reported to CDC (*5,133,134*). In all cases involving rodents, the state or local health department should be consulted before a decision is made to initiate postexposure prophylaxis (*135*).

The offspring of wild animals crossbred to domestic dogs and cats (wild animal hybrids) are considered wild animals by the National Association of State and Public Health Veterinarians and CSTE. Because the period of rabies virus shedding in wild animal hybrids is unknown, when such animals bite humans euthanasia and rabies testing of the hybrid animal is the safest course of action. Vaccination should be discontinued if diagnostic tests of the involved animal are negative for rabies infection. However, because wolves and dogs have very similar genetic makeup and many animals that are advertised as "wolf-dogs" might actually be dogs, each wolf hybrid bite situation should be evaluated individually, taking into account the likelihood that it is a hybrid, the severity of the wound, and the assessment by the bite victim and his or her health-care provider. State or local health departments should be consulted before a decision is made to euthanize and test an animal. Wild animals and wild animal hybrids should not be kept as pets (128) or be publicly accessible. Humans who work with wild animals maintained in United States Department of Agriculture-licensed research facilities or accredited zoological parks should be educated on preventing bites and should receive rabies pre-exposure vaccinations. Rabies exposures of these animal handlers might require booster postexposure vaccinations in lieu of euthanasia and testing of the animal depending on employment requirements.

Domestic Dogs, Cats, and Ferrets. The likelihood of rabies in a domestic animal varies regionally, and the need for postexposure prophylaxis also varies on the basis of regional epidemiology. The number of reported cases of rabies in domestic dogs has decreased substantially in the United States, primarily because of improved canine vaccination and stray animal control programs (5). In the continental United States, rabies among dogs has been reported sporadically along the United States-Mexico border and in areas of the United States with enzootic wildlife rabies (5). During 2000-2006, more cats than dogs were reported rabid in the United States (6). The majority of these cases were associated with the epizootic of rabies among raccoons in the eastern United States. The large number of rabid cats compared with other domestic animals might be attributed to a lower vaccination rate among cats because of less stringent cat vaccination laws; fewer confinement or leash laws; and the nocturnal activity patterns of cats placing them at greater risk for exposure to infected raccoons, skunks, foxes, and bats. In certain developing countries, dogs remain the major reservoir and vector of rabies and represent an increased risk for rabies exposure in such countries (136).

A healthy domestic dog, cat, or ferret that bites a person should be confined and observed for 10 days (*128,137,138*).

Those that remain alive and healthy 10 days after a bite would not have been shedding rabies virus in their saliva and would not have been infectious at the time of the bite (25). All domestic dogs, cats, and ferrets kept as pets should be vaccinated against rabies. Even if they are not, such animals might still be confined and observed for 10 days after a bite to reliably determine the risk for rabies exposure for the person who was bitten. Any illness in the animal during the confinement period before release should be evaluated by a veterinarian and reported immediately to the local public health department. If signs suggestive of rabies develop, postexposure prophylaxis of the bite victim should be initiated. The animal should be euthanized and its head removed and shipped, under refrigeration, for examination by a qualified laboratory. If the biting animal is stray or unwanted, it should either be confined and observed for 10 days or euthanized immediately and submitted for rabies diagnosis (128).

**Other Domestic Animals.** In all instances of exposure to other domestic animal species, local or state health department should be consulted before a decision is made to euthanize and test the animal or initiate postexposure prophylaxis (*128*).

### Circumstances of Biting Incident and Vaccination Status of Exposing Animal

An unprovoked attack by an animal might be more likely than a provoked attack to indicate that the animal is rabid. Bites inflicted on a person attempting to feed or handle an apparently healthy animal should generally be regarded as provoked. Other factors to consider when evaluating a potential rabies exposure include the epidemiology of rabies in the area, the biting animal's history and health status (e.g., abnormal behavior and signs of illness), and the potential for the animal to be exposed to rabies (e.g., presence of an unexplained wound or history of exposure to a rabid animal). A dog, cat, or ferret with a history of continuously current vaccination (i.e., no substantial gaps in vaccination coverage) is unlikely to become infected with rabies (*128,137,139–141*). Even after an initial rabies vaccination, young or naïve animals remain at risk for rabies because of the potential exposures preceding vaccination or before adequate induction of immunity during the 28 days after primary vaccination (*128*).

### **Treatment of Wounds and Vaccination**

The essential components of rabies postexposure prophylaxis are wound treatment and, for previously unvaccinated persons, the administration of both HRIG and vaccine (Table 4) (142). Administration of rabies postexposure prophylaxis is a medical urgency, not a medical emergency, but decisions must not be delayed. Incubation periods of more than 1 year have been reported in humans (143). Therefore, when a documented or likely exposure has occurred, postexposure prophylaxis should be administered regardless

Vaccination status	Treatment	Regimen*
Not previously vaccinated	Wound cleansing	All postexposure prophylaxis should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidine-iodine solution should be used to irrigate the wounds.
	Rabies immune globulin (RIG)	Administer 20 IU/kg body weight. If anatomically feasible, the full dose should be infiltrated around the wound(s) and any remaining volume should be administered intramuscularly (IM) at an anatomical site distant from vaccine administration. Also, RIG should not be administered in the same syringe as vaccine. Because RIG might partially suppress active production of antibody, no more than the recommended dose should be given.
	Vaccine	Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) 1.0 mL, IM (deltoid area§), one each on days $0^{1}$ , 3, 7, 14, and 28.
Previously vaccinated <sup>†</sup>	Wound cleansing	All postexposure prophylaxis should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidine-iodine solution should be used to irrigate the wounds.
	RIG	RIG should not be administered.
	Vaccine	HDCV or PCECV 1.0 mL, IM (deltoid area§), one each on days 0 $^{\P}$ and 3.

 TABLE 4. Rabies postexposure prophylaxis schedule — United States, 2008

\* These regimens are applicable for all age groups, including children.

<sup>†</sup>Any person with a history of a complete pre-exposure or postexposure vaccination regimen with HDCV, PCECV, or rabies vaccine adsorbed, or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination.

<sup>§</sup>The deltoid area is the only acceptable site of vaccination for adults and older children. For younger children, the outer aspect of the thigh can be used. Vaccine should never be administered in the gluteal area.

<sup>¶</sup>Day 0 is the day the first dose of vaccine is administered.

of the length of the delay, provided that compatible clinical signs of rabies are not present in the exposed person. The administration of postexposure prophylaxis to a clinically rabid human patient has demonstrated consistent ineffective-ness (*25*).

In 1977, WHO recommended a regimen of RIG and 6 doses of HDCV over a 90-day period. This recommendation was based on studies in Germany and Iran (19,21). When used in this manner, the vaccine was safe and effective in persons bitten by animals proven to be rabid and induced an adequate antibody response in all recipients (19). Studies conducted in the United States by CDC have documented that a regimen of 1 dose of HRIG and 5 doses of HDCV over a 28-day period was safe and induced an adequate antibody response in all recipients (18). Clinical trials with PCECV have demonstrated immunogenicity equivalent to that of HDCV (144).

Cell culture vaccines have been used effectively with HRIG or RIG of equine origin (ERIG) worldwide to prevent rabies in persons bitten by various rabid animals (18,19). Worldwide, WHO estimates that postexposure prophylaxis is initiated on 10–12 million persons annually (144). An estimated 16,000–39,000 persons in the United States receive a full postexposure course each year (11). Although postexposure prophylaxis has not always been properly administered in the United States, no failures have been documented since current biologics have been licensed.

### **Treatment of Wounds**

Regardless of the risk for rabies, the optimal medical treatment of animal bite wounds includes the recognition and treatment of serious injury (e.g., nerve or tendon laceration), avoidance or management of infection (both local and systemic), and approaches that will yield the best possible cosmetic results (145). For many types of bite wounds, immediate gentle irrigation with water or a dilute water povidone-iodine solution markedly decrease the risk for bacterial infection (146). Care should be taken not to damage skin or tissues. Wound cleansing is especially important in rabies prevention because thorough wound cleansing alone without other postexposure prophylaxis markedly reduce the likelihood of rabies in animal studies (147,148). Consideration should be given to the need for a booster dose of tetanus vaccine (149,150). Decisions regarding the use of antibiotic prophylaxis (151) and primary wound closure (152) should be individualized on the basis of the exposing animal species, size and location of the wound(s), and time interval since the bite. Suturing should be avoided, when possible.

### Vaccination

Postexposure antirabies vaccination should always include administration of both passive antibody and vaccine, with the exception of persons who have ever previously received complete vaccination regimens (pre-exposure or postexposure) with a cell culture vaccine or persons who have been vaccinated with other types of vaccines and have previously had a documented rabies virus neutralizing antibody titer. These persons should receive only vaccine (i.e., postexposure for a person previously vaccinated). The combination of HRIG and vaccine is recommended for both bite and nonbite exposures reported by persons who have never been previously vaccinated for rabies, regardless of the interval between exposure and initiation of prophylaxis. If postexposure prophylaxis has been initiated and appropriate laboratory diagnostic testing (i.e., the direct fluorescent antibody test) indicates that the exposing animal was not rabid, postexposure prophylaxis can be discontinued.

Rabies IgG Use. HRIG is administered only once (i.e., at the beginning of antirabies prophylaxis) to previously unvaccinated persons to provide immediate, passive, rabies virusneutralizing antibody coverage until the patient responds to HDCV or PCECV by actively producing antibodies. If HRIG was not administered when vaccination was begun (i.e., day 0), it can be administered up to and including day 7 of the postexposure prophylaxis series (153). Beyond the seventh day, HRIG is not indicated because an antibody response to cell culture vaccine is presumed to have occurred. Because HRIG can partially suppress active production of antibody, the dose administered should not exceed the recommended dose (154). The recommended dose of HRIG is 20 IU/kg (0.133 mL/kg) body weight. This formula is applicable to all age groups, including children. If anatomically feasible, the full dose of HRIG should be thoroughly infiltrated in the area around and into the wounds. Any remaining volume should be injected IM at a site distant from vaccine administration. This recommendation for HRIG administration is based on reports of rare failures of postexposure prophylaxis when less than the full amount of HRIG was infiltrated at the exposure sites (155). HRIG should never be administered in the same syringe or in the same anatomical site as the first vaccine dose. However, subsequent doses of vaccine in the 5-dose series can be administered in the same anatomic location where the HRIG dose was administered, if this is the preferable site for vaccine administration (i.e., deltoid for adults or anterolateral thigh for infants and small children).

**Vaccine Use.** Two rabies vaccines are available for use in the United States (Table 1); either can be administered in conjunction with HRIG at the beginning of postexposure pro-

phylaxis. A regimen of 5 one-mL doses of HDCV or PCECV should be administered IM to previously unvaccinated persons. The first dose of the 5-dose course should be administered as soon as possible after exposure. This date is then considered day 0 of the postexposure prophylaxis series. Additional doses should then be administered on days 3, 7, 14, and 28 after the first vaccination. For adults, the vaccination should always be administered IM in the deltoid area. For children, the anterolateral aspect of the thigh is also acceptable. The gluteal area should never be used for HDCV or PCECV injections because administration of HDCV in this area results in lower neutralizing antibody titers (*156*).

### Deviations from Recommended Postexposure Vaccination Schedules

Every attempt should be made to adhere to the recommended vaccination schedules. Once vaccination is initiated, delays of a few days for individual doses are unimportant, but the effect of longer lapses of weeks or more is unknown (157). Most interruptions in the vaccine schedule do not require reinitiation of the entire series (158). For most minor deviations from the schedule, vaccination can be resumed as though the patient were on schedule. For example, if a patient misses the dose scheduled for day 7 and presents for vaccination on day 10, the day 7 dose should be administered that day and the schedule resumed, maintaining the same interval between doses. In this scenario, the remaining doses would be administered on days 17 and 31. When substantial deviations from the schedule occur, immune status should be assessed by performing serologic testing 7-14 days after administration of the final dose in the series.

# Postexposure Prophylaxis Outside the United States

Persons exposed to rabies outside the United States in countries where rabies is enzootic might receive postexposure prophylaxis with regimens or biologics that are not used in the United States, including purified vero cell rabies vaccine (Verorab<sup>TM</sup>, Imovax – Rabies vero<sup>TM</sup>, TRC Verorab<sup>TM</sup>), purified duck embryo vaccine (Lyssavac N<sup>TM</sup>), and different formulations of PCECV (Rabipur<sup>®</sup>) or HDCV (Rabivac<sup>TM</sup>). This information is provided to familiarize physicians with some of the regimens used more widely abroad. These regimens have not been submitted for approval by the U.S. Food and Drug Administration (FDA) for use in the United States (*37*,*74*,*159–168*). If postexposure prophylaxis is initiated outside the United States using one of these regimens or vaccines of nerve tissue origin, additional prophylaxis might be necessary when the patient presents for care in the United

States. State or local health departments should be contacted for specific advice in such cases. Rabies virus neutralizing antibody titers from specimens collected 1–2 weeks after preexposure or postexposure prophylaxis would be considered adequate if complete neutralization of challenge virus at a 1:5 serum dilution by RFFIT occurs.

Purified ERIG or fractions of ERIG have been used in developing countries where HRIG might not have been available. The incidence of adverse reactions after ERIG administration has been low (0.8%-6.0%), and most of those that occurred were minor (169-171). In addition, unpurified antirabies serum of equine origin might still be used in some countries where neither HRIG nor ERIG are available. The use of this antirabies serum is associated with higher rates of serious adverse reactions, including anaphylaxis (172).

Although no postexposure prophylaxis failures have occurred in the United States since cell culture vaccines and HRIG have been routinely used, failures have occurred abroad when less than potent biologics were used, if some deviation was made from the recommended postexposure prophylaxis protocol, or when less than the recommended amount of RIG was administered (155,173-175). Specifically, patients who contracted rabies after postexposure prophylaxis might not have had adequate local wound cleansing, might not have received rabies vaccine injections in the deltoid area (i.e., vaccine was administered in the gluteal area), or might not have received appropriate infiltration of RIG around the wound site. Substantial delays between exposure and initiation of prophylaxis are of concern, especially with severe wounds to the face and head, which might provide access to the central nervous system through rapid viral neurotropism.

### **Rabies Pre-Exposure Prophylaxis**

Pre-exposure rabies prophylaxis is administered for several reasons. First, although pre-exposure vaccination does not eliminate the need for additional medical evaluation after a rabies exposure, it simplifies management by eliminating the need for RIG and decreasing the number of doses of vaccine needed. This is particularly important for persons at high risk for being exposed to rabies in areas where modern immunizing products might not be available or where cruder, less safe biologics might be used, placing the exposed person at increased risk for adverse events. Second, pre-exposure prophylaxis might offer partial immunity to persons whose postexposure prophylaxis is delayed. Finally, pre-exposure prophylaxis might provide some protection to persons at risk for unrecognized exposures to rabies. Pre-exposure vaccination should be offered to persons in high-risk groups, such as veterinarians and their staff, animal handlers, rabies researchers, and certain laboratory workers. Pre-exposure vaccination also should be considered for persons whose activities bring them into frequent contact with rabies virus or potentially rabid bats, raccoons, skunks, cats, dogs, or other species at risk for having rabies. In addition, some international travelers might be candidates for pre-exposure vaccination if they are likely to come in contact with animals in areas where dog or other animal rabies is enzootic and immediate access to appropriate medical care, including rabies vaccine and immune globulin, might be limited. Routine pre-exposure prophylaxis for the general U.S. population or routine travelers to areas where rabies is not enzootic is not recommended (*176,177*).

### **Primary Vaccination**

Three 1.0-mL injections of HDCV or PCECV should be administered IM (deltoid area), one injection per day on days 0, 7, and 21 or 28 (Table 5). The immunogenicity of IM primary vaccination with PCECV and HDCV has been reviewed. Vaccine preparations for ID administration are no longer available in the United States.

### **Pre-Exposure Booster Doses of Vaccine**

Persons who work with rabies virus in research laboratories or vaccine production facilities (continuous risk category [Table 6]) (178) are at the highest risk for inapparent exposures. Such persons should have a serum sample tested for rabies virus neutralizing antibody every 6 months. An IM booster dose (Table 5) of vaccine should be administered if the serum titer falls to maintain a serum titer corresponding to a value of at least complete neutralization at a 1:5 serum dilution by the RFFIT. The frequent-risk category includes other laboratory workers (e.g., those performing rabies diagnostic testing), cavers, veterinarians and staff, and animalcontrol and wildlife officers in areas where animal rabies is enzootic. The frequent-risk category also includes persons who frequently handle bats, regardless of location in the United States or throughout the world, because of the existence of lyssaviruses on all continents except Antarctica. Persons in the frequent-risk group should have a serum sample tested for rabies virus neutralizing antibody every 2 years. If the titer is less than complete neutralization at a 1:5 serum dilution by the RFFIT, the person also should receive a single booster dose of vaccine. Veterinarians, veterinary students, and terrestrial animal-control and wildlife officers working in areas where rabies is uncommon to rare (infrequent exposure group) and certain at-risk international travelers who have completed a full pre-exposure vaccination series with licensed vaccines and according to schedule do not require routine serologic verification of detectable antibody titers or routine pre-exposure booster doses of vaccine. If they are exposed to rabies in the future, they are considered immunologically primed against rabies and simply require postexposure prophylaxis for a person previously vaccinated (i.e., days 0 and 3 vaccination).

### Postexposure Prophylaxis for Previously Vaccinated Persons

If a person is exposed to rabies, local wound care remains an important part of postexposure prophylaxis, even for previously vaccinated persons. Previously vaccinated persons are those who have received one of the recommended pre-exposure or postexposure regimens of HDCV, PCECV, or RVA or those who received another vaccine and had a documented rabies virus neutralizing antibody titer. These persons should receive 2 IM doses (1.0 mL each in the deltoid) of vaccine, one immediately and one 3 days later. Administration of RIG is unnecessary and should not be administered to previously vaccinated persons because the administration of passive antibody might inhibit the relative strength or rapidity of an expected anamnestic response (77). For previously vaccinated persons who are exposed to rabies, determining the rabies virus neutralizing antibody titer for decision-making about prophylaxis is inappropriate for at least three reasons. First, several days will be required to collect the serum and determine the test result. Second, no "protective" titer is known. Finally, although rabies virus neutralizing antibodies are important

TABLE 5. Rabies pre-exposure prophylaxis schedule — United States, 2008

Type of vaccination	Route	Regimen
Primary	Intramuscular	Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV); 1.0 mL (deltoid area), one each on days 0,* 7, and 21 or 28
Booster <sup>†</sup>	Intramuscular	HDCV or PCECV; 1.0 mL (deltoid area), day 0 only
*Day 0 is the day the first doce of vaccine is administered		

<sup>1</sup>Day 0 is the day the first dose of vaccine is administered.

<sup>†</sup>Persons in the continuous-risk category should have a serum sample tested for rabies virus neutralizing antibody every 6 months, and persons in the frequent-risk category should be tested every 2 years. An intramuscular booster dose of vaccine should be administered if the serum titer falls to maintain a value of at least complete neutralization at a 1:5 serum dilution by rapid fluorescent focus inhibition test.

Risk category	Nature of risk	Typical populations	Pre-exposure recommendations
Continuous	Virus present continuously, often in high concentrations. Specific exposures likely to go unrecognized. Bite, nonbite, or aerosol exposure.	Rabies research laboratory workers; rabies biologics production workers.	Primary course. Serologic testing every 6 months; booster vaccination if antibody titer is below acceptable level.*
Frequent	Exposure usually episodic, with source recognized, but exposure also might be unrecognized. Bite, nonbite, or aerosol exposure.	Rabies diagnostic laboratory workers, cavers, veterinarians and staff, and animal-control and wildlife workers in areas where rabies is enzootic. All persons who frequently handle bats.	Primary course. Serologic testing every 2 years; booster vaccination if antibody titer is below acceptable level.*
Infrequent (greater than population at large) Exposure nearly always episodic with source recognized. Bite or nonbite exposure.		Veterinarians and animal-control staff working with terrestrial animals in areas where rabies is uncommon to rare. Veterinary students. Travelers visiting areas where rabies is enzootic and immediate access to appropriate medical care including biologics is limited.	Primary course. No serologic testing or booster vaccination.
Rare (population at large)	Exposure always episodic with source recognized. Bite or nonbite exposure.	U.S. population at large, including persons in areas where rabies is epizootic.	No vaccination necessary.

#### TABLE 6. Rabies pre-exposure prophylaxis guide — United States, 2008

\* Minimum acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by the rapid fluorescent focus inhibition test. A booster dose should be administered if the titer falls below this level.

components, other immune effectors also are operative in disease prevention.

# Vaccination and Serologic Testing

### **Post-Vaccination Serologic Testing**

In CDC studies, all healthy persons tested 2-4 weeks after completion of pre-exposure and postexposure rabies prophylaxis in accordance with ACIP guidelines demonstrated an adequate antibody response to rabies (18,73,179,180). Therefore, no testing of patients completing pre-exposure or postexposure prophylaxis is necessary to document seroconversion unless the person is immunosuppressed. Patients who are immunosuppressed by disease or medications should postpone pre-exposure vaccinations and consider avoiding activities for which rabies pre-exposure prophylaxis is indicated. When that is not possible, immunosuppressed persons who are at risk for exposure to rabies should be vaccinated and their virus neutralizing antibody titers checked. In these cases, failures to seroconvert after the third dose should be managed in consultation with appropriate public health officials. When titers are obtained, specimens collected 1-2 weeks after pre-exposure or postexposure prophylaxis should completely neutralize challenge virus at a 1:5 serum dilution by the RFFIT. Antibody titers might decline over time since the last vaccination. Small differences (i.e., within one dilution of sera) in the reported values of rabies virus neutralizing antibody titer (most properly reported according to a standard as IU/mL) might occur among laboratories that provide antibody determination using the recommended RFFIT. Rabies antibody titer determination tests that are not approved by FDA are not appropriate for use as a substitute for RFFIT in suspect human rabies antemortem testing because discrepant results between such tests and measures of actual virus neutralizing activity by RFFIT have been observed (*181*).

### Serologic Response and Pre-Exposure Booster Doses of Vaccine

Although virus neutralizing antibody levels might not definitively determine a person's susceptibility or protection from a rabies virus exposure, titers in persons at risk for exposure are used to monitor the relative rabies immune status over time (182). To ensure the presence of a primed immune response over time among persons at higher than normal risk for exposure, titers should be checked periodically, with booster doses administered only as needed. Two years after primary pre-exposure vaccination, a complete neutralization of challenge virus at a dilution of 1:5 (by the RFFIT) was observed among 93%–98% of persons who received the 3-dose pre-exposure series intramuscularly and 83%–95% of persons who received the 3-dose series intradermally (68). If the titer falls below the minimum acceptable antibody level of complete neutralization at a serum dilution of 1:5, a single pre-exposure booster dose of vaccine is recommended for persons at continuous or frequent risk for exposure to rabies (Table 6). The following guidelines are recommended for determining when serum testing should be performed after primary pre-exposure vaccination:

- A person in the continuous-risk category should have a serum sample tested for rabies virus neutralizing antibody every 6 months (178).
- A person in the frequent-risk category should have a serum sample tested for rabies virus neutralizing antibody every 2 years (183).

State or local health departments or CDC can provide the names and addresses of laboratories performing appropriate rabies virus neutralizing serologic testing.

## Management and Reporting of Adverse Reactions to Rabies Biologics

Once initiated, rabies prophylaxis 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 anti-inflammatory, antihistaminic, and antipyretic agents.

When a person with a history of hypersensitivity to rabies vaccine must be revaccinated, empiric intervention such as pretreatment with antihistamines might be considered. Epinephrine should be readily available to counteract anaphylactic reactions, and the person should be observed carefully immediately after vaccination (*184*).

Although serious systemic, anaphylactic, or neuroparalytic reactions are rare during and after the administration of rabies vaccines, such reactions pose a serious dilemma for the patient and the attending physician (14). A patient's risk for acquiring rabies must be carefully considered before deciding to discontinue vaccination. Advice and assistance on the management of serious adverse reactions for persons receiving rabies vaccines can be sought from the state or local health department or CDC.

All clinically significant adverse events occurring following administration of rabies vaccine should be reported to VAERS, even if causal relation to vaccination is not certain. Although VAERS is subject to limitations common to passive surveillance systems, including underreporting and reporting bias, it is a valuable tool for characterizing the safety profile of vaccines and identifying risk factors for rare serious adverse reactions to vaccines (94). VAERS reporting forms and information are available at http://www.vaers.hhs.gov or by telephone (800-822-7967). Web-based reporting is available and health-care providers are encouraged to report electronically at https://secure.vaers.org/VaersData Entryintro.htm. Clinically significant adverse events following HRIG administration should be reported to the Food and Drug Administration's MedWatch. Reports can be submitted electronically to http://www.fda.gov/MedWatch.

## **Precautions and Contraindications**

### Immunosuppression

Corticosteroids, other immunosuppressive agents, antimalarials, and immunosuppressive illnesses can interfere with the development of active immunity after vaccination (185,186). For persons with immunosuppression, pre-exposure prophylaxis should be administered with the awareness that the immune response might be inadequate. Patients who are immunosuppressed by disease or medications should postpone pre-exposure vaccinations and consider avoiding activities for which rabies pre-exposure prophylaxis is indicated. When this course is not possible, immunosuppressed persons who are at risk for rabies should have their virus neutralizing antibody titers checked after completing the pre-exposure series. A patient who fails to seroconvert after the third dose should be managed in consultation with their physician and appropriate public health officials. No cases of rabies postexposure prophylaxis failure have been documented among persons immunosuppressed because of human immunodeficiency virus infection.

Immunosuppressive agents should not be administered during postexposure prophylaxis unless essential for the treatment of other conditions. When postexposure prophylaxis is administered to an immunosuppressed person, one or more serum samples should be tested for rabies virus neutralizing antibody to ensure that an acceptable antibody response has developed. If no acceptable antibody response is detected, the patient should be managed in consultation with their physician and appropriate public health officials.

### Pregnancy

Because of the potential consequences of inadequately managed rabies exposure, pregnancy is not considered a contraindication to postexposure prophylaxis. Certain studies have indicated no increased incidence of abortion, premature births, or fetal abnormalities associated with rabies vaccination (187– 189). If the risk for exposure to rabies is substantial, pre-exposure prophylaxis also might be indicated during pregnancy. Rabies exposure or the diagnosis of rabies in the mother should not be regarded as reasons to terminate the pregnancy (157).

### Allergies

Persons who have a history of serious hypersensitivity to components of rabies vaccine or to other vaccines with components that are also present in rabies vaccine should be revaccinated with caution (184).

# **Indigent Patient Programs**

Both rabies vaccine manufacturers have patient assistant programs that provide medications to uninsured or underinsured patients. Sanofi pasteur's Indigent Patient Program (providing Imogam<sup>®</sup> Rabies-HT and Imovax<sup>®</sup> Rabies) is administered through the National Organization for Rare Disorders. Information is available by telephone (877-798-8716) or e-mail (nnadiq@rarediseases.org). Information on Novartis Pharmaceuticals Patient Assistance Program for RabAvert<sup>®</sup> is available at http://www.corporatecitizenship. novartis.com/patients/drug-pricing/assistance-programs.shtml.

### **Treatment of Human Rabies**

Rabies is associated with the highest case fatality rate of any infectious disease. No proven effective medical treatment is recognized after the development of clinical signs. Combined with intensive care, experimental measures have included administration of vidarabine, multisite ID vaccination with cell-culture vaccines, human leukocyte interferon, RIG by the intravenous and intrathecal routes, antithymocyte globulin, inosine pranobex, ribavirin, ketamine, and high doses of steroids (190–197). Initiation of rabies vaccination after onset of clinical symptoms in patients with confirmed rabies diagnoses is not recommended and might be detrimental.

Survival has been well documented for only six patients. In five of these cases, the persons had received rabies vaccination before the onset of disease (198–202). Only one patient has recovered from rabies without the institution of rabies vaccination (9,203). Despite these successes, rabies is not considered curable. Treatment of clinical rabies remains an extreme challenge. Rapid antemortem diagnosis is a priority. When a definitive diagnosis is obtained, primary health considerations should focus, at a minimum, on comfort care and adequate sedation of the patient in an appropriate medical facility. Sedation is often necessary because patients might become extremely agitated, especially in the presence of stimuli such as loud noises, air currents, and the sight or sound of running water, particularly during the acute neurologic phase of the disease (25). Beyond the overt clinical situation associated with progressive encephalitis, during fluctuating periods of lucidity, patient stress might be compounded by the psychological trauma resulting from a sense of personal isolation and hopelessness from the prognosis. As new potential treatments become available, medical staff at specialized tertiary care hospitals might consider institution of an aggressive approach to experimental therapies, especially in confirmed cases in young healthy persons at an early stage of clinical disease, after in depth discussions and informed consent by the patient, family or legal representatives (http:// www.mcw.edu/display/router.asp?DocID=11655). Parties authorized to give permission for such treatment also should be aware of the high probability for treatment failure, the anticipated expenses, and that in the rare instances of patient survival, the recovery might be associated with a variety of neurologic deficits requiring a lengthy period of rehabilitation (204). Continued efforts focusing on the elimination of exposure to sources of virus and the institution of appropriate and timely prophylaxis after exposure occurs remain the most effective public health measures to prevent human rabies.

## Precautions for Safe Clinical Management of Human Rabies Patients

Human rabies patients do not pose any greater infection risk to health-care personnel than do patients with more common bacterial and viral infections (25). Medical staff should adhere to standard precautions as outlined by the Hospital Infection Control Practices Advisory Committee (126). Staff should wear gowns, goggles, masks, and gloves, particularly during intubation and suctioning (25). Postexposure prophylaxis is indicated only when the patient has bitten another person or when the patient's saliva or other potentially infectious material such as neural tissue has contaminated an open wound or mucous membrane.

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# **Appendix**

# **Abbreviations Used in This Report**

ABL	Australian bat lyssavirus
ACIP	Advisory Committee on Immunization Practices
ARAV	Aravan bat virus
CPRV	Chromatographically purified Vero-cell rabies vaccine
CSTE	Council of State and Territorial Epidemiologists
CVS	Challenge standard virus
EBL	European bat lyssavirus
FDA	Food and Drug Administration
GMT	Geometric mean titer
HDCV	Human diploid cell vaccine
HRIG	Human rabies immune globulin
IgG	Immune globulin
IM	Intramuscular
IRKV	Irkut bat virus
KHUV	Khujand bat virus
NTV	Nerve tissue rabies vaccine
PCECV	Purified chick embryo cell vaccine
РНКС	Purified hamster kidney cell
RFFIT	Rapid fluorescent focus inhibition test
RIG	Rabies immune globulin
RVA	Rabies vaccine adsorbed
VAERS	Vaccine Adverse Events Reporting System
WCBV	West Caucasian bat virus
WHO	World Health Organization

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Recommendations and Reports May 23, 2008 / Vol. 57 / RR-3

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- 6. Submit your answers no later than May 23, 2010.
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### DEPARTMENT OF HEALTH AND HUMAN SERVICES CENTERS FOR DISEASE CONTROL AND PREVENTION

#### **Goal and Objectives**

This report provides recommendations for preventing rabies among humans. These recommendations were developed by CDC staff members and the Rabies Working Group of the Advisory Committee on Immunization Practices. The goal of this report is to guide clinical practice and policy development related to appropriate management of persons at risk for rabies. Upon completion of this educational activity, the reader should be able to1) describe groups for whom rabies pre-exposure prophylaxis are indicated, 2) describe groups for whom rabies serologic testing are indicated, 3) describe groups for whom booster dosing are indicated, 4) describe some of the common rabies reservoirs in the United States, and 5) describe the essential elements of rabies postexposure prophylaxis.

#### To receive continuing education credits, please answer all of the following questions.

1. Evidence from controlled, double-blinded clinical studies among humans indicates that the administration of postexposure prophylaxis after an exposure to a virulent dose of rabies virus is an effective means of preventing a productive infection.

A. True.

- B. False.
- 2. On the basis of available evidence from field observations or animal studies, postexposure prophylaxis is most likely to be beneficial when initiated as soon as possible after exposure, and in the majority of cases, should not be initiated if >\_\_\_\_ days have elapsed since the exposure.
  - A. 2.
  - B. 3.
  - C. 7.
  - D. 10.
  - E. None of the above.
- 3. Contact of which of the following body sites with rabies virus-infected materials constitutes a legitimate exposure?
  - A. Facial lesion.
  - B. Eye.
  - C. Intact skin.
  - D. Hand scratch.
  - E. A, B, and D.
- 4. In a rabid animal, potentially infectious material include...
  - A. Brain.
  - B. Saliva.
  - C. Salivary glands.
  - D. All of the above.
  - E. None of the above.
- 5. Which of the following lists of potential exposure types by animals are correctly ordered from the likely greatest risk for rabies virus infection to the least risk for infection?
  - A. Raccoon scratches are greater than licks to the skin, which are greater than bites.
  - B. Dog licks to the skin are greater than scratches, which are greater than bites.
  - C. Skunk scratches are greater than bites, which are greater than licks to the skin.
  - D. Bat licks to the skin are greater than scratches, which are greater than bites.
  - E. None of the above.

# 6. The recommended duration of routine rabies postexposure prophylaxis in the naïve person is over a period of...

- A. 3 days.
- B. 7 days.
- C. 14 days.
- D. 28 days.
- E. None of the above.

- 7. A runner reports an 'unprovoked bite' from a neighborhood dog. The dog was captured by local animal control authorities, and it appears healthy. What are the appropriate actions? (*Indicate all that are true*.)
  - A. Confine and observe the dog for 10 days for signs suggestive of rabies.
  - B. Begin postexposure prophylaxis of the bitten person.
  - C. Immediately euthanize the dog.
  - D. Because canine rabies has been eliminated in the United States, dog bites are no longer an indication for postexposure prophylaxis, and no further action is needed.
  - E. None of the above.
- 8. Which of the following statements are true about rabies pre-exposure prophylaxis in the United States? (*Indicate all that are true.*)
  - A. It is indicated for all international visitors if they will be in this country for >30 days.
  - B. It consists of 5 doses of rabies vaccine administered intramuscularly or intradermally.
  - C. In the event of an exposure, persons who have received preexposure prophylaxis still require 2 booster doses of rabies vaccine, but no rabies immune globulin.
  - D. Veterinarians in areas where rabies is enzootic should have titers checked every 10 years.
  - E. None of the above.
- 9. Which of the following animals are commonly reported rabid in the United States? (*Indicate all that are true.*)
  - A. Squirrels.
  - B. Raccoons.
  - C. Rabbits.
  - D. Swine.
  - E. Rats.
- 10. Which of the following statements about rabies are true? (*Indicate all that are true*.)
  - A. Human rabies is a fatal disease <50% of the time.
  - B. During the previous 2 decades, the majority of indigenous human rabies cases in the United States have been associated with canine variants of the rabies virus.
  - C. U.S. citizens traveling abroad can be at serious risk for exposure to avian rabies.
  - D. Although human rabies cases in the United States are rare, exposure to rabid or potentially rabid animals remains a relatively common event.
  - E. Postexposure prophylaxis is effective after the onset of clinical illness in the majority of cases.

#### 11. Which best describes your professional activities?

- A. Physician.
- B. Nurse.
- C. Health educator.
- D. Veterinarian.
- E. Other.

#### 12. I plan to use these recommendations as the basis for . . . (Indicate all that apply.)

- A. Health education materials.
- B. Insurance reimbursement policies.
- C. Local practice guidelines.
- D. Public policy.
- E. Other.

#### 13. Overall, the length of the journal report was...

- A. Much too long.
- B. A little too long.
- C. Just right.
- D. A little too short.
- E. Much too short.

#### 14. After reading this report, I am confident I can describe groups for whom rabies preexposure prophylaxis is indicated.

- A. Strongly agree.
- B. Agree.
- C. Neither agree nor disagree.
- D. Disagree.
- E. Strongly disagree.

#### 15. After reading this report, I am confident I can describe groups for whom rabies serologic testing and booster dosing are indicated.

- A. Strongly agree.
- B. Agree.
- C. Neither agree nor disagree.
- D. Disagree.
- E. Strongly disagree.

#### 16. After reading this report, I am confident I can describe groups for whom booster dosing are indicated.

- A. Strongly agree.
- B. Agree.
- C. Neither agree nor disagree.
- D. Disagree.
- E. Strongly disagree.

#### 17. After reading this report, I am confident I can describe some of the common rabies reservoirs in the United States.

- A. Strongly agree.
- B. Agree.
- C. Neither agree nor disagree.
- D. Disagree.
- E. Strongly disagree.
- 18. After reading this report, I am confident I can describe the essential elements of rabies postexposure prophylaxis.
  - A. Strongly agree.
  - B. Agree.
  - C. Neither agree nor disagree.
  - D. Disagree.
  - E. Strongly disagree.

#### 19. The learning outcomes (objectives) were relevant to the goal of this report.

- A. Strongly agree.
- B. Agree.
- C. Neither agree nor disagree.
- D. Disagree.
- E. Strongly disagree.

(Continued on pg CE-4)

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# 20. The instructional strategies used in this report (text, tables, and references) helped me learn the material.

- A. Strongly agree.
- B. Agree.
- C. Neither agree nor disagree.
- D. Disagree.
- E. Strongly disagree.

#### 21. The content is appropriate given the stated objectives of the report.

- A. Strongly agree.
- B. Agree.
- C. Neither agree nor disagree.
- D. Disagree.
- E. Strongly disagree.

#### 22. The content expert(s) demonstrated expertise in the subject matter.

- A. Strongly agree.
- B. Agree.
- C. Neither agree nor disagree.
- D. Disagree.
- E. Strongly disagree.

#### 23. Overall, the quality of the journal report was excellent.

- A. Strongly agree.
- B. Agree.
- C. Neither agree nor disagree.
- D. Disagree.
- E. Strongly disagree.

#### 24. These recommendations will improve the quality of my practice.

- A. Strongly agree.
- B. Agree.
- C. Neither agree nor disagree.
- D. Disagree.E. Strongly disagree.
- 25. The availability of continuing education credit influenced my decision to read this report.

D. Disagree.

E. Strongly disagree.

- A. Strongly agree.
- B. Agree.
- C. Neither agree nor disagree.

#### 26. The MMWR format was conductive to learning the content.

- A. Strongly agree.
  - D. Disagree. E. Strongly disagree.
- B. Agree.C. Neither agree nor disagree.
- 27. Do you feel this course was commercially biased? (*indicate yes or no; if yes, please explain in the space provided*)
  - A. Yes B. No

#### 28. How did you learn about this continuing education activity?

- A. Internet.
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- D. Conference presentation.
- E. MMWR subscription.
- F. Other.

IB; 2E; 3E; 4D; 5E; 6D; 7A; 8C; 9B; 10D.

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Recommendations and Reports

March 19, 2010 / Vol. 59 / No. RR-2

# Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies

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# Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies

# **Recommendations of the Advisory Committee on Immunization Practices**

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### Summary

This report summarizes new recommendation and updates previous recommendations of the Advisory Committee on Immunization Practices (ACIP) for postexposure prophylaxis (PEP) to prevent human rabies (CDC. Human rabies prevention—United States, 2008: recommendations of the Advisory Committee on Immunization Practices. MMWR 2008;57[No. RR-3]). Previously, ACIP recommended a 5-dose rabies vaccination regimen with human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV). These new recommendations reduce the number of vaccine doses to four. The reduction in doses recommended for PEP was based in part on evidence from rabies virus pathogenesis data, experimental animal work, clinical studies, and epidemiologic surveillance. These studies indicated that 4 vaccine doses in combination with rabies immune globulin (RIG) elicited adequate immune responses and that a fifth dose of vaccine did not contribute to more favorable outcomes. For persons previously unvaccinated with rabies vaccine, the reduced regimen of 4 1-mL doses of HDCV or PCECV should be administered intramuscularly. The first dose of the 4-dose course should be administered as soon as possible after exposure (day 0). Additional doses then should be administered on days 3, 7, and 14 after the first vaccination. ACIP recommendations for the use of RIG remain unchanged. For persons who previously received a complete vaccination series (pre- or postexposure prophylaxis) with a cell-culture vaccine or who previously had a documented adequate rabies virus-neutralizing antibody titer following vaccination with noncell-culture vaccine, the recommendation for a 2-dose PEP vaccination series has not changed. Similarly, the number of doses recommended for persons with altered immunocompetence has not changed; for such persons, PEP should continue to comprise a 5-dose vaccination regimen with 1 dose of RIG. Recommendations for pre-exposure prophylaxis also remain unchanged, with 3 doses of vaccine administered on days 0, 7, and 21 or 28. Prompt rabies PEP combining wound care, infiltration of RIG into and around the wound, and multiple doses of rabies cell-culture vaccine continue to be highly effective in preventing human rabies.

# Introduction

Rabies is a zoonotic disease caused by RNA viruses in the family *Rhabdoviridae*, genus *Lyssavirus* (1). Virus is transmitted in the saliva of rabid mammals via a bite. After entry to the central nervous system, these viruses cause an acute, progressive encephalomyelitis. The incubation period usually ranges from 1 to 3 months after exposure, but can range from days to

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years. Rabies can be prevented by avoidance of viral exposure and initiation of prompt medical intervention when exposure does occur. In the United States, animal rabies is common. In a recent study, approximately 23,000 persons per year were estimated to have been exposed to potentially rabid animals and received rabies postexposure prophylaxis (PEP) (2). With the elimination of canine rabies virus variants and enzootic transmission among dogs, human rabies is now rare in the United States, with an average of one or two cases occurring annually since 1960 (3).

Prompt wound care and the administration of rabies immune globulin (RIG) and vaccine are highly effective in preventing human rabies following exposure. A variety of empirical schedules and vaccine doses have been recommended over time, based in part on immunogenicity and clinical experience in areas of the world with enzootic canine or wildlife rabies (4). As more potent vaccines were developed, the number of vaccine doses recommended for PEP has decreased, and studies aimed at further revision and reduction of PEP schedules and doses in humans have been encouraged. By the latter half of the 20th century, a 4- to 6-dose, intramuscular regimen using human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) was being recommended (5-8). In the United States, a 5-dose PEP vaccine regimen was adopted during the 1980s (9-12). In 2007, when human rabies vaccine was in limited supply, an ad hoc National Rabies Working Group was formed to reassess the recommendations for rabies prevention and control in humans and other animals. In 2008, a smaller Advisory Committee on Immunization Practices (ACIP) Rabies Workgroup was formed to review rabies vaccine regimen options. This report provides updated ACIP recommendations regarding the use of a 4-dose vaccination regimen, replacing the previously recommended 5-dose regimen, for rabies PEP in previously unvaccinated persons.

### **Methods**

The ACIP Rabies Workgroup\* was formed in October 2008 to review 1) previous recommendations; 2) published and unpublished data from both national and global sources regarding rabies PEP; and 3) the immunogenicity, effectiveness, and safety of a 4-dose PEP rabies vaccination regimen. The ACIP Rabies Workgroup used an evidence-based process for consideration of a reduced vaccination regimen in human rabies PEP. This approach consisted of a review of information available from basic and applied studies of rabies prevention. Because rabies is almost always fatal among immunologically naïve persons once clinical symptoms of rabies occur, randomized, placebo-controlled efficacy studies of vaccine in humans cannot be conducted. The ACIP Rabies Workgroup reviewed six areas: 1) rabies virus pathogenesis, 2) experimental animal models, 3) human immunogenicity studies, 4) prophylaxis effectiveness in humans, 5) documented failures of prophylaxis in humans, and 6) vaccine safety. Studies for review were identified by searching the PubMed database and other relevant references and by consulting subject-matter experts. When definitive research evidence was lacking, the recommendations incorporated the expert opinion of the ACIP Rabies Workgroup members. The ACIP Rabies Workgroup also sought advice and comment from representatives of the vaccine industry, the National Association of State Public Health Veterinarians, the Council of State and Territorial Epidemiologists, state and local public health officials, additional national stakeholder groups, and other national and international experts. The proposed revised recommendations and a draft statement from the ACIP Rabies Workgroup were presented to the full ACIP during February 2009. After review and comment by ACIP, a revised draft, recommending a reduced regimen of 4 1-mL doses of rabies vaccine for PEP in previously unvaccinated persons, was prepared for consideration. These recommendations were discussed and accepted by ACIP at the June 2009 meeting (13).

## Rationale for Reduced Doses of Human Rabies Vaccine

A detailed review of the evidence in support of a reduced, 4-dose schedule for human PEP has been published (14). The totality of the evidence, obtained from the available peerreviewed literature, unpublished data sources, epidemiologic reviews, and expert opinion strongly supports a reduced vaccination schedule (Table 1). Since the 19th century, prophylactic interventions against rabies have recognized the highly neurotropic characteristics of lyssaviruses and have aimed at neutralizing the virus at the site of infection before it can enter the human central nervous system (Figure 1) (4,15,16). To accomplish this, immunologic interventions must be prompt and must be directed toward local virus neutralization, such as local infiltration with RIG and vaccination. Modern recommended rabies PEP regimens emphasize early wound care and passive immunization (i.e., infiltration of RIG in and around the wound) combined with active immunization (i.e., serial doses of rabies vaccine). Accumulated scientific evidence indicates that, following rabies virus exposure, successful neutralization and clearance of rabies virus mediated via appropriate PEP generally ensures patient survival (8).

<sup>\*</sup>A list of the membership appears on page 9 of this report.

Evidence	Conclusion	Sources
Rabies virus pathogenesis	High neurotropism of rabies virus requires immediate immunization (local infiltration with human rabies immune globulin [HRIG] and vaccination) to neutralize virus at the site of infection and prevent viral entry into the central nervous system.	Published literature,* expert national and international opinion, and historic observations
Experimental animal models	Protection in animal models was elicited without regard to the absolute number of vaccine doses used.	Published literature, <sup>†</sup> expert national and international opinion, and unpublished data
Human clinical studies	All patients develop adequate levels of virus-neutralizing antibodies by day 14, without any additive value of a 5th dose of vaccine administered at day 28 (in regards to any substantive increase in measured virus-neutralizing antibody levels).	Published literature, <sup>§</sup> expert national and international opinion, and unpublished data
Epidemiologic surveillance	No human rabies cases were identified in patients who received appropriate wound care, HRIG, and 4 doses of vaccine.	Published literature, <sup>¶</sup> expert national and international opinion, and unpublished data
Health economics	Expected positive national benefits are related to omission of a 5th dose (e.g., minimized travel expenses, reduced time out of work, health-care workers have more time for other patients, and fewer adverse reactions)	Published literature** and expert national opinion

#### TABLE 1. Summary of evidence in support of a 4-dose postexposure prophylaxis regimen — United States, 2010

\* SOURCES: Lyles DS, Rupprecht CE. Rhabdoviridae. In: Knipe D, Howley P, eds. Fields virology. 5th ed. Philadelphia, PA: Lippincott, Williams, & Wilkins; 2007:1363–408. Plotkin SA, Koprowski H, Rupprecht CE. Rabies vaccines. In: Plotkin SA, Orenstein WA, Offit PA, eds. Vaccines. 5th ed. Philadelphia, PA: Saunders; 2008:687–714. World Health Organization. WHO Expert Consultation on Rabies. 1st report. WHO Technical Report Series, No. 931. Geneva, Switzerland: World Health Organization; 2005. Rupprecht CE, Briggs D, Brown C, et al. Evidence for a 4-dose vaccine schedule for human rabies post-exposure prophylaxis in previously non-vaccinated individuals. Vaccine 2009;27:7141–8. Charlton KM, Nadin-Davis S, Casey GA, Wandeler AI. The long incubation period in rabies: delayed progression of infection in muscle at the site of exposure. Acta Neuropathol 1997;94:73–7. Dietzschold B, Schnell M, Koprowski H. Pathogenesis of rabies. Curr Top Microbiol Immunol 2005;292:45–56.

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- SOURCES: Plotkin SA, Koprowski H, Rupprecht CE. Rabies vaccines. In: Plotkin SA, Orenstein WA, Offit PA, eds. Vaccines. 5th ed. Philadelphia, PA: Saunders; 2008:687–714. World Health Organization. WHO Expert Consultation on Rabies. 1st Report. WHO Technical Report Series, No. 931. Geneva, Switzerland: World Health Organization; 2005. Rupprecht CE, Briggs D, Brown C, et al. Evidence for a 4-dose vaccine schedule for human rabies post-exposure prophylaxis in previously non-vaccinated individuals. Vaccine 2009;27:7141–8.
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- \*\* SOURCES: Meltzer MI, Rupprecht CE. A review of the economics of the prevention and control of rabies: I: global impact and rabies in humans. PharmacoEconomics 1998:14:365–83. Dhankhar P, Vaidya SA, Fishbien DB, Meltzer MI. Cost effectiveness of rabies post exposure prophylaxis in the United States. Vaccine 2008;26:4251–5.

The induction of a rabies virus-specific antibody response is one important immunologic component of response to vaccination (4). Development of detectable rabies virus-specific neutralizing antibodies is a surrogate for an adequate immune response to vaccination. Clinical trials of human rabies vaccination indicate that all healthy persons develop detectable rabies virus-neutralizing antibody titer rapidly after initiation of PEP. For example, in a literature review conducted by the ACIP Rabies Workgroup of at least 12 published rabies vaccination studies during 1976–2008 representing approximately1,000 human subjects, all subjects developed rabies virus-neutralizing antibodies by day 14 (14). Observational studies indicate that PEP is universally effective in preventing human rabies when administered promptly and appropriately. Of the >55,000 persons who die annually of rabies worldwide, the majority either did not receive any PEP, received some form of PEP (usually without RIG) after substantial delays, or were administered PEP according to schedules that deviated substantially from current ACIP or World Health Organization recommendations (*17*). For example, a review of a series of 21 fatal human cases in which patients received some form of PEP indicated that 20 patients developed signs of illness, and most died before day 28 (Figure 2). In such cases, in which widespread infection of the central



FIGURE 1. Schematic of dynamics of rabies virus pathogenesis\* in the presence and absence of postexposure prophylaxis (PEP)–mediated immune responses<sup>†</sup>

\* Rabies can progress through five stages: incubation period (5 days to >2 years: U.S. median ~35 days), prodrome state (0–10 days), acute neurologic period (2–7 days), coma (5–14 days), and death.

<sup>+</sup>Once in tissues at the entry site, rabies virus can be neutralized by passively administered rabies immune globulin (RIG). Active immunization (vaccine) stimulates the host immune system, and, as a result, virus-neutralizing antibodies (VNA) are produced approximately 7–10 days after initiation of vaccination. By approximately day 14–28 (after administration of 4 vaccine doses), VNAs peak. In the absence of early and adequate PEP, virus enters host neurons, spreads to the central nervous system (CNS), and causes disease, with inevitably fatal consequence.

§ Human rabies immune globulin.

<sup>¶</sup> Day vaccine administered.

nervous system occurs before the due date (i.e., day 28) of the fifth vaccine dose, the utility of that dose must be nil. In the United States, of the 27 human rabies cases reported during 2000–2008, none of the patients had a history of receiving any PEP before illness, and this is the most common situation for human rabies deaths in both developed and developing countries (3,8). In India, an analysis from two animal bite centers during 2001-2002 demonstrated that in 192 human rabies cases, all deaths could be attributed to failure to seek timely and appropriate PEP, and none of them could be attributed to a failure to receive the fifth (day 28) vaccine dose (18). Even when PEP is administered imperfectly or not according to established scheduled dose recommendations, it might be generally effective. Several studies have reported cases involving persons who were exposed to potentially rabid animals and who received less than 5, 4, or even 3 doses of rabies vaccine but who nevertheless did not acquire rabies (Table 2). For example, in one series from New York, 147 (13%) of 1,132 patients had no report of receiving the complete 5-dose vaccine regimen. Of these patients, 26 (18%) received only 4 doses of vaccine, and two of these patients were exposed to animals with laboratoryconfirmed rabies. However, no documented cases of human rabies occurred (CDC, unpublished data, 2003). The ACIP Rabies Working Group estimates that >1,000 persons in the United States receive rabies prophylaxis annually of only 3 or 4 doses, with no resulting documented cases of human rabies, even though >30% of these persons likely have exposure to confirmed rabid animals (14). In addition, no case of human rabies in the United States has been reported in which failure of PEP was attributable to receiving less than the 5-dose vaccine course. Worldwide, although human PEP failures have been reported very rarely, even in cases in which intervention

FIGURE 2. Number of documented rabies postexposure prophylaxis (PEP) failures — Burma, India, the Philippines, South Africa, Sri Lanka, and Thailand, 1984–2007\*



**SOURCES:** Wilde H. Failures of post-exposure rabies prophylaxis. Vaccine 2007;25:7605–9; Wilde H, Sirikawin S, Sabcharoen A, et al. Failure of postexposure treatment of rabies in children. Clin Infect Dis 1996;22:228–32; Matha IS, Salunke SR. Immunogenicity of purified vero cell rabies vaccine used in the treatment of fox-bite victims in India. Clin Infect Dis 2005;40:611–3.

\* Of 21 reported PEP failures described, 20 patients had symptoms and 15 died before day 28.

appeared both prompt and appropriate (8), no cases have been attributed to the lack of receipt of the fifth human rabies vaccine dose on day 28 (4,17).

In vivo laboratory animal studies using multiple animal models from rodents to nonhuman primates have underscored the importance of timely PEP using RIG and vaccine, regardless of the absolute number of vaccine doses used or the schedule (14, 19). For example, in a study in which 1, 2, 3, 4, or 5 doses of rabies vaccine were used in a Syrian hamster model in combination with human rabies immune globulin (HRIG), no statistically significant differences in elicited protection and consequent survivorship were observed among groups receiving different doses (20). In the same study, using a murine model, no differences were detected in immunogenicity and efficacy of PEP with 2, 3, or 4 vaccine doses. In another study using a nonhuman primate model, 1 dose of cell-culture vaccine, in combination with RIG administered 6 hours postexposure, provided substantial protection (21). In another study, a 3-dose regime was evaluated in a canine model and determined to be effective in preventing rabies (22).

Compared with older, nerve tissue-based products, adverse reactions associated with modern human rabies vaccination are uncommon (4). A review by the Workgroup of published and unpublished human rabies vaccine clinical trials and Vaccine Adverse Event Reporting System data identified no adverse events that were correlated to a failure to receive the fifth vaccine dose. As some adverse reactions might be independent clinical events with each vaccine administration, the omission of the vaccine dose on day 28 might have some positive health benefits. Otherwise, the overall safety of human rabies PEP is expected to be unchanged from the evidence provided in the 2008 ACIP report (12).

Preliminary economic assessments support the cost savings associated with a reduced schedule of vaccination (23,24). The ACIP Rabies Workgroup has estimated that, assuming 100% compliance with a recommended vaccine regimen, a change in recommendation from a 5-dose schedule to a 4-dose schedule would save approximately \$16.6 million in costs to the U.S. health-care system. Persons who receive rabies vaccination might see some savings related to deletion of the fifth recommended dose of vaccine, measured in both the cost of the vaccine and the costs associated with the additional medical visit.

# Revised Rabies Postexposure Prophylaxis Recommendations

This report presents revised recommendations for human rabies PEP (Table 3). Rabies PEP includes wound care and administration of both RIG and vaccine.

## Postexposure Prophylaxis for Unvaccinated Persons

For unvaccinated persons, the combination of RIG and vaccine is recommended for both bite and nonbite exposures, regardless of the time interval between exposure and initiation

TABLE 2. Number and percentage of patients with suspected rabies exposures who received <5 doses of vaccine — India, 2003; New York, 1998–2000; and Puerto Rico, 2008\*

	No. of persons	Persons who received <5 doses of vaccine	No. of documented
Location (year)	exposed	No. (%)	rabies deaths
New York (1998–2000) <sup>†</sup>	1,132	147 (13)	0
India (2003)§	439	261 (59)	0
Puerto Rico (2008) <sup>¶</sup>	191	30 (16)	0

\* No cases of human rabies were recorded that were attributable to receipt of only 4 doses of vaccine.

\* SOURCE: CDC, unpublished data, 2003.

SOURCE: Association for the Prevention and Control of Rabies (APCRI) in India. Assessing the burden of rabies in India: WHO sponsored national multicentric rabies survey 2003. Final report May 2004. Available at http://rabies.org.in. Accessed March 8, 2010. Sudarshan MK, Madhusudana SN, Mahendra BJ, et al. Assessing the burden of human rabies in India: results of a national multi-center epidemiological survey. Intl J Infect Dis 2007;11:29–35.

**SOURCE:** CDC, unpublished data, 2008.

Vaccination status	Intervention	Regimen*
Not previously vaccinated	Wound cleansing	All PEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent (e.g., povidine-iodine solution) should be used to irrigate the wounds.
	Human rabies immune globulin (HRIG)	Administer 20 IU/kg body weight. If anatomically feasible, the full dose should be infiltrated around and into the wound(s), and any remaining volume should be administered at an anatomical site (intramuscular [IM]) distant from vaccine administration. Also, HRIG should not be administered in the same syringe as vaccine. Because RIG might partially suppress active production of rabies virus antibody, no more than the recommended dose should be administered.
	Vaccine	Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) 1.0 mL, IM (deltoid area <sup>†</sup> ), 1 each on days 0,§ 3, 7 and 14. <sup>¶</sup>
Previously vaccinated**	Wound cleansing	All PEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidine-iodine solution should be used to irrigate the wounds.
	HRIG	HRIG should not be administered.
	Vaccine	HDCV or PCECV 1.0 mL, IM (deltoid area <sup><math>\dagger</math></sup> ), 1 each on days 0 <sup>§</sup> and 3.

TABLE 3. Rabies postexposure prophylaxis (PEP) schedule — United States, 2010

\* These regimens are applicable for persons in all age groups, including children.

<sup>†</sup> The deltoid area is the only acceptable site of vaccination for adults and older children. For younger children, the outer aspect of the thigh may be used. Vaccine should never be administered in the gluteal area.

§ Day 0 is the day dose 1 of vaccine is administered.

<sup>1</sup> For persons with immunosuppression, rabies PEP should be administered using all 5 doses of vaccine on days 0, 3, 7, 14, and 28.

\*\* Any person with a history of pre-exposure vaccination with HDCV, PCECV, or rabies vaccine adsorbed (RVA); prior PEP with HDCV, PCECV or RVA; or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination.

of PEP. If PEP has been initiated and appropriate laboratory diagnostic testing (i.e., the direct fluorescent antibody test) indicates that the animal that caused the exposure was not rabid, PEP may be discontinued.

### Vaccine Use

A regimen of 4 1-mL vaccine doses of HDCV or PCECV should be administered intramuscularly to previously unvaccinated persons (Table 3). The first dose of the 4-dose regimen should be administered as soon as possible after exposure. The date of the first dose is considered to be day 0 of the PEP series. Additional doses then should be administered on days 3, 7, and 14 after the first vaccination. Recommendations for the site of the intramuscular vaccination remain unchanged (e.g., for adults, the deltoid area; for children, the anterolateral aspect of the thigh also is acceptable). The gluteal area should not be used because administration of vaccine in this area might result in a diminished immunologic response. Children should receive the same vaccine dose (i.e., vaccine volume) as recommended for adults.

### **HRIG Use**

The recommendations for use of immune globulin in rabies prophylaxis remain unchanged by the revised recommendation of a reduced rabies vaccine schedule. HRIG is administered once to previously unvaccinated persons to provide rabies virusneutralizing antibody coverage until the patient responds to vaccination by actively producing virus-neutralizing antibodies. HRIG is administered once on day 0 at the time PEP is initiated, in conjunction with human rabies vaccines available for use in the United States. If HRIG was not administered when vaccination was begun on day 0, it can be administered up to and including day 7 of the PEP series (*12,25*). If anatomically feasible, the full dose of HRIG is infiltrated around and into any wounds. Any remaining volume is injected intramuscularly at a site distant from vaccine administration. HRIG is not administered in the same syringe or at the same anatomic site as the first vaccine dose. However, subsequent doses (i.e., on days 3, 7, and 14) of vaccine in the 4-dose vaccine series can be administered in the same anatomic location in which HRIG was administered.

## Postexposure Prophylaxis for Previously Vaccinated Persons

Recommendations for PEP have not changed for persons who were vaccinated previously. Previously vaccinated persons are those who have received one of the ACIP-recommended pre- or postexposure prophylaxis regimens (with cell-culture vaccines) or those who received another vaccine regimen (or vaccines other than cell-culture vaccine) and had a documented adequate rabies virus-neutralizing antibody response. Previously vaccinated persons, as defined above, should receive 2 vaccine doses (1.0 mL each in the deltoid), the first dose immediately and the second dose 3 days later. Administration of HRIG is unnecessary, and HRIG should not be administered to previously vaccinated persons to avoid possible inhibition of the relative strength or rapidity of an expected anamnestic response (26). Local wound care remains an important part of rabies PEP for any previously vaccinated persons.

# Vaccination and Serologic Testing

# **Postvaccination Serologic Testing**

All healthy persons tested in accordance with ACIP guidelines after completion of at least a 4-dose regimen of rabies PEP should demonstrate an adequate antibody response against rabies virus (14). Therefore, no routine testing of healthy patients completing PEP is necessary to document seroconversion (12). When titers are obtained, serum specimens collected 1-2 weeks after prophylaxis (after last dose of vaccine) should completely neutralize challenge virus at least at a 1:5 serum dilution by the rapid fluorescent focus inhibition test (RFFIT). The rabies virus-neutralizing antibody titers will decline gradually since the last vaccination. Minimal differences (i.e., within one dilution of sera) in the reported values of rabies virus-neutralizing antibody results might occur between laboratories that provide antibody determination using the recommended RFFIT. Commercial rabies virus antibody titer determination kits that are not approved by the Food and Drug Administration are not appropriate for use as a substitute for the RFFIT. Discrepant results might occur after the use of such tests, and actual virus-neutralizing activity in clinical specimens cannot be measured.

# Management of Adverse Reactions, Precautions, and Contraindications

### **Management of Adverse Reactions**

Recommendations for management and reporting of vaccine adverse events have not changed. These recommendations have been described in detail previously (12).

### Immunosuppression

Recommendations for rabies pre- and postexposure prophylaxis for persons with immunosuppression have not changed. General recommendations for active and passive immunization in persons with altered immunocompetence have been summarized previously (27,28). This updated report discusses specific recommendations for patients with altered immunocompetence who require rabies pre- and postexposure prophylaxis. All rabies vaccines licensed in the United States are inactivated cell-culture vaccines that can be administered safely to persons with altered immunocompetence. Because corticosteroids, other immunosuppressive agents, antimalarials, and immunosuppressive illnesses might reduce immune responses to rabies vaccines substantially, for persons with immunosuppression, rabies PEP should be administered using a 5-dose vaccine regimen (i.e., 1 dose of vaccine on days 0, 3, 7, 14, and 28), with the understanding that the immune response still might be inadequate. Immunosuppressive agents should not be administered during rabies PEP unless essential for the treatment of other conditions. If possible, immunosuppressed patients should postpone rabies preexposure prophylaxis until the immunocompromising condition is resolved. When postponement is not possible, immunosuppressed persons who are at risk for rabies should have their virus-neutralizing antibody responses checked after completing the preexposure series. Postvaccination rabies virus-neutralizing antibody values might be less than adequate among immunosuppressed persons with HIV or other infections (29,30). When rabies pre- or postexposure prophylaxis is administered to an immunosuppressed person, one or more serum samples should be tested for rabies virus-neutralizing antibody by the RFFIT to ensure that an acceptable antibody response has developed after completing the series. If no acceptable antibody response is detected after the final dose in the pre- or postexposure prophylaxis series, the patient should be managed in consultation with their physician and appropriate public health officials.

# Variation from Human Rabies Vaccine Package Inserts

These new ACIP recommendations differ from current rabies vaccine label instructions, which still list the 5-dose series for PEP. Historically, ACIP review and subsequent public health recommendations for the use of various biologics has occurred after vaccine licensure and generally are in agreement with product labels. However, differences between ACIP recommendations and product labels are not unprecedented. For example, during the early 1980s, ACIP review and recommendations concerning the intradermal use of rabies vaccines occurred well in advance of actual label claims and licensing (9). On the basis of discussions with industry representatives, alterations of current product labels for HDCV and PCEC are not anticipated by the producers of human rabies vaccines licensed for use in the United States.

Please note: An erratum has been published for this issue. To view the erratum, please click here.

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#### MMWR

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#### Advisory Committee on Immunization Practices Membership as of June 24, 2009

Chair: Dale Morse, MD, New York State Department of Health, Albany, New York.

Executive Secretary: Larry Pickering, MD, National Center for Immunization and Respiratory Diseases, CDC, Atlanta, Georgia.

Members: Carol Baker, MD, Baylor College of Medicine, Houston, Texas; Robert Beck, JD, Consumer Representative, Palmyra, Virginia; Lance Chilton, MD, University of New Mexico, Albuquerque, New Mexico; Paul Cieslak, MD, Oregon Public Health Division, Portland, Oregon; Kristen Ehresmann, MPH, Minnesota Department of Health, St. Paul, Minnesota; Janet Englund, MD, University of Washington and Children's Hospital and Regional Medical Center, Seattle, Washington; Franklyn Judson, MD, University of Colorado Health Sciences Center, Denver, Colorado; Susan Lett, MD, Massachusetts Department of Public Health, Boston, Massachusetts; Michael Marcy, MD, UCLA Center for Vaccine Research, Torrance, California; Cody Meissner, MD, Tufts Medical Center, Boston, Massachusetts; Kathleen Neuzil, MD, University of Washington; Seattle, Washington; Mark Sawyer, MD, University of California–San Diego, California; Ciro Valent Sumaya, MD, Texas A&M Health Science Center, College Station, Texas; Jonathan Temte, MD, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin.

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#### ACIP Rabies Workgroup Membership as of June 24, 2009

Chair: Paul Cieslak, MD, Oregon Department of Public Health, Corvallis, Oregon.

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## **Section 4: Vermont Recommendations**

A. School Animal Policy Guide

Vermont Rabies Control Resource Manual 2018

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## What's in this guide?

- **Guidance to schools for developing an animal policy** that will reduce the risk of human exposure to rabies and other diseases transmitted from animals.
- Recommended animals that should be prohibited from schools.
- Guidelines for allowing or prohibiting animals like **dogs**, **cats**, **birds**, **reptiles** and **fish**.
- Links to additional resources for setting healthy and safe school standards and practices.

# Recommendation: Wild, stray or poisonous animals and bats should be prohibited.

The Vermont Department of Health recommends that the following animals be prohibited from schools:

- Wild animals and stray domestic animals Rabies is found regularly in Vermont's wildlife populations. Any fur-bearing animal is susceptible to this very serious fatal disease and, if infected, can transmit it to students and staff. A single wild animal or unvaccinated pet carrying rabies has the potential to expose a large number of children.
  - Because wild animals and stray domestic animals pose a risk for transmitting rabies and other zoonotic diseases, they should not be allowed in schools or handled by staff or children. This includes bats, raccoons, skunks, foxes, coyotes and other wild animals (either live or dead). It also includes any stray domestic animal, such as a stray cat or dog, including kittens and puppies. Wolf-dog hybrids should also be prohibited from schools.
  - Exceptions can be made when a wild animal is part of demonstration and is handled by someone experienced in wildlife handling. However, there should be no contact between the students and the animals, and the animals should be safely enclosed in a cage or other appropriate enclosure. Because of the high incidence of rabies in bats, raccoons, skunks, fox and other carnivores, such animals should never be allowed on school grounds.
- **Poisonous animals** Venomous or toxin-producing spiders, insects, reptiles and amphibians should be prohibited for safety reasons.
- **Bats** Bats pose a high risk for transmitting rabies, and for this reason bat houses should not be installed on school grounds.

## Other animals are up to the school's discretion.

DEPARTMENT OF HEALTH

Each school will determine whether the following animals are allowed or prohibited:

- Domestic dogs, cats, puppies and kittens Puppies and kittens that are too young to be vaccinated for rabies should not be brought into a school unless they were born to a vaccinated mother, and they have been housed indoors, precluding contact with other animals. In addition, young animals are more likely to shed harmful bacteria and parasites in their stool, and so they may pose an unacceptably high risk for young children.
  - Adult dogs and cats could be occasional visitors to a school but must be under the control of their owner or handler. Before allowing a dog or cat on the school premises, it is important to make sure the animal has the proper temperament for that setting. In addition, cats and dogs should be under the care of a veterinarian, and proof of current rabies vaccination should be made available to the school staff. They should also be on a program of proper flea, tick and intestinal parasite control.
- Ferrets Ferrets can be allowed to visit a classroom, but they should be handled by the person responsible for them. Ferrets should be under the care of a veterinarian, and proof of current rabies vaccination should be made available to school staff. Because they startle easily and may bite, school children should not be allowed to hold ferrets.
- **Birds** Birds in the classroom should be housed in appropriate cages and not allowed to fly free. Psittacine birds, such as parakeets, parrots, cockatiels and cockatoos can be carriers of psittacosis, a potentially serious disease that can be transmitted to people. People usually become infected by breathing in dust from dried bird feces. Sick birds should never be brought into school, but birds that appear healthy can also be carriers of this disease. Any birds brought into a classroom should be healthy, kept in a cage, and bird waste should be frequently cleaned out and safely discarded. Species that are less likely to carry psittacosis may be more appropriate for the classroom.
- Reptiles and Amphibians Reptiles (iguanas, snakes, lizards and turtles) and amphibians (frogs, salamanders and toads) are common carriers of *Salmonella* bacteria. Even healthy animals can carry these bacteria. There are many confirmed reports of transmission of *Salmonella* from pet reptiles to people. Reptiles and amphibians may not be appropriate in schools, especially if young children are in attendance.
  - In people, infection with Salmonella usually causes diarrhea and fever. The illness can be life-threatening in very young children, the elderly, and people with weakened immune systems, but anybody can become seriously ill. These animals should not be handled by children, pregnant women, or individuals with infants at home. They should be housed in cages which provide a physical barrier between the animal and the children (such as glass or plastic). Anyone handling a reptile or amphibian should wash their hands thoroughly and immediately after contact with the animal or anything in its living space.
- Chicks and ducklings Chicks and ducklings, even if they appear healthy, can spread Salmonella bacteria to people. Salmonella infections can be life-threatening in young children, the elderly,

and people with weakened immune systems, but anyone can become seriously ill. These animals should not be handled by children, pregnant women, or individuals with infants at home. Anyone handling chicks or ducklings should wash their hands thoroughly, immediately after contact with the animal or anything in its living space. There have been many documented outbreaks of illness after contact with chicks and ducklings, and they may not be appropriate in schools, especially if young children are in attendance.

- Guinea pigs, hamsters, gerbils, rabbits Healthy guinea pigs, hamsters, gerbils and rabbits pose a limited health risk. Such animals may be allowed as classroom pets or as occasional visitors. However, even tame animals may react aggressively in strange situations, so student contact with animals should always be closely supervised, and animals should not be allowed to run loose in the classroom. Students should not be allowed to "kiss" these animals. Students and staff must wash their hands after handling these animals or anything in their living space.
- Fish Fish pose a very limited health risk and may be allowed in the classroom. Tank water should not be disposed of in sinks that are used for food preparation or for obtaining drinking water. Gloves should be worn when cleaning the tank, and hands should be washed thoroughly afterwards.

### **Recommendations on animal care:**

- Any animal present in the school or on school grounds must be clean and healthy so that the risk of transmission of disease to students and teachers is minimal. Animals that become ill should be removed from the school and seen by a veterinarian.
- Animals must be under routine veterinary care. Preventive care, including vaccination and parasite control, appropriate for the species, should be provided. Consider requiring a health certificate from a veterinarian before allowing the animal in the classroom.
- Staff responsible for the animals should be very familiar with the behavior of the animals and proper husbandry practices.
- The school must be able to provide proper housing and nutrition for the animals. There must be a plan to care for the animals when school is not in session, such as weekends and holidays.
- Animal cages or tanks should be cleaned thoroughly on a regular basis. Young children should not be allowed to handle or clean up any form of animal waste (feces, urine, blood, etc.), and older children should be closely supervised. Animal waste and used bedding should be disposed of in a plastic bag or container with a lid. Anyone who cleans a cage or tank should wash their hands immediately after completing the task.

## **General recommendations:**

• Hand washing facilities should be conveniently located so that staff and students can wash their hands immediately after having contact with an animal.

- In the event of an animal bite or scratch, procedures for first aid and notification of parents or legal guardians should be followed. In addition, animal bites must be reported to the local health officer in the town where the bite occurred **within 24 hours**.
- Animals should not be allowed in food preparation areas at any time. Food handlers should not be responsible for clean-up of animal wastes. Cages and tanks should not be cleaned in areas where food is prepared.
- Children with immune deficiencies or those with allergies may be especially susceptible to diseases transmitted by animals or allergic reactions. Therefore, special precautions may be needed to minimize risks. Consultation with the school nurse and the child's parents about precautionary measures is strongly advised.
- Consider notifying parents or obtaining their written consent prior to allowing animals in a classroom.

## Visit the Health Department online for more information.

To effectively protect students and staff, it is recommended that adherence to the school's animal policy be required for the entire school community. Parents, teachers, school nurses and other staff should be reminded of the policy on a regular basis and know of its provisions.

This document is intended to be a guideline and does not address all potential situations. Please contact Vermont Department of Health, Infectious Diseases Epidemiology at **1-800-640-4374 or 802-863-7240** if you have any questions.

For information about school health services standards: www.healthvermont.gov/family/school/standards-practice-school-health-services-manual

For additional information, please see the "Compendium of Measures to Prevent Disease Associated with Animals in Public Settings, 2017", JAVMA Vol. 251/No. 11/December 1, 2017: <a href="https://www.nasphv.org/Documents/AnimalContactCompendium2017.pdf">www.nasphv.org/Documents/AnimalContactCompendium2017.pdf</a>

Acknowledgement: This document is based, in part, on guidelines from the Kansas Department of Health and Environment. For the most up-to-date version of this resource manual and more information, visit the <u>Vermont Department of Health</u> rabies webpage.

Revised July 2018

## **Section 5: Rabies Exposure Protocols**

- A. Human Rabies Exposure Management by Animal Type
- B. Management of Potential Human Exposures to Rabies
- C. Rabies Exposure Management for Bat-related Incidents
- D. Management of Potential Pet Exposures to Rabies

### Human Rabies Exposure\* Management by Animal Type



Animal Type	Situation	Rabies Postexposure Prophylaxis (rPEP) Recommendations			
Dogs, cats, ferrets	Animal available for testing or 10 day confinement and observation.	If the animal is exhibiting symptoms consistent with rabies <sup>**</sup> , immediately euthanize and test. If the animal is not exhibiting symptoms, a 10 day confinement period can be instituted. If the animal exhibits signs of rabies during the 10 day confinement period it should be euthanized immediately and tested. If results are positive, unsuitable, or indeterminate administer rPEP. If the animal does not exhibit clinical signs during the 10 day confinement period, rPEP is not recommended, since the animal was not shedding virus at the time of the bite or saliva exposure.			
( L	Animal unavailable (waiting up to 72 hours to capture the animal may be reasonable, assuming the correct animal can be identified).	If the animal is not available for confinement or testing, consider rPEP and contact the Health Department at 802-863-7240.			
Horses, other farm animals	If the animal exhibits signs of rabies or dies suddenly, test the animal for rabies.	Defer administration of rPEP until outcome of testing. If results are positive, unsuitable, or indeterminate, administer rPEP.			
	All other cases, contact Health Department for guidance.	Contact Health Department at 802-863-7240.			
Skunk, racoon,	Euthanize and test animal.	Defer administration of rPEP until outcome of testing. If results are positive, unsuitable, or indeterminate, administer rPEP.			
fox, coyote	Animal unavailable for testing.	Administer rPEP immediately.			
Large rodents (beavers, muskrats, groundhogs)	Euthanize and test animal.	Defer administration of rPEP until outcome of testing. If results are positive, unsuitable, or indeterminate, administer rPEP.			
	Animal unavailable for testing.	Contact Health Department at 802-863-7240.			
Small rodents (squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, rabbits, opossum)	Provoked bite and animal behaving normal.	No rPEP is recommended, as these species almost never carry rabies.			
	Unprovoked bite or animal behaving abnormal.	Contact Health Department at 802-863-7240.			

\*Exposure: a bite or saliva/nervous tissue contact to an open wound or mucous membrane.

\*\*Rabies virus causes an acute encephalitis in all mammalian hosts and the outcome is almost always fatal. The first symptoms of rabies may be nonspecific and include lethargy, fever, vomiting, and anorexia. Signs progress within days to cerebral dysfunction, cranial nerve dysfunction, ataxia, weakness, paralysis, seizures, difficulty swallowing, excessive salivation, abnormal behavior, aggression, and/or self-mutilation.

NOTE: If the patient was bitten above the shoulders, the Health Department recommends that the healthcare provider consider starting rPEP immediately. rPEP can be discontinued if the animal tests negative for rabies or is healthy at the end of the quarantine period. Thoroughly wash all wounds with soap and water and, if available, flush with povidone iodine solution (or other virucidal solution). Evaluate tetanus vaccination status, update if needed.





rabies, or die during

observation period?

NO

Questions? Call the Rabies Hotline at 1-800-4-RABIES (800-472-2437) or the Vermont Department of Health at 802-863-7240.

The animal is considered noninfectious at the time of bite.



Management of Potential Bat-related Rabies Exposures\*









Questions? Call the **Rabies Hotline at 1-800-4-RABIES** (800-472-2437) or the **Vermont Department of Health at 802-863-7240**.

\*Exposure is when saliva or neural tissue from a confirmed or suspected rabid animal is introduced into bite wounds, open cuts in skin, or onto mucous membranes. Wild mammalian carnivores not available for testing should be regarded as rabid.

## **Section 6: Rabies Testing and Reporting Forms**

- A. Rabies Specimen Lab Testing and Shipping Instructions
- **B.** Request for Rabies Examination
- C. Rabies Postexposure Prophylaxis Report Form
- D. Town Health Officer Animal Bite Report Form

## INSTRUCTIONS FOR PREPARING, PACKAGING & SHIPPING RABIES SPECIMENS

#### RABIES KITS 10 & 12

All specimens submitted to the Vermont Department of Health Laboratory for rabies diagnostic testing **must be pre-approved** by calling the Vermont Department of Health Epidemiology Program at **1-800-640-4374** or **802-863-7240**. Test results are usually available within 24-48 hours of receipt.

Vermont Department of Health Laboratory hours are Monday-Friday from 7:45am-4:30pm, except for state holidays. If submission of specimens is necessary after the Laboratory is closed, please call the Epidemiology Program to make arrangements. Only human exposure cases require testing on weekends and holidays.

Testing may not be possible if the head of the animal has been damaged or is badly decomposed.

## **RABIES KITS**

Rabies kits can be obtained from the Vermont Department of Health Laboratory. Many State Police barracks and Vermont Department of Health District Offices also have kits on hand. Please call ahead to inquire.

#### Kit 10 – Whole Animal Carcass or Animal Head Kit contains:

- 1 thick black or blue plastic bag in which to place the animal specimen
- 1 clear plastic bag in which to place the bagged specimen
- 2 pieces of filament tape for preparing the carton for shipping
- 6 polyfoam panels and plastic bag which line the cardboard shipping container
- 2 unfrozen 20-ounce ice packs (store frozen until needed)
- 1 Rabies Request for Examination requisition form
- 1 envelope addressed to the Vermont Department of Health Laboratory

#### Kit 12 – Small Animal or Livestock Brain Tissue Kit contains:

- 1 clear, plastic zip lock bag
- 1 plastic zip lock Biohazard bag
- 1 insulated cardboard shipping box
- 1 unfrozen 20-ounce ice pack (store frozen until needed)
- 1 Rabies Request for Examination requisition form
- 1 envelope addressed to the Vermont Department of Health Laboratory

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Mailing address: P.O. Box 1125 Burlington, VT 05402-1125



## **PREPARING SPECIMENS FOR RABIES TESTING**

**Do not submit live animals**. Animals should be euthanized prior to shipment. Handle all specimens or with disposable gloves.

Specimens must be kept refrigerated, not frozen, until shipment. Freezing may damage the brain tissue and may compromise the test and/or delay testing.

Determine which test kit is needed for each specimen:

#### Kit 10 – Whole Animal Carcass or Animal Head Kit

- Domestic pets and small livestock (sheep, goats, pigs, dogs, cats, etc.)
- Wild animals (raccoons, foxes, skunks, etc.)

#### Kit 12 – Small Animal or Livestock Brain Tissue Kit

- Bats
- Small rodents
- Large livestock brain tissue (cows, horses)
- Heads of small wild or domestic animals (skunks, cats, etc.)

Bats: whole bodies are acceptable.

Small rodents: whole bodies or heads are acceptable.

**Domestic pets and small livestock (sheep, goats, pigs, dogs, cats, etc.):** submit entire head or brain only. A qualified person shall separate the animal head from the body as soon as possible after death, prior to submission to the laboratory.

**Large livestock (cows, horses):** brain tissue (brainstem and cerebellum via the foramen magnum) is acceptable. Samples of all three lobes of the cerebellum and a complete cross-section of the brainstem are required. Removal of brain sections should be performed by a veterinarian. Avoid brain tissue damage as it may compromise the test.

**Wild animals (raccoons, foxes, woodchucks, etc.):** whole carcasses are acceptable if they fit into the rabies box. Animals that do not fit must be decapitated.

**Skunks:** Whole bodies must be deodorized prior to submission by submerging the whole animal in a mixture of 1 qt. peroxide, ¼ c. baking soda, and 1 tsp. liquid soap.

## **PACKAGING SPECIMENS FOR RABIES TESTING**

- 1. Only one specimen should be placed in a box.
- 2. If two specimens must be placed in the same box:
  - a. Fill out a separate Rabies Request for Examination form for each specimen.

Mailing address: P.O. Box 1125 Burlington, VT 05402-1125



- b. Under the "Animal Information" section on the Request for Rabies Examination form, check "yes" under "More than One Specimen in Box?"
- c. Mark in large letters on the outside of the box the number of specimens in the box.
- 3. Do not overstuff the shipping box.
- 4. The specimen must be placed into the thick, black or blue plastic bag (Kit 10) or into the clear zip lock bag (Kit 12). Twist and tightly knot the top of the bag or seal the zip lock bag to prevent leaks.
- 5. Place the bag inside the clear plastic bag that lines the inside of the insulated cardboard box (Kit 10) or inside the biohazard zip lock bag and into the insulated cardboard shipping box (Kit 12). Place the frozen ice packs on top of the plastic bag containing the specimen. Twist and tightly knot the top of the clear plastic bag or seal the zip lock bag to prevent leaks.
- 6. Place the polyfoam lid on top of the side panels and close the top of the cardboard box completely. Tightly seal the top of the box with tape.
- 7. Fill out the Rabies Request for Examination form completely.
- 8. Place the form in the self-addressed envelope and seal. Attach the envelope to the top of the shipping box. Do not place the envelope inside the box. Department of Transportation regulations state the "UN3373 Biological Substances, Category B" label located on the envelope must be displayed for all rabies submissions during transport to the Laboratory.

## **SHIPPING SPECIMENS FOR RABIES TESTING**

#### Prior arrangements must be made through the Epidemiology Program.

- Rabies specimens **should not** be shipped by U.S. Mail or UPS.
- Rabies specimens must be delivered to the laboratory by the fastest means possible and may be shipped in one of four ways:
  - o Delivered by submitter
  - Delivered by the University of Vermont Medical Center Courier Service (through a local hospital)
  - Shipped by FedEx at the submitter's expense
  - o Sent via Vermont Greyhound Bus

For comments or questions, call the Department of Health Laboratory. For questions about submission of a specimen for rabies testing, please call the Epidemiology Program or the Rabies Hotline at 1-800-4-RABIES.

#### Micro 430 (July 2018)

Mailing address: P.O. Box 1125 Burlington, VT 05402-1125



#### Vermont Department of Health Laboratory Request for Rabies Examination



Mailing Address: PO Box 1125, Burlington, VT 05402-1125

Shipping and Drop Off Address: 359 South Park Drive, Colchester VT 05446 • (802) 338-4724 or (800) 660-9997 in VT only

#### NOTE: All rabies testing requests must be pre-approved by Infectious Disease Epidemiology Check here if request has been approved by calling: (802) 863-7240 or 1-800-640-4374 (available 24/7)

Submitter Information (e.g. Game Warden, Veterinarian)						
Facility or Agency Name:						
Last Name: First Name:						
Mailing Address:		City/Town:				
State:	Zip Code:	Telephone Number (Day):		Telephone Number (Evening):		
Shipping Address (If Different from Mailing Address):						
Large Rabies Box Animal Kit (Indicate number needed):			Small Rabies Box Ar	nimal Kit (Indicate number needed):		

Complainant Information (e.g. Animal Owner)						
Last Name:		First Name:				
Address:						
City/Town:			State:	Zip Code:		
Telephone Number (Day):		Telephone number (	(Evening):			
Reason for Test:						
Human Exposure *	Contact With Pet or Domestic Animal		Diagnostic	Surveillance		
Human Exposure Information						
Date of Exposure:	Type of Exposure:	1	Name of Person(s) Exposed:			
	Bite Contact with Saliva/Nervous T	īissue				
Telephone Number of Exposed (	Day): Telephone Number of Exposed (Ev	vening):				

Animal Information						
Animal Type:		Age of Bovine (If Applic	able):	Animal/USDA ID Number:		
Date of Death:	Town Captured/Found:			County Captured/Found:		State Captured/Found:
Latitude (USDA): Longitude (USDA):		Porcu	ipine Quills Present? YES INO	More than One	Specimen in Box?	

**Comments** (additional comments may be written on the back of this document):

\*Human Exposure is only when wet saliva or nervous tissue from a suspect animal is directly introduced into open wounds and/or mucous membranes (e.g. mouth, nose, eyes), or exposure to a bat where there is uncertainty of a bite.

VERM(	ONT Ra	abies Po	stexposure	e Pronhv	laxis Report Form	VDH Use Only:
DEPARTMENT OF HEALTH						
Reporting Informat	tion	, ,				
Date of report:		]/				
Name of person re	oorting:			Phone:	()	_
Facility/Institution:				Provider	(if not reporter):	
Patient Informatio	n					
Last name:			First nam	ne:	MI:	
Street address: _					Town:	
State:			Zip:		Phone: ()	
Sex: 🗆 Male 🗆	Female 🗆 No	answer	Age:	_	Date of birth:/	/
Clinical Informatio	n					
U Vaccine U Vac	cine + Immune	globulin (R	IG) Is th	ie patient im	munosuppressed? 🗆 Yes 🗆	No 🗆 Unknown
Date of vaccine (fir	st dose):	_//				
Date of (RIG):	Same date	as vaccine	□ Ot	her date, spe	ecify://	
Has the patient eve	er received rabio	es vaccine b	efore? 🗆 Yes	🗆 No	🗆 Unknown	
If yes, reason:	🗆 Animal p	professional	□ Travel [	□ Previous ra	abies exposure 🛛 Other:	
Exposure Informat	ion					
Date of exposure:	Date of exposure:// Geographic location of exposure:					
Type of exposure:	ype of exposure: 🗆 Bite 🛛 Mucous membrane 🖓 Saliva or brain tissue into wound 🖓 Scratch 🖓 Unknown					
	🗆 Bat in bedr	oom		Other:		
Exposure site:	🗆 Leg	□ Head	Torso	🗆 Arm	🗆 Hand/Finger 🛛 🗆 U	Inknown
	$\Box$ Other:					
Animal type:	Raccoon	🗆 Skunk	🗆 Bat		Woodchuck     Bobca	at
	□ Cow	🗆 Cat	□ Horse	Sheep	□ Dog    □ Ferre	t
	🗆 Unknown	$\Box$ Other:				
Animal status:   Owned  Stray  Wild  Unknown						
If owned, owner's name: Owner telephone: ()						
Animal disposition: 🗆 10-day confinement 🗆 Euthanized and tested 🗆 At large/unavailable 🗆 Unknown						
Describe exposure scenario:						
Has a <u>Town Health</u>	Has a <u>Town Health Officer</u> been notified? (required for animal bites):  Yes  No  Unknown					

Fax or scan form to (802) 951-4061 or <u>AHS.VDHEpiLabRabies@vermont.gov</u>. Direct questions to the Infectious Disease Epidemiology Program (802) 863-7240.

VERMONT DEPARTMENT OF HEALTH	Town Health Offi Animal Bite Repo	cer ort Form	AFFIX PATIENT LABEL HERE		
Reporting Information					
Date of report://	′ Town:		Health Officer name:		
Work phone: ()	A	Iternative phone:	()		
Person reporting bite:	Health care provider	Veterinarian	□ Bite victim/parent or guardian □ Other		
Reporter name:	Facility	:	Phone: ()		
Bite Victim Information					
Last name:	F	irst name:	MI:		
Street address:			Town:		
State:	Zip:		Phone: ()		
Sex: 🗆 Male 🗆 Female	□ No answer Age:		Date of birth:///		
Bite Information					
Date of bite:///	Where bite occurre	ed:	Provoked bite? 🗆 Yes 🗆 No 🛛 Unknown		
Location of bite: 🗆 Leg	🗆 Head 🗆 To	orso 🗆 Arm	Hand/Finger     Other:		
Animal type: 🛛 🗆 Dog	🗆 Cat 🛛 Co	ow 🗆 Horse	Sheep     Gerret     Unknown		
🗆 Racco	on 🗆 Skunk 🗆 Ba	at 🗆 Fox	□ Other:		
Animal status: 🛛 Owne	d 🗆 Stray 🗆 W	ʻild 🗆 Unknov	wn		
If owned, owner's name:		If c	owned, animal's name:		
Street address:		То	wn:		
State:	Zip:	Ov	vner telephone: ()		
Animal disposition: 🗆 10-da	y confinement 🛛 Eutha	anized and tested	At large/unavailable Unknown		
Veterinarian name:	Fac	ility:	Phone: ()		
Has the animal received a rabies vaccine in the past?   Yes  No  Unknown					
If yes, date of last rabies shot:// Rabies Tag #:					
Describe bite scenario:					
Action taken by Health Office	r:				

Report animal bites to the local <u>Town Health Officer</u>.

Health Officers: Please keep a completed copy of this form in your town clerk's office.

Direct questions to the Infectious Disease Epidemiology Program at (802) 863-7240.