Recommendations of the Canadian Council of Chief Veterinary Officers Subcommittee for the Management of Potential Domestic Animal Exposures to Rabies

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Background

In the summer of 2014, shortly after the Canadian Food Inspection Agency (CFIA) withdrew from risk assessment, collection of rabies suspect samples, and animal control activities of rabies-exposed animals, a subcommittee of the Canadian Council of Chief Veterinary Officers (CCVO) was struck. The committee was directed by the CCVO to discuss approaches to dealing with domestic animal exposures to rabies in order to promote, where appropriate, consistency in the approaches employed in each province/territory. This document seeks to consolidate the committee's discussions, findings, and recommendations. While several recommendations mirror those found in the CFIA Rabies Manual of Procedures (2011), each was thoroughly considered for its merit. The evidence and justifications for each recommendation are provided so as to be enduring and readily apparent. Where scientific evidence was lacking or inconclusive, the committee relied on expert experiences and opinion. The committee's recommendations are the product of consensus.

The recommendations focus on the most common exposure scenarios and do not address all potential circumstances and species. "Pocket pets" (e.g., hamsters, guinea pigs, etc.), exotic pets, and zoo species are not discussed.

The committee recognizes that national consistency may not necessarily be achievable in all situations. The epidemiology and risk of rabies varies across provinces and territories as evidenced by the range in number and species of animal rabies cases confirmed annually. This variability includes the rabies virus variants, the reservoir species for rabies and the prevalence of rabies virus in the respective reservoir species. The ability to place or enforce quarantines varies across jurisdictions. These epidemiologic and practical factors are important considerations in rabies management. The recommendations and rationale in this document are, therefore, intended only for consideration by the relevant authorities of each province/territory, along with other relevant factors, when designing their rabies response plan. It is also the committee's expectation that the content will contribute to future updates of the Canadian Rabies Management Plan.

Investigation of a Possible Rabies Exposure

The recommendations below are intended for use in situations where there is a reasonable suspicion of exposure to rabies. This requires a thorough investigation of the exposure incident by a competent individual to evaluate the risk of exposure/transmission having occurred. Not all potential exposure events (i.e. wildlife contacts) carry a significant risk of transmission, and thus the implementation of these recommendations may not be required. For example, contact with a species that does not commonly transmit rabies in that geographic area and did not display any abnormal behavior may not warrant any follow-up action, or may warrant only education and informal recommendations to the owner.

Owner education

In all situations where a domestic animal has potentially been exposed to rabies, it is critical that the owners be educated about the potential health risks to themselves, their family, the public, and other

domestic animals. The only way to negate the risks entirely would be to promptly euthanize the exposed animal(s). The recommendations given below assume that owners have been educated about, and accepted, these risks.

Owners of potentially exposed animals should be educated regarding the possible signs of the disease and provided appropriate contact information to report any concerns. They should also be instructed to report appropriately in the event that the exposed animal bites a human or another domestic animal. In this document, the term quarantine has been used to indicate measures that restrict contact between an exposed animal and humans or other animals. Where the committee has recommended that no contact restrictions (i.e., quarantine) be imposed, owner education should still be provided. In all cases, owner education should be reinforced periodically to ensure continued vigilance.

Executive Summary

Recommendation #1: Immediate Vaccination or Revaccination of Dogs, Cats, and Ferrets

All animals (dogs/cats/ferrets) that have been exposed or potentially exposed to rabies, whether previously vaccinated or not, should receive a post-exposure vaccination for rabies immediately, ideally within seven days after the exposure event. A vaccination can still be administered after this seven day period; however any delay may decrease the efficacy of the vaccine to prevent rabies, and thus affect the requirement for and/or duration of quarantine.

Animals that have received a vaccination shortly before the exposure event should be treated on a caseby-case basis with consideration given to the time elapsed since the vaccination, age of the animal, total number of previous rabies vaccinations, and overall health status.

Recommendation #2: Vaccination and/or Quarantine of Dogs, Cats, and Ferrets Current on Rabies Vaccination

Any animal is considered currently vaccinated if it has been administered a licensed rabies vaccine in accordance with the label directions and at least 14 days have elapsed since the animal's vaccination. The time between the animal's vaccination and the labelled duration of immunity of the vaccine must not have elapsed. Both primary and fully vaccinated animals are considered currently vaccinated.

Currently vaccinated dogs, cats, and ferrets that have been exposed, or potentially exposed, to rabies should receive a post-exposure vaccination immediately, as in Recommendation #1. Currently vaccinated animals that receive a post-exposure vaccination within seven days of exposure do not require quarantine. Owner education and follow-up should still occur.

Currently vaccinated animals that <u>do not</u> receive a post-exposure vaccination within seven days of exposure should be quarantined for a period of three months (with the possible exception of animals that received a vaccination shortly before exposure – see Recommendation #1).

Recommendation #3: Quarantine of Dogs, Cats, and Ferrets Not Current on Rabies Vaccination

Dogs and cats exposed to rabies that have no known history of previous rabies vaccination should be vaccinated immediately, as in Recommendation # 1, and quarantined for a period of three months. Consideration should be given to the administration of a second rabies vaccination in the 3rd week following exposure. If not vaccinated within seven days of the exposure event, these animals should be quarantined for six months.

Note: The committee recognizes that the World Organization for Animal Health (OIE) considers the incubation period for rabies to be six months. (OIE, 2014)

Ferrets exposed to rabies that have no known history of previous rabies vaccination should be vaccinated immediately, as in Recommendation # 1, and quarantined for a period of six months. Consideration should be given to the administration of a second rabies vaccination in the 3rd week following exposure.

Animals that are out-of-date on their vaccination should be assessed on a case by case basis. All other things being equal, a shorter duration since the animal's vaccination status lapsed, a higher number of previous rabies vaccinations, minimal delay between exposure and revaccination, and better overall health status of the animal would each generally be expected to result in better immunity. The expected level of protection against rabies should be assessed and the animal placed under a six month, three month, or no quarantine as deemed appropriate.

Recommendation #4: Conditions of a Rabies Quarantine for a Companion Animal

See the Considerations section of this document for the recommended minimum conditions that should apply to companion animal quarantines (Pg 14)

Recommendation #5: Vaccination of an Animal during a Public Health Observation Period

Under normal circumstances, when an animal is under a public health observation period following a bite to a human, it should not be vaccinated. Uncommonly, an animal both is potentially exposed to rabies and bites a human. In these infrequent circumstances, rabies vaccination should be administered to the animal immediately, as in Recommendation #1, in consultation with relevant public health authorities.

Recommendation #6: Quarantine of Livestock Species Regardless of Rabies Vaccination Status

All livestock species, regardless of vaccination status, that are exposed or potentially exposed to rabies should be quarantined for 60 days from the time of exposure, if known, or 40 days from the time of the first diagnosis if the index case is within the herd/group.

While specific evidence is lacking to support the use of post-exposure rabies vaccination in livestock species, evidence does support this practice in dogs and cats. Post-exposure vaccination of livestock species immediately following an exposure event may similarly reduce the risk of these animals developing rabies.

The conditions of livestock quarantines should be set on a case-by-case basis with consideration given to the type of livestock and intended use, with the primary goals of minimizing direct contact with people and other animals outside of the quarantined group, and ensuring handler safety should the animal(s) develop neurological disease.

For the purposes of this recommendation, horses, donkeys, and their hybrid offspring are considered to be "livestock species".

#6 a. Slaughter of livestock animals following rabies exposure

Livestock animals that are not exhibiting any clinical abnormalities consistent with rabies can be slaughtered for human consumption under standard procedures within seven days of exposure to rabies. After this time, animals should not be slaughtered for human consumption until after completion of the appropriate quarantine period.

#6 b. Utilization of Milk from Dairy Animals under Quarantine for Rabies Exposure

Milk from quarantined animals can continue to enter standard processing channels but should not be used in raw milk products.

A reference table displaying committee recommendations alongside those in the CFIA Manual of Procedures (2011) has been provided as Appendix 1.

Recommendations with Committee Considerations and Justification

Recommendation #1: Immediate Vaccination or Revaccination of Dogs, Cats, and Ferrets

All animals (dogs/cats/ferrets) that have been exposed or potentially exposed to rabies, whether previously vaccinated or not, should receive a post-exposure vaccination for rabies immediately, ideally within seven days after the exposure event. A vaccination can still be administered after this seven day period; however any delay may decrease the efficacy of the vaccine to prevent rabies, and thus affect the requirement for and/or duration of quarantine.

Animals that have received a vaccination shortly before the exposure event should be treated on a caseby-case basis with consideration given to the time elapsed since the vaccination, age of the animal, total number of previous rabies vaccinations, and overall health status.

Considerations

- Evidence exists to suggest that post-exposure vaccination, especially for previously vaccinated animals, can reduce the risk of developing rabies.
 - Manikam et al. (2008) experimentally exposed 8-12 month old naïve Indian street dogs to rabies and subsequently administered post-exposure prophylaxis (PEP) in the form of rabies vaccinations. Ten dogs in each of 4 groups were inoculated into the masseter muscle, through a surgical laceration, with rabid dog brain suspension. The dogs received either, placebo, 5 doses of Rabisin (Merial), or 3 or 5 dose of Nobivac Rabies (Intervet) on days 0, 3, 7, 14, 28, or on days 0, 5, and 28. All vaccinated dogs showed titres >0.5 IU/ml by 7 days and none showed signs of rabies or died. Six of ten control dogs died of rabies between 32 and 58 days post-exposure. The remaining 4 showed only mild, transient neurological signs between 2 and 4 weeks post exposure, and were confirmed negative for negri-bodies at euthanasia 90 days post-exposure. This suggests possible coevolution of the viral strain with the street dogs, since most evidence suggests 100% case fatality.
 - Conversely, Hanlon et al. (2002) found that PEP with vaccine only (5 doses: days 0, 3, 7, 14, and 35) was not effective in preventing rabies in 5 experimental beagles. They did find that 4/5 animals survived administration of monoclonal antibodies (mAb) at the site of inoculation, and that 5/5 beagles survived after administration of both mAb and vaccine. Vaccine only dogs developed signs of rabies on days 9 or 10, while control dogs did so on days 11, 12, or 13.
 - The contrasting findings of Manikam et al. (2008) and Hanlon et al. (2002) may be due to differences in challenge dose, viral strain, experimental animal genetics, or co-evolution of host and viral strain.
 - The CFIA Rabies Manual of Procedures (2011) states, "Research has found that vaccination or revaccination following exposure of a pet dog, cat or ferret may offer some protection to the animal, and it is therefore recommended. The sooner this can be performed the better. A window of seven days is suggested; however, slightly longer time-lines may be required" (Section 6.2.1)

- Dr. Fehlner-Gardiner, current Head of the CFIA Centre of Expertise for Rabies in Ottawa (2014, personal communication) stated:
 - "It is anticipated that the vast majority of dogs, cats and ferrets that have been vaccinated with a licensed rabies vaccine will mount an adequate immune response that will be protective. The re-vaccination following exposure would be expected to induce a memory immune response. The same rationale is the basis for booster shots in a person who has previously received rabies vaccination (either pre-exposure or post-exposure regimens)."
 - "To have a vaccine licensed, the manufacturer would have had to demonstrate that under the protocol described (i.e. the label claim), that the majority of animals are protected from disease following a virulent challenge (e.g. US regulations 9CFR requires 88% [23/25 or 26/30, or statistical equivalent if higher number of animals are used] of challenged vaccinates to survive a challenge that kills 80% of the unvaccinated controls). Therefore, animals that are vaccinated according to the manufacturer's instructions would be expected to be protected, however a booster vaccination would be expected to increase this likelihood. [...]"
- In the study by Moore *et al.* (2015), discussed further under Recommendation #2, several currently vaccinated animals were found to have anti-rabies antibody titres <0.5 IU/ml. All such animals developed titres above this level when revaccinated and sampled between 5 and 15 days later.
- See data from Texas under Recommendation #3 regarding efficacy of post-exposure vaccination.
- For unvaccinated animals exposed to rabies, the Compendium of Animal Rabies Control and Prevention written by the National Association of State Public Health Veterinarians (NASPHV, 2011, Section 5 a) (1)) advises vaccination immediately, or up to 28 days prior to release from quarantine.
- Consideration was given to the merits of titre testing of animals following potential rabies exposure.
 It is the opinion of the committee that measuring an animal's Rabies Neutralizing Antibody (RNA) (aka antirabies antibody) titre is of very limited value.
 - "Although the presence of antibodies after vaccination is important, a specific level may not directly correlate with complete assurance of protection against the disease in every individual because the quality of antibodies (their ability to stop infection) and their duration (how long they remain high) is different for every individual. This is because there are other immunological factors which are involved in the protection from rabies infection." (Kansas State University Rabies Laboratory, 2014).
 - The eighth report of the WHO Expert Committee recommends that fully vaccinated humans that are exposed to rabies receive two post-exposure booster vaccinations (on days 0 and 3). There are no distinctions made based on the exposed individual's RNA titre (WHO, 2015).
 - The availability of RNA testing for animal samples is limited, as no Canadian laboratories offer this service. Samples are generally sent to Kansas State University (KSU). Testing is also relatively expensive compared to the cost of vaccination. Clinic cost for a Stat RNA Titre test through IDEXX (who submits their samples to KSU) is \$189.95 (November 28, 2014), with a turnaround time of 10-14 days.

The CFIA Rabies Manual of Procedures (2011) (Sections 2.2.2/2.2.4) addresses titre testing and provides it as an option for fully vaccinated pets. It cautions "...that an elevated titre means there was a measurable immune response to a stimulus, but it permits no conclusion about protection." In the Manual, a titre >0.5 IL/ml in a fully vaccinated animal (without revaccination) carries the same recommendation as that for a vaccinated animal that receives a post-exposure booster—a 45 day "owner observation". If the animal's titre is <0.5 IU/ML, a 3 month quarantine is recommended. It would, therefore, be unwise to await titre results prior to revaccination, since this would preclude doing so within an appropriate time period after exposure (i.e. <7 days).

 In some cases, the owner of an animal that has been exposed to rabies may not be able to afford the cost of post-exposure vaccination. Consideration should be given to whether vaccination in these situations should be paid for with public funds, as such an action is for the protection of public health.

Recommendation #2: Vaccination and/or Quarantine of Dogs, Cats, and Ferrets Current on Rabies Vaccination

Any animal is considered currently vaccinated if it has been administered a licensed rabies vaccine in accordance with the label directions and at least 14 days have elapsed since the animal's vaccination. The time between the animal's vaccination and the labelled duration of immunity of the vaccine must not have elapsed. Both primary and fully vaccinated animals are considered currently vaccinated.

Currently vaccinated dogs, cats, and ferrets that have been exposed, or potentially exposed, to rabies should receive a post-exposure vaccination immediately, as in Recommendation #1. Currently vaccinated animals that receive a post-exposure vaccination within seven days of exposure do not require quarantine. Owner education and follow-up should still occur.

Currently vaccinated animals that <u>do not</u> receive a post-exposure vaccination within seven days of exposure should be quarantined for a period of three months (with the possible exception of animals that received a vaccination shortly before exposure – see Recommendation #1).

Considerations

- Not all animals will mount a sufficient immune response to vaccination. Rabies disease has very rarely been observed in exposed, previously vaccinated, animals.
 - Murray et al. (2009) collected available data in the USA between 1997 and 2001. "A total of 264 rabid dogs and 840 rabid cats were identified during the study period. Thirteen (4.9%) rabid dogs and 22 (2.6%) rabid cats had a history of rabies vaccination. Of these, 2 dogs and 3 cats were classified as currently vaccinated. Overall, 6 animals (1 dog and 5 cats) had a history of receiving 2 doses of rabies vaccine in their lifetime, including 2 cats that were

classified as currently vaccinated." The dog and remaining 3 cats were not currently vaccinated.

- Texas has experienced high rates of rabies in domestic animals for many years. Among confirmed cases of rabies in domestic animals between 1991 and 2009, there were 11 animals that developed rabies despite current vaccination status. Among these were 5 dogs, 2 cats, and 1 horse that had only received a primary vaccine and were not yet due for a booster. Another 2 dogs had received two previous rabies vaccines each, and the final dog had received multiple doses. In the instances where the date of exposure was known, the incubation periods were reported to have been 17 days, 20 days, "one month", and 70 days. See the complete summary of the data and references under Recommendation #3.
- Dr. Fehlner-Gardiner, current Head of the CFIA Centre of Expertise for Rabies in Ottawa (2014, personal communication) stated:
 - "...However, not all vaccinated animals will respond adequately to the initial vaccination (see Berndtsson et al. 2011, Acta Vet. Scand. 53:22 -- 91% of 6789 vaccinated dogs had titers >0.5 IU/ml; Kennedy et al. 2007, Vaccine 25:8500 – over 10K animals tested, dependent on vaccine used, failure rate [ie. titer <0.5 IU/ml] ranged from 0.01 to 0.2), not all vaccine is administered properly, the health of the animal at the time of exposure may compromise its ability to resist infection, etc. For these reasons, most jurisdictions recommend an observation period for exposed dogs/cats/ferrets, even with a booster vaccination immediately after the exposure."
- The Compendium of Animal Rabies Control and Prevention (NASPHV, 2011) (pg 8) states, "Dogs, cats, and ferrets that are currently vaccinated should be revaccinated immediately, kept under the owner's control, and observed for 45 days. The rationale for an observation period is based in part on the potential for: overwhelming viral challenge, incomplete vaccine efficacy, improper vaccine administration, variable host immunocompetence, and immune-mediated fatality (i.e., early death phenomenon) (12,45-47)."
- The CFIA Rabies Manual of Procedures (2011) advises a 45 day 'observation period' for currently vaccinated animals that received a booster vaccination and a 3 month quarantine for those who do not receive a booster vaccination. The committee felt the likelihood of vaccine breakthrough in a currently vaccinated animal that receives a booster vaccination within seven days of exposure is so low that these animals do not require quarantine. However, thorough education of the owner(s) and periodic informal follow-up (such as by phone or email) is advised.
- There was uncertainty among committee members as to whether animals that do not receive a booster vaccine should be quarantined for 45 or 90 days. Given that documented incubation periods in the data examined were generally less than 45 days, some committee members felt such duration was adequate. This would also provide further distinction between the management of vaccinated and unvaccinated animals. Other members felt that the data available did not sufficiently support this deviation from the CFIA Rabies Manual of Procedures (2011), and a majority preferred to recommend a 90 day quarantine. Enforcement of such a quarantine should only be occasionally necessary, since booster vaccinated animals.

- The committee acknowledges that currently vaccinated animals that have received two or more doses of rabies vaccine (termed "fully vaccinated" in the CFIA Rabies MOP, 2011) may be better protected than those that have only received one dose ("primary vaccinated"). However, primary vaccinates are still in compliance with labeled directions under which the vaccine efficacy has been tested. They are therefore subject to the same recommendations, as they were in the CFIA Rabies MOP (2011).
- The CFIA Rabies Manual of Procedures (2011) defines a primary vaccinated animal to have received its first rabies vaccine at least 30 days prior to exposure. Similarly, dogs (but not cats) entering the USA are required to have proof of rabies vaccination, with the first vaccine having been administered not less than 30 days prior (CDC, 2014). However, the committee feels that this duration is excessively conservative for the purposes of post-exposure management. Manikam et al. (2008) demonstrated titres greater than 0.5 IU/ml only seven days after initial vaccination in 30/30 naïve Indian street dogs. Note that these animals had received two doses of vaccine by this point in the experiment (day 0 and 3 or 0 and 5), and had also been challenged with rabies virus on day 0 (additional discussion under Recommendation #1). Minke et al. (2008) vaccinated a total of 30 laboratory beagles (13-18 weeks of age) with a single dose of commercial rabies vaccine (either RABISIN (Merial) or NOVIBAC Rabies (Intervet)). When measured on day 14 after vaccination, 29 dogs had RNA titres >0.5 IU/ml. The remaining dog failed to demonstrate a titre >0.5 IU/ml at any point during the 120 day follow-up. While titre cannot be solely relied upon as a measure of protection against rabies, these findings support the committee's recommendation that animals be considered as currently vaccinated 14 days after primary rabies vaccination. Note that current labels of animal rabies vaccines available in Canada do not provide insight into this question.

Recommendation #3: Quarantine of Dogs, Cats, and Ferrets Not Current on Rabies Vaccination

Dogs and cats exposed to rabies that have no known history of previous rabies vaccination should be vaccinated immediately, as in Recommendation # 1, and quarantined for a period of three months. Consideration should be given to the administration of a second rabies vaccination in the 3rd week following exposure. If not vaccinated within seven days of the exposure event, these animals should be quarantined for six months.

Note: The committee recognizes that the World Organization for Animal Health (OIE) considers the incubation period for rabies to be six months. (OIE, 2014)

Ferrets exposed to rabies that have no known history of previous rabies vaccination should be vaccinated immediately, as in Recommendation # 1, and quarantined for a period of six months. Consideration should be given to the administration of a second rabies vaccination in the 3rd week following exposure.

Animals that are out-of-date on their vaccination should be assessed on a case by case basis. All other things being equal, a shorter duration since the animal's vaccination status lapsed, a higher number of previous rabies vaccinations, minimal delay between exposure and revaccination, and better overall health status of the animal would each generally be expected to result in better immunity. The expected level of protection against rabies should be assessed and the animal placed under a six month, three month, or no quarantine as deemed appropriate.

Considerations

- There is evidence to support post-exposure prophylactic vaccination (PEP) of animals to reduce the likelihood of developing rabies (see recommendation #1).
- While there is some evidence to suggest efficacy, rabies immunoglobulin (RIG) is not used for PEP in animals in North America at this time. This is likely due to a lack of ready availability, high cost, and a limited body of research on its use in animals.
- There is significant precedent for the use of a 6 month quarantine period following rabies exposure due to the variable incubation period of the disease. Six months quarantine is the current recommendation of the National Association of State Public Health Veterinarians (NASPHV) (2011)
- As noted by Dr. Fehlner-Gardiner (personal communication, 2014), the incubation period (from a regulatory standpoint) is generally considered to be up to 6 months for <u>unvaccinated animals</u>. There is evidence to suggest that for animals that receive a vaccine but still succumb to the disease there is a shorter incubation period. The phenomenon is known as 'early death'. There appears to be a pathologic component of the immune response to rabies viral infection that plays a role in causing virally induced dysfunction/death. Vaccinated, but non-immunized animals are thought to mount a more vigorous immune response to rabies infection and accelerate the progression of the disease (Prabhakar, 1981). As a result, animals that develop rabies despite prophylaxis (either pre or post exposure) appear to have an incubation period shorter than that of naïve animals.
 - Field experience during canid rabies epizootics in Texas in the 1970s indicated that vaccination may hasten the onset of clinical signs (when disease occurred) (Clark et al, 1981, as cited by Wilson *et al.*, 2010)
 - Historical literature had indicated that although the incubation period for naturally exposed dogs typically ranged from 21 to 60 days, an animal exposed to rabies prior to vaccination would develop rabies within 1 month after vaccination (Johnson, 1965, as cited by Wilson *et al.*, 2010)
- This reduced/minimal incubation period in animals that receive post-exposure vaccination has been substantiated by 30 years' worth of data from Texas:
 - Texas Administrative Code 169.30 states
 - "(a) Not currently vaccinated animals that have been bitten by, directly exposed by physical contact with, or directly exposed to the fresh tissues of a rabid animal shall be: (1) euthanatized; or (2) immediately vaccinated against rabies, placed in confinement for 90 days, and given booster vaccinations during the third and eighth weeks of confinement. For young animals, additional vaccinations may be necessary to ensure that the animal receives at least two vaccinations at or after the age prescribed by the United States Department of Agriculture (USDA) for the vaccine administered.
 - (b) Currently vaccinated animals that have been bitten by, directly exposed by physical contact with, or directly exposed to the fresh tissues of a rabid animal shall

be: (1) *euthanatized; or* (2) *immediately given a booster rabies vaccination and placed in confinement for 45 days."*

- Note, however, that prior to 1988 the protocol involved only one vaccination upon entry into a 6 month quarantine and another 1 month prior to release.
- Clark and Wilson (1996):
 - In Texas, from 1979 to 1987, there were 856 laboratory confirmed cases of rabies in domestic animals. From 1988 to 1994 there were an additional 618 laboratory confirmed positives.
 - From 1979 to 1987 in Texas, 440 dogs, 57 cats, and 216 livestock animals that were previously unvaccinated were exposed to rabies and subsequently received PEP. Exposure to rabies meant exposure to an animal confirmed as rabid by laboratory diagnosis. Of these, one 3 month old puppy and one 6yr old dog developed rabies, with incubation times of 23 and 17 days, respectively (time from exposure to death/euthanasia due to rabies).
 - From 1988 to 1994, 406 dogs, 106 cats, and 120 livestock animals that were previously unvaccinated received PEP. Of these, three dogs developed rabies. Ages were 7 months, 1 year, and 2 years and incubation periods ranged from were 14 to 16 days. PEP was found to be 99.7 and 99.5% effective in these two time periods, respectively.
 - Between 1991 and 1994, there were also 6 animals (5 dogs, 1 cat) that developed rabies while currently vaccinated. These animals were all between 1 and 3 years old. Three of the dogs and the cat had only received one previous rabies vaccine, while the remaining two dogs had received two doses previously. In only one case was a likely exposure date reported **70 days** prior to onset of clinical symptoms.
- Wilson and Clark (2001):
 - From 1995 to 1999, there were 286 confirmed cases of rabies in domestic animals in Texas.
 - During this time, 621 dogs, 71 cats, and 138 livestock animals that were previously unvaccinated were exposed to rabies and subsequently received PEP. The same definition of exposure was used as in the 1996 paper. There were 4 cases of rabies among these animals, all in dogs. Ages were 1 year, 8 months, 8 weeks, and 5 weeks at the time they died/were euthanized due to rabies. In two of these cases, 8 and 9 days elapsed between exposure and administration of the first PEP vaccination. Incubation times ranged from 15 to 25 days.
 - During this same time period, there were also 4 pre-exposure vaccination failures, including a 1 year old horse and 3 dogs with ages of 11 months to 6 years. The horse and two of the dogs had had only one dose of vaccine prior to exposure. In one of the dog cases, the suspected exposure event occurred **17 days** prior to the onset of symptoms, and another was possible exposed by a skunk "one month" prior. The exposure event was not known in the other cases. Only the six year old

dog experienced vaccine failure after having had multiple dose of vaccine. In this time period, there were 286 confirmed cases of rabies in domestic animals.

- Wilson et al. (2010):
 - From 2000 to 2009 there were 523 cases of rabies confirmed in domestic animals in Texas.
 - During this time, 769 dogs, 126 cats, and 119 livestock animals that were previously unvaccinated were exposed to rabies and subsequently received PEP. None of these animals developed rabies. All of these cases involved exposure to a confirmed rabid animal. 295 were 'direct exposures,' meaning that the exposed animal was bitten or otherwise attacked by a rabid animal, attacked or killed the rabid animal, or was found chewing on/playing with the carcass of a rabid animal.
 - During this same time period, there was one pre-exposure vaccine failure in a 15.5 month old cat, 10.5 months after vaccination with a 3 year vaccine. In addition, there was a case of rabies in a dog 2y9m after primary vaccination with a 3yr vaccine, but there was no booster given at 1 yr as per label instructions. The dog had suspected exposure to a rabid skunk and received a booster vaccination 12 days later. It developed rabies and died 8 days after the booster vaccine; total incubation period was **20 days**. There was a similar case in a cat who developed rabies 2y3m after receiving a single dose of a 3 yr vaccine (again no booster was given as per the label).
- The above data from Texas collected over 30 years is observational in nature, but had appropriately defined inclusion criteria in that only animals exposed to confirmed positive animals were included. The data from Texas is unique owing to their high rate of rabies in domestic animals along with a well-established and well documented PEP program. Out of the nine previously unvaccinated animals that developed rabies despite PEP, the longest incubation period observed (from exposure to death/euthanasia due to rabies) was 25 days.
- The CCVO committee was of the opinion that there was inadequate rationale behind the additional doses of vaccine given at 3 and 8 weeks. Note that none of the animals that developed rabies were alive long enough to make it to 8 weeks. Wilson et al. (2010) state "prompt administration of the first rabies vaccine and adherence to the booster schedule are important components for successful PEP. However, future considerations may include whether the booster vaccination on the eighth week is necessary and whether modification to a shorter isolation period is warranted." Prior to 1988, there was only a single dose of vaccine administered after exposure, yet there appears to be fairly minimal difference in the failure rate between the pre and post 1988 Texas data. Furthermore, additional doses of vaccine may increase the likelihood of owner noncompliance.
 - While the committee was in general agreement about excluding the 8th week vaccination from its recommendation, there was considerable discussion about whether to exclude the 3rd week vaccine also. The majority opinion was to exclude the 3rd week vaccine, thus the recommendation was written in its current form.

- Also see the summaries of the Mannikam et al (2008) and Hanlon et al. (2002) experimental studies of rabies PEP under Recommendation #1. All 30 dogs that received PEP vaccination survived in the former study, while in the latter, 5/5 developed rabies on day 9 or 10 after exposure.
- There are several problems associated with using a longer than required quarantine period (i.e. 6 months)
 - Longer quarantines are likely to increase incidents of non-compliance with the quarantine conditions
 - The threat of long quarantines may decrease the likelihood of exposure incidents being reported and properly investigated.
 - Extended periods of isolation from outside contacts (both with other animals and humans) may lead to problems with socialization of pets. This is especially concerning for young animals in critical developmental periods of their lives.
- The Texas Administrative Code utilizes the same post-exposure protocol for all animals, regardless of species. However, in the data presented for 1979 to 2009, there were no reports of ferrets receiving PEP. A literature search was also unable to find any data to support the efficacy of post-exposure vaccination of naïve ferrets. While three, rather than six, months quarantine may be sufficient in naïve ferrets that receive a vaccination within 7 days of exposure, the committee elected not to extrapolate the supporting data from dogs and cats to ferrets. Thus, the recommendation is that naive ferrets be quarantined for a period of six months.
- The Compendium of Animal Rabies Control and Prevention (NASPHV, 2011) states that, "because a rapid anamnestic response is expected, an animal is considered currently vaccinated immediately after a booster vaccination (34)."
- Moore et al. (2015) conducted a study to evaluate the non-inferiority of anamnestic antibody responses to rabies vaccination in dogs and cats with out-of-date compared to current vaccination status. An anti-rabies antibody titre was measured in serum collected immediately prior to administration of a rabies vaccination and then again between 5 and 15 days later. For the 19 dogs with out-of date vaccination status, compared to 55 that were current, the proportional hazards ratio was 0.53 (95% CI 0.20-1.12, H_0 : HR<1.25), indicating a non-inferior anamnestic response in out of date animals. There were 7 cats with current and 26 with out-of-date vaccine status included in the study. At follow-up sampling, >80% of cats in each group had titres >12 IU/ml (upper limit of quantification), and all were >2 IU/ml. The low number of cats and high proportion that exceeded the upper limit of quantification precluded proportional hazards analysis. Nine dogs with current and 5 with out-of-date vaccine status had titres <0.5 IU/ml at baseline, but all were >0.5 IU/ml at follow-up. One current and one out-of date cat had baseline titres <0.5 IU/ml, both were >12 IU/ml at follow-up. Based on the evidence they present, the authors recommend that animals with out-ofdate rabies vaccinations be treated in the same manner as those with current vaccination following a rabies exposure event. Specifically, they should receive a booster vaccination immediately after exposure, maintained under owner control, and observed for 45 days with no contact restrictions.

- The serological data from this study suggests that the immune memory as it relates to humoral immunity is similar in animals with out-of date and current rabies vaccine status. However, sample size was limited and the authors do not discuss whether other aspects of the immune response might differ between the groups. The relative importance of humoral versus cell mediated immunity in protection from rabies challenge is not fully understood. A comprehensive investigation would necessarily include a challenge study, however, such an undertaking would suffer from logistic and financial challenges that may well be insurmountable. They type of data presented in this paper may represent the best evidence available to make decisions about the post exposure management of animals with out-of-date vaccine status.
- The committee discussed whether the conclusions of this paper should be adopted into the recommendations. Some members were prepared to do so, and indicated that they will act accordingly in their jurisdictions going forwards. However, some committee members were uncomfortable with this course for various reasons, including the serological nature of the study, the relatively small sample size, and the limited number of animals that were substantially overdue for revaccination. It was questioned whether the recommendation would apply equally to an animal one year overdue for a booster versus one that is ten years overdue, and if not, where we should place a cut off and why? It was decided that the study does not yet lend itself to a broad recommendation. Instead, it should be interpreted relative to the circumstances of an individual situation. The recommendation was thus maintained as written.

Recommendation #4: Conditions of a Rabies Quarantine for a Companion Animal

Most rabies quarantines are carried out on the owners' property. The committee advises that the following minimum conditions apply to all such quarantines of companion animals. Should the owner(s) feel that these conditions cannot be met, consideration should be given to carrying out the quarantine at an alternate location, such as a kennel or veterinary clinic.

In situations where quarantine is warranted, it is prudent to inform the relevant public health authorities in a timely manner.

While not all provinces/territories will utilize legally enforceable quarantines, the conditions specified can be equally employed as recommendations provided to the owners' of exposed animals.

Note that the sub-bullets under conditions 2 and 3 have been prefaced by 'should' rather than 'must'. While these conditions represent the desired state, practical considerations in some situations may make owner compliance unsustainable.

Rabies Vaccination:

1. The Subject Animal must be vaccinated as per Recommendations #1-3.

- 2. All other animals in the household must also be brought/kept up to date on rabies vaccination as per the manufacturer's recommendations.
 - a. Animals not yet eligible for rabies vaccination according to label directions (i.e. <12 weeks of age), or not currently vaccinated, should not have contact with the subject animal. Contact may be permitted following an appropriate interval after vaccination of the non-exposed animal, which must be determined on a case-by-case basis based on total number of previous rabies vaccinations (if any), duration of immunity of rabies vaccine given (1 versus 3 years), duration since last rabies vaccination, and overall health status of the animal.</p>

Control/Limit Human Exposure to the Animal:

- 3. The Subject Animal must not have direct contact with persons outside the permanent members of the household.
 - a. A primary care giver, and an alternate person if necessary, should be designated to care for the Subject Animal. Ideally, other persons in the household should not have contact with the animal.
- 4. The Subject Animal must not be allowed to roam freely outdoors at any time.
- 5. The Subject Animal must not be left unsupervised for extended periods in a building/room/enclosure from which escape may reasonably be considered possible. Reasonable precautions must also be taken (if necessary) to prevent accidental escape of the Subject Animal when the building/room/enclosure is entered by a person.
- 6. The Subject Animal may leave the property at which the quarantine is carried out for the purposes of basic exercise and necessary veterinary care, but must be kept muzzled, on-leash, and under control at all times, or in a securely closed pet carrier.

Record Keeping:

7. If accidental contact occurs between the subject animal and persons or animals other than the permanent household members, the name and contact information for these parties, as well as the type of contact that occurred, must be recorded by the owner or caregiver and retained for a minimum of 2 weeks after the human contact.

Reporting:

- 8. Any clinical signs of disease or changes in behaviour must be reported to the appropriate authorities.
- 9. If the subject animal bites a human, the exposure must be reported to the appropriate provincial/territorial health authorities.

Recommendation #5: Vaccination of an Animal during a Public Health Observation Period

Under normal circumstances, when an animal is under a public health observation period following a bite to a human, it should not be vaccinated. Uncommonly, an animal both is potentially exposed to rabies and bites a human. In these infrequent circumstances, rabies vaccination should be administered to the animal immediately, as in Recommendation #1, in consultation with relevant public health authorities.

Considerations

- Following a bite from a domestic animal to a human, the animal is commonly observed for symptoms of rabies for several days. This can be an accurate method to rule out rabies transmission from the offending animal. For example, cats/dogs will not shed rabies virus in the saliva more than 10 days prior to showing overt clinical signs and/or dying of the disease. In some situations, an animal is both potentially exposed to rabies and bites a human. For instance, a dog with a bite wound from a wild animal that then bites a person attempting to assess/treat the wound. While this situation suggests the bite should be considered 'provoked' and thus the risk of rabies very low, a 10 day observation is often still employed. Under normal circumstances, animals should not be vaccinated while under observation in order to avoid confusing rare adverse reactions with clinical signs of rabies. If such a reaction occurred, post-exposure prophylaxis would likely be initiated in the bitten human and the animal would likely be euthanized and tested for rabies (for which it would be negative). Therefore the negative outcomes from confusing a vaccine reaction with symptoms of rabies would be unnecessary euthanasia of the animal and the expense and risk associated with human PEP. As the likelihood of confusing a vaccine reaction with symptoms of rabies is considered very low, the committee deems this recommendation to be an appropriate balance of risks.
- The Compendium of Animal Rabies Control and Prevention (NASPHV, 2011, Section 6 (a)) states that, "administration of rabies vaccine to the animal is not recommended during the observation period to avoid confusing signs of rabies with rare adverse reactions (13)."
- This reference refers to post-marketing surveillance data reported by Frana et al. (2008). The following table is taken from this article. During the three year study period (April 1, 2003 to March 31, 2007), the US Centre for Veterinary Biologics received 217 adverse effects reports in dogs in which rabies vaccine was considered "possibly related". In ~72%, the rabies vaccine was administered alongside one or more additional vaccines or other medical products. It can be seen by evaluation of the reactions in the table that the majority would be very unlikely to be confused with clinical signs of rabies.

Clinical terms used to describe adverse events	No. of dogs (%)*		
Vomiting	61 (28.1)		
Facial swelling	57 (26.3)		
Injection site swelling or lump	42 (19.4)		
Lethargy	26 (12.0)		
Urticaria	22 (10.1)		
Circulatory shock	18 (8.3)		
Injection site pain	16 (7.4)		
Pruritus	16 (7.4)		
Injection site alopecia or hair loss	15 (6.9)		
Death	12 (5.5)		
Lack of consciousness	12 (5.5)		
Diarrhea	10 (4.6)		
Hypersensitivity (not specified)	10 (4.6)		
Anorexia	9 (4.1)		
Fever	9 (4.1)		
Anaphylaxis	6 (2.8)		
Ataxia	6 (2.8)		
Lameness	6 (2.8)		
General signs of pain	5 (2.3)		
Hyperactivity	5 (2.3)		
Injection site scab or crust	5 (2.3)		
Muscle tremor	5 (2.3)		
Tachycardia	5 (2.3)		
Thrombocytopenia	5 (2.3)		
*Based on 217 adverse event reports.			

Table 1—Clinical terms used to describe possibly related adverse events in dogs vaccinated against rabies and reported to the USDA CVB from April 1, 2004, through March 31, 2007.

• Dr. Fehlner-Gardiner also offered the following perspective (personal communication, 2014) (Note that the web address provided in the text was updated on 19 Sept 2014)):

In the above scenario, the predominant rabies risk to the person is from the potential for transfer of saliva or neural tissue from the wild animal (perhaps around the mouth of the dog that fought with the rabid animal) into the wound received from the biting dog, or into other cuts or mucous membranes. However, I assume by asking this question, you are postulating that the biting dog may also have rabies.

There are three possible outcomes here:

1) The wild animal tests positive for rabies. The medical practitioner will have to decide whether to administer PEP to the person due to a possible exposure via the dog (acting as a "fomite", if you will). I expect most MOH would err on the side of caution and give PEP (consider the recent case of laboratory-confirmed raccoon rabies in New Brunswick where two family dogs were potentially exposed because they were seen interacting with the raccoon [see: <u>http://www.healthywildlife.ca/rabies-in-a-raccoon-in-new-brunswick/</u>]. Afterwards the dogs licked popsicles being eaten by the children; the children were given PEP). The dog would be subject to whatever disease control measures are required depending on its vaccination status at the time of the exposure to the wild animal. The 10d observation period does not apply in this scenario because due to the potential risk to the human from the rabid wild animal, PEP

has likely been given. Therefore, even in the unlikely event that the dog was also rabid at the same time it fought with the rabid animal, the person bitten by the dog is still protected by PEP.

2) The wild animal tests negative for rabies. In this case, one has to consider the risk that the biting dog may have rabies. In this case, the 10 d observation period would be applicable, provided the dog is otherwise healthy and the case history is not suggestive of rabies. There is no concern about exceeding the 7d "window" for revaccination of the dog, because the dog was not at risk of rabies from the wild animal.

3) The wild animal is unavailable for testing. In this case the relevant authorities need to carefully examine the circumstances surrounding the event and tailor the response accordingly. Again, I would expect most MOH to err on the side of caution and treat the event as in outcome (1), but depending on the type of wildlife involved (e.g. rodent vs carnivore reservoir species), local epizootiology, etc., the event may be treated as in outcome (2). I think it important to keep in mind that post-exposure management guidelines are guidelines, they are not hard and fast rules that can never be broken. At all times the professional judgment of medical and veterinary professionals should take precedence in the determination of disease control measures for both animals and people.

Recommendation #6: Quarantine of Livestock Species Regardless of Rabies Vaccination Status

All livestock species, regardless of vaccination status, that are exposed or potentially exposed to rabies should be quarantined for 60 days from the time of exposure, if known, or 40 days from the time of the first diagnosis if the index case is within the herd/group.

While specific evidence is lacking to support the use of post-exposure rabies vaccination in livestock species, evidence does support this practice in dogs and cats. Post-exposure vaccination of livestock species immediately following an exposure event may similarly reduce the risk of these animals developing rabies.

The conditions of livestock quarantines should be set on a case-by-case basis with consideration given to the type of livestock and intended use, with the primary goals of minimizing direct contact with people and other animals outside of the quarantined group, and ensuring handler safety should the animal(s) develop neurological disease.

For the purposes of this recommendation, horses, donkeys, and their hybrid offspring are considered to be "livestock species".

Considerations

• Experimental and observational evidence suggests these time periods are sufficiently long to allow the vast majority of infected animals to develop clinical signs of rabies. (The following, including the species specific references, were provided by Dr. Fehlner-Gardiner, personal communication 2014).

- In general, incubation periods for the experimental infections ranged from 2-6 weeks. In Pépin et al. (1984) it is noted that the incubation period they observed following experimental infection of cattle (average of 19 days) was rarely observed in the field in France (but only a personal communication is cited). However, they do reference another study where three bovines succumbed after 17, 19 and 26 days following a bite from a rabid animal. As well, they provide data reported from another study (by Zundel, reported in Fermi, 1950 "La Rabbia") on 579 cases of bovine rabies caused by the dog variant rabies virus, in which 5% had an incubation period of <15 d, 23% 15-30 d, 39% 40-45 d, 13% 45-60 d, 17 % 3-6 mo, 1% longer than 6 mo. Eighty-two percent of the cattle had incubation periods falling within a 60d period.
- \circ Cattle
 - Martell MA, Di Batalla C, Baer GM, Benignos y Acuna J. 1974. Experimental bovine paralytic rabies – "derringue". Vet. Rec. 95:527-530 (and references therein). Incubation period of 15-43 d, average 15.1 d, experimental infection.
 - Hudson LC, Weinstock D, Jordan T, Bold-Fletcher NO. 1996. Clinical features of experimentally inducted rabies in cattle and sheep. J. Vet. Med 43:85-95 (and references therein). Incubation period in non-vaccinated cattle 12-15 d, average 12.5 d. Incubation period in vaccinated cattle 9-28 d, average 18.3 d; experimental infections.
 - Blancou J, Pépin M, Soulebot JP, Brun A. 1984. Vaccination des bovins contre la rage. Cinétique des anticorps, résistance à l'épreuve trois ans après vaccination. Ann. Rech. Vét. 15 :543-547. Incubation period 19-23d, experimental infection.
 - Pépin M, Blancou J, Aubert MFA. 1984. Rage expérimentale des bovins: sensibilité, syptômes, réactions immunitaires humorales, lésions et excrétion du virus. Ann. Rech. Vét. 15 :325-333 (and reference therein). Incubation period 2-4 wks, 19 d average, experimental infection.
 - Baer GM. Vampire bat and bovine paralytic rabies. *In* The Natural History of Rabies, 2nd Edition. GM Baer, *ed.* 1991. CRC Press. Boca Raton. p 395. (and references therein). In this chapter there is a small section on incubation period for bovine paralytic rabies. Baer cites several publications (most in Spanish or Portuguese) indicating that the incubation period in naturally infected animals varies from 1-2 months. Another study cited by Baer, in which cattle were experimentally infected with vampire bat variant rabies virus, cattle had incubation periods of 24-154 d, whereas two other studies had incubation periods of 165, 223, 354 (Am. J. Epidemiology 1970 91:203) and 611 days (cited as a personal communication). Baer makes the comments that these incubation periods are unusually long and may reflect "the site and route of inoculation or inherent characteristics of that virus strain in cattle".

o Sheep

 Hudson LC, Weinstock D, Jordan T, Bold-Fletcher NO. 1996. Clinical features of experimentally inducted rabies in cattle and sheep. J. Vet. Med 43:85-95 (and references therein). Incubation period 9-11d, average 10d, experimental infection.

- Soria Baltazar R, Aubert MFA, Blancou J et al. 1986. Rage expérimentale des ovins: sensibilité, symptômes, résponse immunitaire humorale, lésions et exrétion du virus. Revue Méd. Vét.137:847-856 (and references therein). Incubation period 15-19d, experimental infection.
- o Swine
 - Corner AH, Beauregard M, Mitchell HK. 1960. Rabies in piglets. Can. J. Comp. Med. Vet. Sci. 24:364-365. Natural infections – minimum incubation period was 12 d (piglet), maximum was 20 d (sow).
 - Morehouse LG, Kintner, LD, Nelson SL. 1968. Rabies in swine. J. Am. Vet. Med. Assoc. 153:57-64. Natural infections; exact incubation period not determined as date of exposure unknown, but swine died at a rate of approx. 2 per week for a period of 2 months.
- Hudson *et al.* (1996) performed a rabies vaccine trial in horses. Among the test animals, 12 naïve and 9 test-vaccinated horses developed clinical signs. The average incubation period in these animals was 12.3 days, with naïve animals having a significantly shorter incubation period than vaccinates. Muzzle tremor was the most common sign of disease (81%), followed by pharyngeal spasm or paresis (71%, ataxia or paresis (71%), and lethargy or somnolence (71%). Signs associated with furious rabies were seen in 43% of animals. The authors note that the results of this trial do not reflect on the efficacy of commercially licensed equine rabies vaccines.
- If the index case is within the herd/group and the time of exposure is not known, 40 days quarantine is considered sufficient because herbivore to herbivore transmission of rabies is thought to be quite rare. If multiple animals are infected with rabies in the same herd, it is likely due to exposure to the same rabid vector, thus a portion of the 60d quarantine otherwise imposed will have already elapsed.
- These recommendations match those in the CFIA Rabies Manual of Procedures (2011) Section 6.4.1.
- Dr. Kim Knight-Picketts (Disease Control Specialist with the CFIA) provided the following comments (personal communication with Dr. Maureen Anderson, OMAFRA):
 - "The livestock 40/60 day quarantine was introduced early on (in the 70's or earlier) in the rabies program to ensure that owners of livestock would cooperate and report rabies cases without incurring an onerous 6 month quarantine (or euthanasia) which could negatively affect their running their business (the rabies indemnity also helped increase cooperation).
 - The over 50 years of applying these reduced quarantines in livestock without any major issues appears to back up the assumption that these quarantines are adequate and practical (CFIA-AG Canada may have adapted the U.S. quarantine periods for livestock many years ago). Increasing these quarantine periods or requiring euthanasia of exposed livestock herds may lead to confrontations and very uncooperative owners."
- The 2011 Compendium of Animal Rabies Control and Prevention (NASPHV, 2011) advocates a 6 month quarantine for exposed livestock (or immediate euthanasia) (Section 5b 1). The Compendium also advises that, "Multiple rabid animals in a herd or herbivore-to-herbivore transmission are uncommon (48); therefore, restricting the rest of the herd if a single animal has been exposed to or infected by rabies is usually not necessary" (Section 5.b(3))

 The same recommendation for a 6 month quarantine was made by the Rabies Committee of the Conference of Public Health Veterinarians, the AVMA Council of Public Health and Regulatory Veterinary Medicine, and the Rabies Control Unit, National Communicable Disease Center, USPHS in 1970 (Sikes RK. Guidelines for Rabies Control. Am. J. Public Health 60:1133-1138). Various US state recommendations differ; some advocate the 6 month quarantine, others 3 month, others leave it to the judgment of state veterinarians.

#6 a. Slaughter of livestock animals following rabies exposure.

Livestock animals that are not exhibiting any clinical abnormalities consistent with rabies can be slaughtered for human consumption under standard procedures within 7 days of exposure to rabies. After this time, animals should not be slaughtered for human consumption until after completion of the appropriate quarantine period.

- This recommendation is consistent with the 2011 CFIA Rabies Manual of Procedures Section 6.4.1.1.
- Animals that must be culled from a herd during quarantine, and greater than 7 days after exposure, must be euthanized and disposed of appropriately, but should not enter the human food chain. While thorough cooking of rabies infected tissues will inactivate the virus, butchering activities and consumption of uncooked (or possibly undercooked) tissues may pose a risk for rabies transmission.
- 2011 Compendium of Animal Rabies Control and Prevention (NASPHV, 2011, Section 5.b(4)): "Handling and consumption of tissues from exposed animals might carry a risk for rabies transmission. Risk factors depend in part on the site(s) of exposure, amount of virus present, severity of wounds, and whether sufficient contaminated tissue has been excised. If an exposed animal is to be custom or home-slaughtered for consumption, it should be done immediately after exposure, and all tissues should be cooked thoroughly. Persons handling exposed animals, carcasses, and tissues should use barrier precautions (49,50). Historically, federal guidelines for meat inspectors required that any animal known to have been exposed to rabies within 8 months be rejected for slaughter (51). USDA Food and Inspection Service (FSIS) and state meat inspectors should be notified if such exposures occur in food animals before slaughter. Rabies virus is widely distributed in tissues of rabid animals (52-54). Tissues and products from a rabid animal should not be used for human or animal consumption (55,56) or transplantation (57). Pasteurization and cooking will inactivate rabies virus (58); therefore, inadvertently drinking pasteurized milk or eating thoroughly cooked animal products does not constitute a rabies exposure."
- WHO Frequently Asked Questions on Rabies (2013):
 - "There are no evidence-based reports of human rabies occurring due to consumption of milk. Individuals or professionals who slaughter rabies infected animals and handle brain and other infected material may be at risk, but there are no human cases due to consumption of cooked meat."
 - "Q 18: Can consumption of meat from an infected animal transmit rabies? The consumption of raw meat from an infected animal requires PEP. Cooked meat does not transmit rabies; however, it is not advisable to consume meat from an infected animal."

#6 b. Utilization of Milk from Dairy Animals Under Quarantine for Rabies Exposure

Milk from quarantined animals can continue to enter standard processing channels but should not be used in raw milk products.

- The known pathology and progression of rabies virus make it extremely unlikely, if not impossible, for rabies to be shed into the milk. If rabies virus were to be shed into milk, it would be expected to be inactivated by standard pasteurization techniques.
- WHO FAQs on Rabies (2013): "Q 17: Is PEP necessary if milk or milk products from an infected animal are consumed? No. There is no laboratory or epidemiological evidence that the consumption of milk or milk products from rabid animals transmits the disease. However, it is not advisable to consume milk from rabid animals."
- 2011 Compendium of Animal Rabies Control and Prevention (NASPHV, 2011): pg 2 "CDC's Rabies Laboratory is attempting to collect specimens to evaluate the potential for rabies transmission via milk from lactating animals. Over the past 15 years, CDC has received mammary tissue and unpasteurized milk from approximately 1 rabid cow per year. To date, no rabies virus antigen or nucleic acids have been detected." Section 5.b(4) "Pasteurization and cooking will inactivate rabies virus (58); therefore, inadvertently drinking pasteurized milk or eating thoroughly cooked animal products does not constitute a rabies exposure."
- CFIA MOP Section 7.6.2.1: "Milking procedures can be continued in rabies exposure situations involving lactating dairy animals (cattle, goats, sheep, etc.). To date, rabies virus has not been detected in milk."
- While there is no risk to the public from consuming pasteurized milk from exposed animals, the committee considers it prudent to inform the relevant public health authorities of the situation in a timely manner.

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	Animal Exposed and Vaccine Status	Committee Recommendation	CFIA Rabies Manual of Procedures (2011)
1	All animals (dogs/cats/ferrets) exposed or potential exposure to rabies	Vaccinate or revaccinate within 7 days of exposure.	Vaccinate or re-vaccinate. Suggested to be within 7 days of exposure.
2	Dogs/Cats/Ferrets current on rabies vaccination	Revaccinate within 7 days, no quarantine. Owner education and follow-up should still occur. If not revaccinated, quarantine 3 months.	Revaccinate and keep under CFIA-controlled owner observation for 45 days. If not revaccinated, quarantine 3 months
3	Dogs/cats/ferrets not currently vaccinated for rabies	Vaccinate within 7 days and quarantine for: 3 months for dogs and cats; 6 months for ferrets. Consider a second vaccination in the 3 rd week following exposure. If not vaccinated within 7 days, quarantine for 6 months.	Vaccinate and quarantine for 6 months.
4	Conditions of a Rabies Quarantine for a Companion Animal (Only the primary conditions on the exposed animal are listed here. See the full document for additional information.)	 Animal only to have contact with immediate members of the household. (Limiting human contact to a designated primary care giver is desirable). All other animals in household brought/kept up to date on rabies vaccine. No contact with animals not residing in the same household. (Avoiding contact with other animals in household until an appropriate duration after vaccination is desirable.) Must not roam freely or be kept in a manner that could easily allow escape. Must take steps to prevent accidental escape when doors are opened. Animal may leave the property for veterinary care and basic exercise, but must be kept on leash, muzzled, and under control, or in a securely closed pet carrier. 	 Subject animal to be isolated, preferably double gated No contact with any humans or other animals, other than the designated primary care giver. Access to outdoors only if kept leashed and in a fenced area that is part of the premises used for the quarantine. Must not leave the premises of the quarantine unless licenced to do so. If veterinary care is needed, CFIA vet must be notified and should visit the premise to evaluate the situation, notify the private veterinarian of quarantine conditions, and licence the animal to and from the clinic.
5	Vaccination of an Animal during a Public Health Observation Period	Under normal circumstances, when an animal is under a public health observation period following a bite to a human, it should not be vaccinated. Uncommonly, an animal both is potentially exposed to rabies and bites a human. In these infrequent circumstances, rabies vaccination should be administered to the animal immediately (as in #1), in consultation with relevant public health authorities.	Not addressed.
6	Livestock animals regardless of rabies vaccination status	Quarantine for 60 days from the time of exposure if known, or 40 days from the time of the first diagnosis if the index case is within the herd/group. Consider post-exposure rabies vaccination.	Quarantine for 60 days from the time of exposure if known, or 40 days from the time of the first diagnosis if the index case is within the herd/group.
6a	Slaughter of livestock animals following rabies exposure	Can be slaughtered for human consumption under standard procedures within 7 days of exposure.	Can be slaughtered for human consumption under standard procedures within 7 days of exposure.
6b	Utilization of milk from dairy animals under quarantine for rabies exposure	Milk from quarantined animals can continue to enter standard processing channels but should not be used in raw milk products.	Milking procedures can be continued in rabies exposure situations involving lactating dairy animals.

Appendix 1: Quick Reference Comparison Chart of Committee Recommendations versus CFIA Manual of Procedures (2011)