Nebraska Rabies Investigation Guideline (*Including Management of Potential Rabies Exposures*)

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Rabies (Including Management of Potential Exposures) Disease Management and Investigative Guidelines

CASE DEFINITIONS – Animal Rabies (CDC 1997)

Laboratory Criteria for Case Classification:

- A positive direct fluorescent antibody test (preferably performed on central nervous system tissue), or
- Isolation of rabies virus (in cell culture or in a laboratory animal)

Case Classification:

- Confirmed: a case that is laboratory confirmed.

CASE DEFINITIONS – Human Rabies (CDC 2011)

Clinical Evidence:
Rabies is an acute encephalomyelitis that almost always progresses to coma or death within 10 days after the first symptom.

Laboratory Evidence:

- Detection of *Lyssavirus* antigens in a clinical specimen (preferably the brain or the nerves surrounding hair follicles in the nape of the neck) by direct fluorescent antibody test, or
- Isolation (in cell culture or in a laboratory animal) of a *Lyssavirus* from saliva or central nervous system tissue, or
- Identification of *Lyssavirus* specific antibody (i.e. by indirect fluorescent antibody (IFA) test or complete rabies virus neutralization at 1:5 dilution) in the CSF, or
- Identification of *Lyssavirus* specific antibody (i.e. by indirect fluorescent antibody (IFA) test or complete rabies virus neutralization at 1:5 dilution) in the serum of an unvaccinated person, or
- Detection of *Lyssavirus* viral RNA (using reverse transcriptase-polymerase chain reaction [RT-PCR]) in saliva, CSF, or tissue.

Case Classification:

- *Confirmed*: a clinically compatible case that is laboratory confirmed by testing at a state or federal public health laboratory.

LABORATORY ANALYSIS

A. Human Samples:

- The Centers for Disease Control and Prevention (CDC) performs human sample testing for both antemortem and postmortem diagnosis.
- Contact Nebraska Department of Health and Human Services Office of Epidemiology (NDHHS-OE) to coordinate collection/submission of samples.
- For further guidance, refer to the Managing Special Situations – Human Rabies Case.

B. **Animal Testing**:

- The University of Nebraska-Lincoln Veterinary Diagnostic Center (UNL-VDC) performs animal rabies testing for NDHHS.
    - NDHHS pays for testing of certain specimens if a human is exposed but will not cover charges for euthanasia, shipping, or handling.
    - For approval of specimens please contact NDHHS at 402-471-2937. If human exposure criteria are met, NDHHS will designate a Rabies Approval (RA) number which must be included on the UNL-VDC requisition form.
    - Criteria required for NDHHS to assign an RA number:
        - Exposure involves unvaccinated animal or animal not current on rabies vaccine, and penetration of the skin by the teeth or any contamination with saliva or brain material of mucous membranes (eyes, mouth, or nasal passages) or fresh, open cuts in the skin.
        - For exposures involving bats, if the bat bit a person, flew into a person's face, or collided with one's exposed skin; if a person stepped on a bat barefoot or woke to find a bat in a room with them; or if a bat is found in a room with a person unable to communicate.
        - For purposes of assigning RA numbers, finding a bat OUTSIDE of the room the person was in (i.e., hallway or other side of open door) is not considered high risk exposure and does not meet the criteria.
    - PRIOR to preparation and shipping of samples, consult with UNL-VDC at 402-472-1434 to coordinate sample submission.
    - Use the UNL-VDC Rabies Diagnostic Testing Requisition Form for animal testing (Appendix A). Also available on the UNL-VDC website.

- Only dead animals can be tested for rabies. To facilitate testing living animals must be euthanized. A fresh (not formalin-fixed) cross-section of the brainstem and cerebellum is required for testing.
    - Euthanize in accordance with the American Veterinary Medical Association's Guidelines on Euthanasia.
    - For bats, the whole animal should be submitted for testing. For animals larger than a bat, send only the head.
    - Exercise caution when decapitating the animal. Do not damage the brain or brain stem or put yourself or others at risk of exposure.
    - Contact NDHHS-OE (402-471-2937) if only formalin-fixed brains are available (Not preferred).

- Packaging and shipping of animal specimens:
    - Pack the head or small animal in a primary leak-proof container.
    - Place the primary container into a secondary container with enough cold packs to maintain refrigerator temperatures until reaching the lab. (Dry ice is not recommended as it may freeze the head.)
    - Samples should be sent to:

      University of Nebraska-Lincoln Veterinary Diagnostic Center
      Mailing Address: P.O Box 82646, Lincoln, NE 68501-2646
      Delivery Address: Room 230A NVDC
      4040 East Campus Loop North
      Lincoln, NE 68583-0907

RABIES EPIDEMIOLOGY

With few exceptions, rabies occurs worldwide. The World Health Organization estimates that up to 55,000 human deaths occur annually, mostly in rural areas of Africa and Asia. In the United States, the number of human deaths attributed to rabies has declined from 100 or more each year in the early 1900's to a current average of only 2 or 3 per year. Two programs have contributed to this substantial reduction. Animal control and vaccination programs started during the 1940's and more recent oral rabies vaccination programs have eliminated domestic dogs as reservoirs of rabies in the United States. Also, effective human rabies vaccines and immunoglobulins have been developed; modern day prophylaxis has proven nearly 100% successful. From 2008 to June of 2017, 33 cases of human rabies were recorded in the United States and Puerto Rico. On the basis of historic records at NDHHS (which might be incomplete), the last reported human cases of rabies in Nebraska occurred in the 1920s.

During 2015, 50 states and Puerto Rico reported 5,508 rabid animals and 3 human fatal rabies cases to the Centers for Disease Control and Prevention (CDC). Approximately 92% of animal cases were in wildlife; most frequently reported rabid wildlife species were as follows: 1,704 (30.9%) bats, 1,619 (29.4%) raccoons, 1,365 (24.8%) skunks, 325 (5.9%) foxes. Among domestic species, the highest numbers of reported case were 244 (4.4%) cats, 85 (1.5%) cattle, and 67 (1.2%) dogs.

During 2006–2016, 11,579 animals were submitted for testing in Nebraska of which 448 (3.9%) were positive. The proportion of positive tests was highest among skunks (219/307 [71.3%]), followed by horses (16/124 [12.9%]), cattle (43/431 [10.0%]), bats (123/6,669 [1.8%]), cats (33/2,030 [1.6%], raccoons (2/369 [0.5%]), and dogs (6/1,257 [0.1%]). During 2006–2016, median number of bats and skunks testing positive per year was 13 (range, 3–16) and 15 (range, 7–53), respectively. NDHHS paid for 4,932 tests for exposure events with established human risk (median/year, 450; range 371–530). Of these, 4,803 (97.4%) were negative (median/year, 443; range 359–510); risk of rabies was ruled out and costly PEP was avoided. Of the remaining 203 exposure events, 121 (2.5%) were positive (median/year, 11.5; range 7–16 [1.6–4.1%]) and 82 (1.7%) were not testable (median/year, 8; range 4–10 [0.9–2.3%]); PEP was necessary for these potentially exposed persons.

During 2017, a total of 1,154 animals in Nebraska were submitted for testing; 19 (1.6%) were positive including 10 bats (52.6%), 7 skunks (36.8%), and 2 cats (10.5%). These animals originated from 15 of Nebraska's 93 counties. No rabid raccoons were reported. Skunks and bats remain the two primary wildlife reservoirs for the rabies virus in Nebraska. Given ongoing presence of this disease in these reservoir species, rabies remains a potentially serious threat to public health in Nebraska.

A report listing the current year-to-date positive cases and links to both data from previous years and a summary report of rabies in Nebraska from 2006 to 2016 are available on the NDHHS website at the following URL:
http://dhhs.ne.gov/Pages/srd_rabies.aspx

DISEASE OVERVIEW

A. **Agent:**
A *Rhabdovirus* of the genus *Lyssavirus* causes rabies.

B. **Clinical Description:**
Rabies virus infects the central nervous system, causing encephalopathy and ultimately death. Early symptoms of rabies in humans are nonspecific: fever, headache, and general malaise. As the disease progresses, neurological symptoms appear: insomnia, anxiety, confusion, slight or partial paralysis, excitation, hallucinations, agitation, hypersalivation, difficulty swallowing, and hydrophobia. Rabies typically progresses rapidly to death after the onset of neurological symptoms. Some animals may die rapidly with limited symptoms. In animals, there are two types of rabies. One type is encephalitic (furious) rabies where animals are hostile, bite at objects, and have an increase in saliva. The second form is paralytic (dumb) rabies where an animal is timid and shy often rejecting food and exhibiting paralysis of the lower jaw and muscles. Signs of animal rabies include: changes in behavior, general sickness, problems swallowing, an increase in saliva, wild animals appearing abnormally tame or sick, animals that bite at everything if excited, difficulty moving or paralysis, and death.

C. **Reservoirs:**
In the United States, raccoons, skunks, foxes, and bats are the major reservoirs. In developing countries, dogs remain the principal problem. Small rodents and lagomorphs (e.g., squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, wild rabbits, and hares) have not been known to transmit rabies to humans and generally have never been found to be infected with rabies. The exception is rodents and lagomorphs caged outdoors.

D. **Mode(s) of Transmission:**
Rabies is spread through the saliva of infected animals through a bite, scratch, or contact with mucous membranes or a break in the skin. Skin breaks or mucous membrane exposure to nervous tissue (e.g., brain, spinal cord) of an infected animal may also pose a risk of transmission.

E. **Incubation Period:**
In humans, usually 14–56 days; range, 10 days to >1 year. Period tends to shorten as severity of exposure increases and/or proximity to the central nervous system decreases (e.g., a bite to the face). In animals, generally 15–50 days, but variable and in rare cases even several months or longer.

F. **Period of Communicability:**
Dogs, cats, and ferrets can shed the virus in their saliva up to 10 days before onset of clinical signs and throughout the course of disease. Wild animals, such as skunks, bats, and foxes, may have virus present in saliva for longer periods before onset of clinical symptoms.

G. **Susceptibility and Resistance:**
All mammals are susceptible to rabies. Non-mammalian species are not susceptible.

H. **Treatment:**
Experimental treatment options for humans may be available on a case-by-case basis. However, once symptoms occur, the outcome is almost always fatal.

NOTIFICATIONS (ANIMAL RABIES)

The following notifications occur as a result of animal rabies laboratory reports:

1. **Positive, unsuitable, or indeterminate laboratory reports:**
   - UNL-VDC will notify the submitter of the specimen result (e.g., veterinarian, local health department [LHD], animal control authority) both by phone and fax, and NDHHS-OE by fax and by electronic reporting to the NDHHS Electronic Disease Surveillance System (NEDSS).
   - An NDHHS-OE Epidemiologist or administrative assistant will notify the LHD having jurisdiction over the area from which the animal originated by calling, faxing, or e-mailing a copy of the UNL-VDC report indicating the result. Upon such notification, the LHD is responsible to ensure proper follow-up with potentially exposed persons and providing recommendations for case management. NDHHS-OE consultation is available as needed by calling 402-471-2937.

2. **Negative laboratory reports:**
   - UNL-VDC will notify the submitter of the specimen by fax or email.

3. **All laboratory reports (regardless of result)**
   - UNL-VDC will notify NDHHS-OE of all test results by electronic reporting to the NDHHS NEDSS system.
   - Each electronic report of a rabies result will populate the NEDSS Documents Requiring Review queue which serves as notification for LHD surveillance staff.

INVESTIGATION GUIDELINES

Rabies is a fatal disease; any report of an animal bite or exposure, and all positive (or unsuitable) laboratory reports require prompt investigation by the local health department.

Local health departments should conduct the following steps:	**Refer to page(s):**
A. When an animal rabies laboratory report (or a verbal account of a situation involving a potentially rabid animal) is received:	
1. Identify if any human or other animal exposure occurred with the animal.	7
a. Positive laboratory reports: considered a high risk situation if exposure is identified; start PEP and/or begin to manage exposed animals.	
b. Unsuitable reports: investigate as if positive.	
2. For positive rabies laboratory result received in Nebraska's Electronic Disease Surveillance System (NEDSS), create an investigation, enter appropriate information, confirm as a case, and create a notification.	21
B. If a person was bitten or exposed to animal saliva or brain material:	
1. Assess the risk of rabies transmission to the person.	7–9
2. Decide on disposition of the exposing animal (source of exposure).	11
3. Recommend rabies post-exposure prophylaxis (PEP) to those who need it and provide reassurance to those who do not.	12–14
4. If PEP is recommended, follow-up with the patient and/or the medical provider to assure the treatment regime is completed.	
5. Create and complete an Animal Exposure investigation in NEDSS for each exposed person.	21
C. If an animal was bitten or exposed to animal saliva or brain material:	
1. Assess the risk of rabies transmission to the animal.	
2. Decide on disposition of the exposing animal (source of exposure).	7–9
3. Recommend quarantine or other disposition of the animal that was potentially exposed to rabies.	11 15–16
4. Follow-up to assure compliance with recommendations.	
D. **For cases of human rabies, see Managing Special Situations**	17–19

Identify if there was any human or animal exposure

Exposure: Rabies is transmitted only when the virus is introduced into bite wounds, open cuts in skin, or onto mucous membranes from saliva or other potentially infectious material such as neural tissue.

- Rabies virus is found in the saliva and brain matter of infected animals.
- Rabies virus is inactivated by drying, UV irradiation, and other factors, and therefore does not persist in the environment. If the suspect material is dry, the virus can be considered non-infectious.

Bite exposures: any penetration of the skin by the teeth. All bites, regardless of body site or degree of gross trauma, represent potential risk.
Non-bite exposures: surgical recipient of infected tissue, exposure to a large amount of aerosolized virus (laboratory); infectious saliva or brain material in contact with mucous membranes (eyes or mouth) or fresh, open cuts in skin.
Bat exposures: Direct contact of a human with a bat, finding a bat in the same room as a person who might be unaware that a bite or direct contact had occurred (i.e., sleeping person awakes with bat in room or an adult witnesses a bat in the room with a previously unattended, unprotected child, mentally disabled person, or intoxicated person).

- Those in the room that are able to credibly state that they were not in direct contact with the bat are not considered exposed.
- Undetected exposure is less likely when protection like mosquito netting is used while sleeping or when bats are observed outdoors, in a room open to the outside, or in settings where they are normally present.

Assess the risk of rabies transmission

Animal exposures can be classified into three categories as follows: high risk, low risk, and no risk. The boundary between these categories is often unclear and a risk assessment is needed to decide if the animal was rabid and if post exposure prophylaxis (PEP) or other action is needed.
The risk assessment is based upon the following criteria:

- The type of exposure, as defined above.
- The risk that the animal is rabid.

The risk that an animal is rabid depends on the following circumstances:

- Can the animal species be infected with and transmit rabies?
- Did the animal possibly have contact with any rabies vectors?
- Is/was the animal exhibiting signs and symptoms of rabies?
    - Dogs, cats, and ferrets might show a variety of signs, including fearfulness, aggression, excessive drooling, difficulty swallowing, staggering, and seizures.
    - Horses, cattle, sheep, and goats may exhibit the signs above and also depression, self-mutilation, or increased sensitivity to light.
    - Wild animals may only exhibit unusual behavior which may include being fearless of humans or appearing tame.

1. Review the type of animal causing the exposure vs. the nature of rabies:

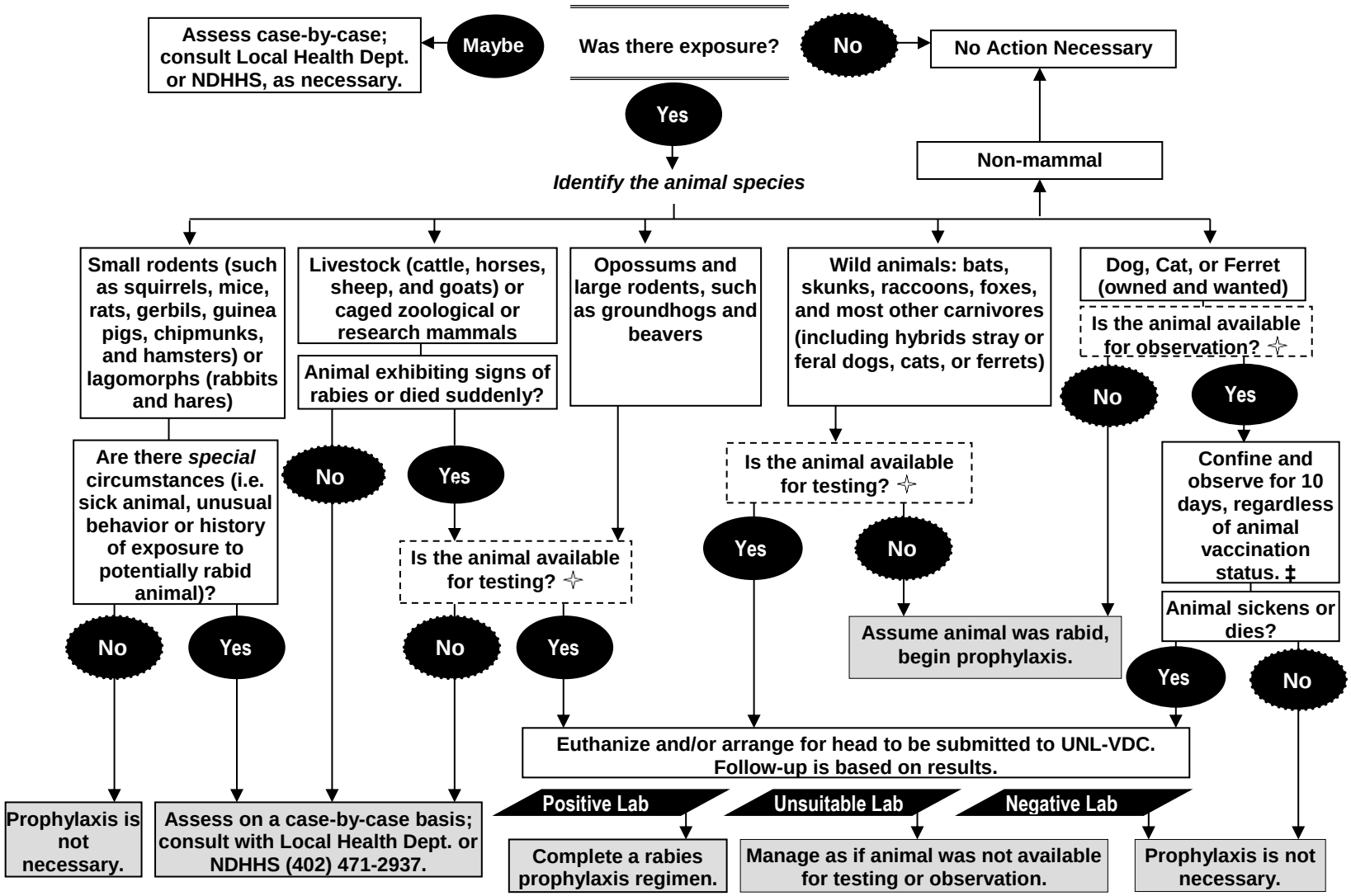
   Bats: Rabid bats are increasingly implicated as an important wildlife reservoir. Transmission can occur from minor, seemingly underappreciated or unrecognized bites from bats. Make every effort to safely capture and test the bat involved in an exposure incident. Encounters with bats are often considered high risk exposures. Regard as rabid unless negative by laboratory tests.
   Wild Terrestrial Carnivores: Wild terrestrial carnivores are an important rabies reservoir and skunks are most often found to be infected with rabies in Nebraska. Suggestive clinical signs of rabies among wildlife cannot be interpreted reliably. Vaccines given to wildlife are of unknown efficacy and should be disregarded. Regard as rabid unless animal is negative by laboratory tests.
   In Nebraska, it is illegal to keep skunks, raccoons, foxes, wolves, coyotes, and other wildlife in captivity except as authorized by permit issued by the Nebraska Game and Parks Commission; animals held in unlawful captivity must be sacrificed and tested.
   Wild animal hybrids: No rabies vaccines are licensed for hybrids of species that transmit rabies and thus vaccines given to hybrids are disregarded. The period of rabies virus shedding in wild animal hybrids is unknown. Hybrids of species that transmit rabies should be managed as wild carnivores and regarded as rabid unless the animal tests negative for rabies. When such animals bite humans, euthanasia and rabies testing of the hybrid is the safest course of action.
   Stray or Feral Dogs, Cats, and Ferrets: More likely to have had contact with wild animals and less likely to have been vaccinated. Manage as wild carnivores and regard as rabid unless the animal tests negative for rabies.
   Domestic Dogs, Cats, and Ferrets: If up-to-date rabies vaccinations, a healthy dog, cat, or ferret is unlikely rabid and therefore is of low risk for rabies and can be observed. However, if signs and symptoms of rabies are present, the animal should be considered rabid unless proven negative by laboratory tests.
   Livestock: Vaccinated and/or healthy animals are unlikely to be rabid. Livestock exhibiting signs of rabies should be investigated as suspect rabies cases. Consult with NDHHS-OE.
   Large rodents (woodchucks and beavers): Large rodents have been found to have rabies in the Eastern U.S. where raccoon-variant rabies virus is circulates. This "raccoon strain" has not been identified in Nebraska. The risk while low should be evaluated in consultation with NDHHS-OE.
   Small rodents and lagomorphs: Squirrels, chipmunks, rats, mice, hamsters, guinea pigs, and gerbils and lagomorphs (rabbits and hares) are rarely infected and have not been known to transmit rabies to humans. No risk; unless the circumstances of the exposure or the animal's history of past exposure to rabies vectors suggest differently. (e.g., past history of pet rabbit exposed to bite of wild carnivore and nursed back to health).
   Non-mammalian animals: Non-mammals do not transmit rabies. No risk.

2. Investigate the circumstances of exposure:
   Talk to the exposed person or other witnesses. Get an account of what occurred. Make a distinction between a provoked and unprovoked bite considering the animal's "normal" behavior. An unprovoked bite may be attributable to rabies. Provoked bites are less likely to reflect behavioral changes associated with rabies. Examples of provoked bites:
   - Bites by unfamiliar or non-domesticated animals the person was interacting with (e.g., petting a stray, feeding or cornering wild animals)
   - Bites by an injured animal (e.g., dog hit by a car).
   - Bites by an animal protecting "their space" (e.g., a front yard, their food)
3. Consider what is known about the exposing animal:
   - Animals up-to-date with an approved vaccine for their species are unlikely to be rabid. (Listing of approved rabies vaccines; *Compendium of Animal Rabies Prevention and Control, 2016*, Appendix 1)
   - Animals having been in contact with wildlife at a higher risk for rabies.
   - Bites by animals with a previous history of menacing or biting are less likely to reflect changes in behavior that may be attributable to rabies.
4. Make a decision (Use "Rabies Exposure Algorithm" provided on p. 10):
   Review information collected to determine the risk of rabies transmission:
   - No risk: PEP, confinement and/or testing is not indicated.
   - Low risk: Confinement or testing is indicated. PEP is offered based on the results of confinement or testing.
   - High risk: Immediate testing of the animal and initiation of prophylaxis is indicated. Prophylaxis can be stopped if testing results are negative.

   Examples of high risk situations:
   - Exposure to a bat or animal testing positive for rabies.
   - Exposure to a mammal exhibiting signs and symptoms of rabies.
   - Bite above the shoulder by wild carnivores or unvaccinated dog or cat.
   - Bite or exposure to a wild carnivore, dog, cat, or ferret that cannot be located and positively identified for testing within at least 72 hours.

   Verify that the investigation information for exposed persons is captured in Nebraska's Electronic Disease Surveillance System (NEDSS).
5. If the exposing animal available for testing, use the "UNL-VDC Rabies Diagnostic Testing Requisition Form" (Appendix A) to collect and record:
   - Name, address, and contact information of submitting clinic/agency;
   - Specimen history
     - Kind of animal, breed/species, and location (town and county);
     - Vaccination status of exposing animal;
     - Symptoms or signs of rabies in exposing animal as appropriate;
     - Exposing animal owner name, address, and contact information;
   - Exposure history
     - Has exposing animal bitten any person? If yes, provide person's name and date bitten or exposed;
     - Incident details (e.g., wound severity/location, exposure extent);
     - Was exposing animal in contact with pets or domestic animals? If yes, provide species, vaccination status, and owner name, address, and contact information.

Rabies Exposure Assessment Algorithm: Human Exposures to Potentially Rabid Animal



✧ **Contact NDHHS at (402) 471-2937 for Rabies Approval (RA) number. Exposed individuals may be offered post-exposure prophylaxis (PEP) at anytime during the period of testing or observation if the situation is considered one of high risk for potential rabies transmission. If the animal is later determined not rabid, treatment should be stopped.**

On a case-by-case basis, it may be allowable to wait up to 72 hours to identify an animal's owner or to capture an offending animal (assuming the correct animal can be positively identified).

‡ **For the 10 day observation period, day 0 is the day that the bite or exposure occurred.**

Notes:

1) **Exposure:** Any penetration of the skin by the teeth or any contamination of mucous membranes or fresh, open cuts in the skin with saliva or brain material. Please refer to note 2) for bats.

2) **Bat Exposure**: Every effort should be made to safely capture and test the bat involved. Please refer the *Rabies Exposure Management of Bat-related Incidents* algorithm (Appendix B) for specific guidance regarding Bat Exposures.

3) **Immediate care**: Proper wound care should always occur (i.e., cleaning area, tetanus booster, and/or antibiotics, as needed).

4) **For consultation**: Contact Local Health Department (Appendix C) or NDHHS Office of Epidemiology at (402) 471-2937.

*Based on "Rabies Exposure Assessment Algorithm" in *Rabies Investigation Guideline*. Kansas Department of Health and Environment. Page 8. (http://www.kdheks.gov/epi/Investigation_Guidelines/Rabies_Disease_Investigation_Guideline.pdf). Accessed June 7, 2016.

Disposition (management) of the exposing animal

*Based on best available current science as determined by 1) *Human Rabies Prevention --- United States, 2008, Recommendations of the Advisory Committee on Immunization Practices*; 2) *Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies* (CDC-ACIP, 2010); and 3) *Compendium of Animal Rabies Prevention and Control, 2016*.

When investigating a potential rabies exposure of a human or other mammal, the management of the animal causing the exposure should be as follows:

Healthy domestic, dog, cat, or ferret that is owned or wanted should be confined and observed daily for 10 days regardless of vaccination status.

- 10-day period begins on day 0, which is the date exposure occurred and is completed at the end of day 10.
- Confined/isolated: animal is kept in an approved location in a manner that would not allow the offending animal to be lost to follow-up during the confinement period. Do not vaccinate during this 10 day period.
- Locations of isolation: Determined by local rabies control authorities.
- Before or during isolation: 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 submitted for testing.
- Release: If, after observation and examination by a veterinarian, at the end of the ten-day period the animal shows no clinical signs of rabies, the animal may be released to its owner. If federal, state, or local laws prohibit ownership of wild or other animals, release of the animal may be prohibited.

Stray dogs, cats or ferrets: Any animal of a species known to be involved in rabies transmission which has bitten a person or caused an abrasion of the skin of a person and is unowned or the ownership of which cannot be determined within 72 hours of the time of the bite or abrasion, must be immediately subject to any tests to determine whether the animal is afflicted with rabies. The 72-hour period includes holidays and weekends and must not be extended for any reason.

- If the stray begins to experience symptoms of rabies before the end of the 72-hour period, it should be sacrificed immediately and tested.
- For high risk situations due to the severity and/or location of the bite, the holding period may be waived in lieu of testing urgency.

Horses, cattle, or sheep: Management should be determined by local health or animal officials in consultation with NDHHS OE.

Other mammals which are known to be involved in rabies transmission should be sacrificed immediately and head submitted for testing. This includes hybrids of species known to transmit rabies and any vaccinated mammal if its virus shedding period is unknown.

Small rodents and lagomorphs (squirrels, chipmunks, mice, rats, gerbils, guinea pigs, hamsters, rabbits, hares and other species not involved in rabies transmission) do not need to be sacrificed; unless circumstances, in the judgment of the LHD or DHHS OE, indicate otherwise.

Recommendations on rabies post-prophylaxis (PEP) treatment – humans

The administration of rabies PEP is a medical urgency, not a medical emergency, but do not delay decisions. When documented or likely exposure has occurred, PEP should be administered regardless of the length of delay, provided that clinical signs of rabies are not present in the exposed person.

The local health department (LHD) and NDHHS only make recommendations about the advisability of PEP. The patient's physician has the final decision; but, during times of limited rabies biologics, NDHHS will follow CDC guidance in limiting the use of rabies biologics to events in which PEP is recommended.

The Advisory Committee on Immunization Practices (ACIP) provides the recommendations on the use of rabies PEP. The recommendations are reported in the CDC Morbidity and Mortality Weekly Report, *Human Rabies Prevention --- United States, 2008, Recommendations of the Advisory Committee on Immunization Practices*.

Rabies biologics are available only by prescription and are not provided by NDHHS. The LHD must refer clients to private physicians, internal or external clinics or hospitals for immediate treatment. Hospitals, especially the larger hospitals, across Nebraska carry Human Rabies Immune Globulin and Human Rabies Vaccine. PEP treatment is a simple, effective, and a relatively painless procedure. However, the financial costs associated with PEP are variable and might exceed $3,000 per case.

Manufacturers of PEP products have patient assistance programs for the uninsured/underinsured. Medicaid or Medicare will likely cover treatment costs.

- Sanofi Pasteur (HRIG and vaccine): Sanofi Foundation Patient Assistance Program by telephone (866-801-5655) or https://www.visitspconline.com/.
- Novartis (vaccine only): Through *RX Hope* by telephone (800-589-0837) and instructions and request forms are available online.

Note: Pregnancy is not a contraindication to PEP.

If PEP is started and laboratory results later show an animal is negative for rabies, PEP should be discontinued.

Rabies immunizing products (Table 1):

1. Human rabies immune globulin (HRIG):
   - Provides rapid passive immunity for a short time (half-life of 21 days).
   - Administered once at beginning of post-exposure prophylaxis to provide immediate antibodies until the patient responds to the vaccine by actively producing antibodies.
   - If not administered on day 0 (i.e., first day of vaccine dose given), HRIG can be administered up to and including day 7.
   - HRIG may partially suppress active production of antibodies; therefore, no more than the recommended dose should be given.
   - **Never administer HRIG in the same syringe as the vaccine or into the same anatomical site.**
   - **Never give HRIG to a person who has been previously vaccinated.**

2. Human diploid cell (HDCV) or purified chick embryo cell (PCECV) vaccine:
   - Induces active immunity which requires >10 days to develop and usually persists for >2 years.
   - Administered intramuscularly (IM) in the deltoid muscle, which is the only acceptable site of vaccination for adults and older children. For younger children the anterolateral aspect of the thigh is acceptable.
   - **Never give rabies vaccine in the gluteal muscle.**

Rabies postexposure prophylaxis schedule – ACIP Recommendations 2010

Note: The 2010 ACIP recommendations for post-exposure prophylaxis do differ from current rabies vaccine label instructions. Refer to the appropriate MMWR for details.

1. Wound Treatment: Immediate and through cleansing with soap and water. If available, a virucidal agent such a povidine-iodine solution should be used to irrigate. Consider a tetanus vaccine booster. Antibiotic prophylaxis and primary wound closure depend on exposing animal, the wound(s) size and location and time interval since the bite. Avoid suturing, when possible.
2. Determine the patient's rabies vaccination status. (A complete pre- or post-exposure vaccination with HDCV, PCECV, or rabies vaccine adsorbed, or previous vaccination with any other type of rabies vaccine and documented antibody response to that vaccination is consider "previously vaccinated".)
3. For previously vaccinated patients:
   a. HRIG: Do not administer.
   b. Vaccine: 1.0 mL, IM, one each day on days 0 and 3*.
4. For patients not previously vaccinated:
   a. HRIG: 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 IM in the deltoid or quadriceps at an anatomical site distant from the vaccine administrations.
   b. Vaccine: 1.0 mL, IM, one each day on days 0, 3, 7, and 14.*[π]

*** For deviations from recommended postexposure vaccination schedules:**

- **<u>Every attempt</u>** should be made to adhere to the schedule.
- Once initiated, a delay of a few days for individual doses is unimportant. Resume as if on schedule maintaining the same interval between doses.
  - Example: Patient for a day 3 dose appears on day 6; give remaining doses on day 10, and day 17.
- The effect of longer lapses is unknown. For substantial deviations, contact the manufacturer (see Table 1) to evaluate the need to restart.
  - When substantial deviations do occur in a series, assess immune status by performing serologic testing 7–14 days after the final dose.

[π] For patients with immunosuppression, vaccine should be administered using all 5 doses of vaccine on days 0, 3, 7, 14, and 28.

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

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

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

† 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).

Quarantine or management of exposed, non-human animal

*Based on best available current science as determined by 1) *Human Rabies Prevention --- United States, 2008, Recommendations of the Advisory Committee on Immunization Practices*; 2) *Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies* (CDC-ACIP, 2010); and 3) *Compendium of Animal Rabies Prevention and Control, 2016*.

When investigating a potential exposure to rabies of a mammal, the management of the animal potentially exposed should be as follows (See also Appendix I: Rabies Exposed Animal Assessment Algorithm):

1. Determine the rabies immunization status of owned and wanted dogs, cats, ferrets, horses, cattle, and sheep. A current vaccination is verified by the owner providing a rabies vaccination certificate that contains the following:
   - Positive identification for each mammal showing current vaccination by a licensed veterinarian with an approved vaccine for species and
   - Expiration date of the rabies vaccine.

   If the initial vaccination was administered at least 28 days previously or booster vaccinations have been administered in accordance with Part III of the *Compendium of Animal Rabies Prevention and Control, 2016*, the animal is considered current on vaccination.

   Without appropriate documentation, an animal might need to be managed as never vaccinated or with the possible use of prospective serologic monitoring. Refer to appropriate actions in the following section.

2. Disposition based on animal and vaccination status:

   - **The animal should be quarantined or observed based on vaccination status, type of species, and ownership status of the animal.**
     - **Observation:** exposed animal is kept by the owner as per normal handling procedures in a manner that allows the animal to be watched for any changes of behavior or health.
     - **Quarantine:** exposed animal is kept in a manner that assures the exposed animal is effectively restricted from any contact with humans or animals known to contract and transmit rabies. This requires that there be no possibility of the animal gaining exit from or another animal gaining entry to the quarantine space (including digging under or climbing over fencing) and that there is no possibility of contact through spaces in a confining fence by the use of solid fencing material or double fence construction with wire mesh. The number of human caretakers should be as few as possible while monitoring the animal for possible development of rabies.
   - **Any illness in an animal under quarantine or observation** should be reported immediately to the local health department or agriculture officials. If signs suggestive of rabies are present, the animal should be euthanized and tested.
   - **Dogs, cats, and ferrets that have appropriate documentation of current rabies vaccination** and are owned and wanted, 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.

- **Dogs and cats that are overdue for a booster vaccination and have appropriate documentation** of having received a USDA-licensed rabies vaccine approved for that species 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.
    - If booster vaccination is delayed past 96 hours, public health officials may consider increasing the observation period, taking into consideration factors such as the severity of exposure, the length of delay in booster vaccination, current health status, and local rabies epidemiology.
- **Dogs and cats that are overdue for a booster vaccination—but do not have appropriate documentation** of having received a USDA-licensed rabies vaccine approved for that species at least once previously—should immediately receive veterinary medical care for: assessment, wound cleansing, and REQUIRED consultation with NDHHS-OE or local public health authorities on the possible use of prospective serologic monitoring.
    - Prior to booster vaccination, the attending veterinarian must request guidance from NDHHS-OE or local public health authorities.
    - During the testing process, the exposed animal must be kept in strict quarantine.
    - With an adequate anamnestic response, the animal is considered as overdue at time of exposure requiring a 45 day observation.
    - If there is inadequate evidence of an anamnestic response, the animal is considered and handled as if they were never vaccinated.
    - The exposed animal who is not a candidate for serological monitoring is treated as if they have never been vaccinated.
- **Dogs, cats, and ferrets that have never been vaccinated** against rabies should be euthanized immediately. If the owner is unwilling to have the animal euthanized, after the receipt of veterinary medical care for assessment, wound cleansing, and an immediate rabies vaccination, the animal should be placed in strict quarantine for 4 months (for dogs and cats) or 6 months (for ferrets). It is recommended that the period from exposure to vaccination not exceed 96 hours.
    - If vaccination is delayed, public health officials may consider increasing the quarantine period from 4 to 6 months, considering factors such as the severity of exposure, the length of delay in vaccination, current health status, and local rabies epidemiology.
    - Dogs, cats, and ferrets in quarantine do not need to receive the rabies vaccination 30 days prior to release from quarantine.
    - Currently, there is no United States Department of Agriculture (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.
- **Ferrets that are overdue for a booster vaccination** should be evaluated and managed on a case-by-case basis by consulting with NDHHS-OE or local public health authorities. Factors to be considered include the severity of exposure; time elapsed since last vaccination, number of previous vaccinations, current health status, and local rabies epidemiology.

- **Stray, unclaimed, or unwanted dogs, cats or ferrets** should be sacrificed immediately.
- **Cattle, sheep and horses that have appropriate documentation** of current rabies vaccination with a USDA-licensed vaccine approved for that species should be given a booster vaccination immediately and observed for 45 days.
- **Cattle, sheep and horses that are overdue for a booster vaccination** should be evaluated and managed on a case-by-case basis by consulting with NDHHS-OE or local public health authorities. Factors to be considered include the severity of exposure, time elapsed since last vaccination, number of previous vaccinations, current health status, and local rabies epidemiology.
- **Horses, cattle, and sheep that have never been vaccinated** with an approved vaccine should be euthanized immediately or quarantined for six months under veterinary supervision and conditions satisfactory to local health officials.
- **Other mammals (not vaccinated)** should be euthanized immediately. Animals maintained in USDA-licensed research facilities or accredited zoological parks should be evaluated and managed on a case-by-case basis by consulting with NDHHS-OE or local public health authorities.
- **Cattle, sheep, and other livestock slaughtered for consumption**: If an exposed animal is to be slaughtered for consumption, it should be done immediately after exposure. Barrier precautions should be used by persons handling the animal, and all tissues should be cooked thoroughly. Historically, federal guidelines have required that any animal known to have been exposed to rabies within the previous 8 months be rejected for slaughter. Notify USDA Food and Inspection Service (FSIS) meat inspectors if any food animals were potentially exposed before slaughter.

Additional Notes:

- ***It is not necessary to test animals that are sacrificed as a result of their rabies exposure <u>unless</u> the animal is also being investigated as a potential "exposing" animal in a separate exposure incident.***
- ***The information in this Guideline is consistent with the Compendium of Animal Rabies Prevention and Control, 2016 which is based on the most current scientific evidence available. These updated guidelines are intended to serve as the basis to dictate quarantine or management of exposed, non-human animals. Questions concerning implementation can be addressed to Rabies Program staff at the NDHHS Division of Public Health, 402-471-2937.***

MANAGING SPECIAL SITUATIONS

A. Human Rabies Case

- As required by law, suspect cases of human rabies shall be reported to NDHHS immediately.
- NDHHS is the primary contact for physicians for consultation about possible human rabies cases and will coordinate sample collection and submission with CDC Rabies Laboratory.

Safe Clinical Management of Human Rabies Patients:

- Human rabies patients **do not pose** any greater risk of infection to health-care personnel than do patients with other infections.
- Adhere to standard precautions. Use gowns, goggles, masks, and gloves, particularly during intubation and suctioning.
- **Post-exposure prophylaxis**: 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.

Initial information needed for consultation:

- Clinical signs and symptoms, including laboratory tests.
- Any suspicious animal exposure: circumstances, species, type of exposure, location and date of exposure.
- Recent travel history and/or activities of case.
- Occupational association with domestic and wild animals.
- Any recent medical procedures.

Additional case investigation (after samples are approved for CDC testing:

1. Patient history:
   - Use CDC Possible Human Rabies --- Patient Information Form (Appendix D).
   - Ensure the physician completes the clinical history of the patient.
   - Provide the name and phone number of the physician who should be contacted with the test results in addition to NDHHS.
   - The form must accompany samples sent to the CDC Rabies Laboratory.
2. Sample Shipment:
   - All samples should be considered as potentially infectious.
   - Test tubes and other sample containers must be securely sealed (tape around the cap will insure that the containers do not open during transit).
   - If immediate shipment is not possible, samples should be stored frozen at -20°C or below.
   - Samples should be shipped frozen on dry ice by an overnight courier in water-tight primary containers and leak-proof secondary containers that meet the guidelines of the International Air Transport Association.
   - NDHHS will coordinate sample collection, submission, and shipment with the CDC Rabies Laboratory.
3. Sample Collection — four clinical specimens (saliva, neck biopsy, serum, and CSF) are required by CDC:
   - Saliva: Using a sterile eyedropper pipette, collect saliva and place in a small sterile container which can be sealed securely. No preservatives or additional material should be added. Laboratory tests to be performed include detection of

rabies RNA (by reverse transcription and polymerase chain reaction, RT/PCR, of extracted nucleic acids) and isolation of infectious virus in cell culture. Tracheal aspirates and sputum are not suitable for rabies tests.

- Neck Biopsy: A section of skin 5 to 6 mm in diameter should be taken from the posterior region of the neck at the hairline. The biopsy specimen should contain a minimum of 10 hair follicles and be of sufficient depth to include the cutaneous nerves at the base of the follicle. Place the specimen on a piece of sterile gauze moistened with sterile water and place in a sealed container. Do not add preservatives or additional fluids. Laboratory tests to be performed include RT/PCR and immunofluorescent staining for antigen in frozen biopsy specimens.
- Serum and cerebral spinal fluid (CSF): At least 0.5 ml of serum or CSF should be collected; no preservatives should be added. Do not send whole blood. If no vaccine or rabies immune serum has been given, the presence of antibody to rabies virus in the serum is diagnostic and tests of CSF are not needed. Antibody to rabies virus in the CSF, regardless of the immunization history, suggests a rabies virus infection. Antibody tests include indirect immunofluorescence and virus neutralization.
- Brain Biopsy: The rarity of rabies and the lack of an effective treatment make the collection of a brain biopsy unwarranted; however, biopsy samples negative for herpes encephalitis should be tested for evidence of rabies infection. The biopsy is placed in a sterile sealed container; do not add preservatives or additional fluids. Laboratory tests to be performed include RT/PCR and immunofluorescent staining for viral antigen in touch impressions.

Note: Postmortem diagnosis of rabies is made by immunofluorescent staining of viral antigen in touch impressions of brain tissue. Portions of the medulla (brain stem), the cerebellum, and the hippocampus should be frozen and shipped on dry ice to a public health laboratory or CDC laboratory. Preservation of tissues by fixation in formalin is not recommended if rabies diagnosis is desired.

B. Euthanasia of owned animals

- When an owner is making arrangements to euthanize a pet for humane reasons, it is important to have the owner sign an animal euthanasia consent form.
- This form will describe the animal and have the owner attest that to their knowledge it has not bitten anyone in the past 10 days.
- If an animal has bitten someone in the past ten days, the animal must undergo post-mortem rabies testing after euthanasia.
- A Sample Animal Euthanasia Consent Form (Appendix E) is included in supporting documents.

C. Educating the Public

- Education of the general public is a good measure to prevent exposures.
- General information can be found on the CDC Rabies website: www.cdc.gov/rabies/
    - Rabies Exposure: www.cdc.gov/rabies/exposure/index.html
    - Animals and Rabies: www.cdc.gov/rabies/exposure/animals/index.html
- Fact sheets based on information from the CDC and the Kansas Department of Health and Environment are available in Appendix F.

D. **Wildlife Die-offs:**

- Local Health Departments are often called because of an animal die-off.
- These seldom have public health significance, and are best handled by contacting local animal control officers or the Nebraska Game and Parks Commission who are trained in these types of investigations.

LABORATORY REPORT AND HUMAN EXPOSURE MANAGEMENT IN NEDSS

Local health departments (LHD) in Nebraska have access to the state's Electronic Disease Surveillance System (NEDSS) which is currently used to capture/document information regarding animal rabies laboratory reports and human exposures. NDHHS has collaborated with the University of Nebraska-Lincoln Veterinary Diagnostic Center to establish electronic laboratory reporting of Nebraska rabies testing results to NEDSS. Such reporting includes all test results (positive, negative, or unsuitable) and serves to notify LHD surveillance staff of testing from within their jurisdictions. All reports of human exposure warrant follow-up regardless of test result to verify that exposed individuals get timely and accurate test result information and appropriate recommendations on the basis of the result. Within the NEDSS system, an animal exposure investigation should be created for such exposed persons to document all information relevant to the investigation. For positive rabies laboratory results, an investigation should be created to capture associated information, confirm the case, and create a notification. Please refer to Appendix G for the *NEDSS Rabies Lab and Investigation Guide* and Appendix H for the *NEDSS Animal Exposure Investigation Process Flow Chart*; both documents provide detailed information regarding NEDSS activities with regard to rabies case management. The following are rabies-associated conditions in NEDSS.

NEDSS Condition: Rabies, Animal

- Used for positive rabies laboratory reports. Create a "Rabies, Animal" investigation from the laboratory report, enter appropriate information, confirm as a case, and send notification.

NEDSS Condition: Animal Exposure (bite or nonbite)

- Used to document information relevant to investigations of exposed persons.

NEDSS Condition: Rabies, Human

- Used to record all information collected on possible HUMAN RABIES cases. (**Only use for human cases of acute encephalomyelitis that could possibly be attributable to rabies.**)
- Information collected on the "Possible Human Rabies--Patient Information Form" should be faxed to NDHHS Epidemiology at (402) 742-2347 (Appendix D).

ADDITIONAL INFORMATION / REFERENCES

- Compendium of Animal Rabies Prevention and Control, 2016
  http://www.nasphv.org/Documents/NASPHVRabiesCompendium.pdf

- Centers for Disease Control and Prevention
  www.cdc.gov/rabies/
  - Human Rabies Prevention Recommendations (CDC-ACIP)
    www.cdc.gov/mmwr/preview/mmwrhtml/rr57e507a1.htm
  - Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies (CDC-ACIP, 2010)
    http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5902a1.htm
  - Information for Doctors
    http://www.cdc.gov/rabies/specific_groups/doctors/index.html
  - Information for Veterinarians
    http://www.cdc.gov/rabies/specific_groups/veterinarians/index.html

- University of Nebraska-Lincoln Veterinary Diagnostic Center
  https://vbms.unl.edu/nvdls
  - Rabies Test Submission Form and General Instructions: sample preparation, packaging, and shipping. This form is available on the UNL-VDC website at the following link: https://vbms.unl.edu/SubmissionForms

- World Health Organization (WHO)
  http://www.who.int/rabies/en/

- American Veterinary Medical Association (AVMA)
  https://www.avma.org/KB/Policies/Pages/Rabies-Policy.aspx
  - Model Rabies Control Ordinances
    https://www.avma.org/KB/Policies/Documents/avma-model-rabies-ordinance.pdf
  - A Community Approach to Dog Bite Prevention
    https://www.avma.org/public/Health/Documents/dogbite.pdf
  - AVMA Guidelines on Euthanasia
    https://www.avma.org/KB/Policies/Documents/euthanasia.pdf

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Supporting Materials

Appendices A–I are available as attachments to this document

- **APPENDIX A: UNL-VDC Rabies Diagnostic Testing Requisition Form for animal testing**
- **APPENDIX B: Rabies Exposure Management of Bat-Related Incidents**
- **APPENDIX C: Map of Nebraska Local Health Departments (LHD)**
  Contact phone numbers provided for inquiries regarding rabies.
- **APPENDIX D: CDC Possible Human Rabies --- Patient Information Form**
- **APPENDIX E: Sample Animal Euthanasia Consent Form**
- **APPENDIX F: Rabies Fact Sheets**
- **APPENDIX G: NEDSS Rabies Lab and Investigation Guide**
- **APPENDIX H: NEDSS Animal Exposure Investigation Process Flow Chart**
- **APPENDIX I: Rabies Exposed Animal Algorithm**

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