# Chronic Wasting Disease Alternative Disease Control Options –Council of Chief Veterinary Officers

## Executive Summary:

Chronic Wasting Disease (CWD) represents a serious threat to free-ranging and farmed cervids* and their associated economies. It is a disease of national importance with concerns regarding animal health, wildlife population sustainability, and food safety and security, particularly for rural Canadians, First Nations, Inuit, and Métis people.

This document was prepared by a working group of the Canadian Council of Chief Veterinary Officers (CCVO) in response to concerns regarding changes to national CWD programming. The intent is to provide regulators with supplemental or alternative options for CWD management and associated benefits and challenges. However, it is important to recognize that this work was done under an extremely limited timeline and as a result, the review does not delve into great detail and engagement of other important stakeholders was not attempted.

The Canadian Food Inspection Agency (CFIA) has spent upwards of $70 million of taxpayer money on programs designed to eradicate the disease, but the disease continues to be detected in farmed cervids and the prevalence of CWD in the wild continues to increase. The prion load in the environment has raised concerns about potential impacts for other industries (e.g. grain and swine producers) that may not have been part of previous task forces or discussions. Management of the disease is incredibly challenging and cannot be attained by any one government agency.

While there is justification to shift from a management goal of eradication to a management goal of control, the proposed option tabled by the CFIA could result in significantly increased risk for spread of the disease to areas where the disease has not been previously detected. There are also many stakeholders that should be involved in collaborative decision making in a One Health context.

There have been more recent scientific advances and general agreement to evaluate progress on recommendations made in *A Proposal for Canada's National Chronic Wasting Disease Control Strategy (2011*). The goal of this document is not to drive decision making regarding CWD management, but to emphasize the importance of this disease nationally with the need for a collaborative, national approach and provide some options for consideration.

Despite the challenges with timelines, the CCVO identified one option that would mitigate concerns associated with the CFIA's proposed approach. The group recommends implementation of an aggressive response to detections of CWD in areas or provinces/territories where the disease has not been previously detected, including an on-farm and wildlife response.

In the longer term, it is the hope of the CCVO that appropriate provincial, territorial, and indigenous governments, not necessarily those limited to currently affected areas, are involved in science-based decision-making processes moving forward. In addition, the CCVO hopes to continue work on longer term options as well as aligning this work with the information developed in the jurisdictional scan

(Appendix 1). We thank all contributors to this document and acknowledge the persistent efforts of those who have been involved in CWD management to date.

*For the purposes of this document, "cervid" includes species that have been determined to be naturally susceptible to the development of CWD via experimental infection (fallow deer are not included) or are considered to be susceptible based upon studies in very closely related species (caribou are considered susceptible based upon studies in reindeer).

## Purpose:

On June 30, 2017, the CFIA announced updates to the federal control program for CWD in farmed cervids. The changes, initially to be implemented January 1, 2018, entail the CFIA only offering their response measures to producers enrolled in a Voluntary Herd Certification Program (VHCP). The CFIA's initial response will include placement of movement controls and tracing to determine whether there is any involvement of the VHCP compartment. Offer of further disease control activities such as ordering destruction and disposal of animals, and providing compensation to producers will be limited to those who are successfully enrolled in the VHCP. Cervid producers not enrolled or meeting the requirements of the VHCP or that refuse CFIA control measures will not be subject to federal CWD response.

The Regulatory Assistant Deputy Ministers (ADM) Committee recommended to delay implementation of the VHCP and the CWD Control Program changes to April 1, 2018 and allow the Council of Chief Veterinary Officers (CCVO) to develop an options paper or white paper with alternative or supplemental disease control options for CWD. Coincidentally, there was an expressed need to delay the implementation date to allow Regional Administrators of the VHCP to implement the changes required for the new program. Ultimately, the implementation date of the new VHCP and disease control changes was delayed to April 1, 2018.

## Background:

**Introduction**

Chronic wasting disease is an invariably fatal, contagious disease of white-tailed deer, mule deer, elk, reindeer, moose and relatives (cervids). The disease is similar to bovine spongiform encephalopathy (BSE), which has caused lasting economic impacts on the Canadian cattle industry. While the link between the consumption of BSE-contaminated materials and human disease was proven, the potential for humans to develop disease from the consumption of CWD-contaminated meat remains unclear. The causative agent, a prion, is a misfolded protein aggregate that causes progressive neurodegenerative disease. The misfolded nature of the prion makes it nearly impossible to break down and the prion will remain infective in the environment for extended periods of time, which can result in new cases in other animals.

In 2011, a proposal for *Canada's National Chronic Wasting Disease Strategy* was developed with the following six goals:

1. Prevention of further expansion of CWD to new locations or species and the prevention of emergence of new forms or variants of CWD
2. Effective surveillance for CWD
3. Planned management and response program

4. Research in support of CWD management
5. Education and Training
6. Communication and Consultation

After more than 5 years from the proposal of the strategy, the disease prevalence and geographic spread have increased with negligible progress in these six goals across the country. Management of CWD is challenging, particularly once it is found in wild cervids, and the CFIA has been reviewing the effectiveness of the national program.

Due to the limited effect on geographic spread and prevalence in wild and farmed cervids, CFIA has proposed changes to the national CWD control program by moving from a goal of eradication of the disease from domestic cervids to one of control within the VHCP compartment. Eradication of CWD is no longer seen as an option in farmed cervids in areas where eradication of the disease in wildlife is unattainable. However, with no treatment or vaccine currently available for this disease, prevention of spread to new areas should remain a key objective.

**Prion Diseases and Pathogenesis**

Chronic wasting disease is caused by a prion, a variant of a host protein that is the infectious particle that causes transmissible spongiform encephalopathies (TSE's). The prion is a misfolded protein, often abbreviated as $PrP^{Sc}$ that can convert normal host proteins ($PrP^{C}$) into abnormal versions that accumulate and disrupt cellular functions (Sigurdson 2008). The resulting lesions include neuronal vacuolation (spongiform vacuolar changes in the brain) (Williams and Young, 1993). The time between infection to the development of clinical disease (incubation period) can be prolonged and infection is invariably fatal. Other TSE's include scrapie in sheep, BSE in cattle (mad cow disease), and Creutzfeldt-Jakob disease (CJD) in humans. A variant of CJD (v-CJD) has been linked with consumption of BSE-contaminated meat by humans (Aguzzi and Heikenwalder 2006). In general, TSE's tend to target the brain and other nervous tissue, but replication can occur at many sites throughout the body, particularly associated with the lymphoreticular system (a network of tissues and vessels associated with the immune system).

**Transmission**

The $PrP^{Sc}$ prion can be found and be infective in many non-neuronal organs including meat (Angers et al. 2006), saliva and blood (Mathiason et al. 2006), and feces and urine (Hayley et al. 2009). The CWD prion can be transmitted vertically from dam to offspring (Nalls et al. 2013). Nasal secretions and milk are other likely routes of transmission (Gough and Maddison 2010). Although the potential for transmission of CWD prion in semen has not been specifically investigated, semen transmission has been demonstrated with scrapie and it is considered possible (Rubenstein et al. 2012). Prions have also been detected in elk velvet (Napier et al. 2009). Infected animals likely shed prions for the duration of infection, which can be prolonged in many cases (Tamgüney et al. 2009).

Oral transmission is thought to be the predominant form of transmission and the most likely route of human exposure through the consumption of CWD-positive meat (Saunders et al. 2012). However, prion transmission is possible by blood transfusions and organ transplants, which could serve as alternative routes of human exposure and impact health programs (Llewelyn et al. 2004). Horizontal transmission between cervids is thought to play a large role in CWD epidemiology, but environmental reservoirs in water (via adherence to particulates), soil, forage or other fomites contaminated by carcasses, urine or feces of CWD-positive animals could act as sources of infection and remain infective for years (Miller et

al. 2004). Recent publications on soil and plant uptake will be further discussed within the subsection on recent research findings.

**History and Possible Origin**

Chronic wasting disease was first documented in the 1960s by animal health professionals in farmed mule deer that developed a wasting syndrome prior to death at a Colorado research facility (Williams and Young 1980). Although the origin is unknown, scientists speculate that CWD could have been present prior to the 1960s and been undetected (Williams and Miller 2003). Challenges associated with surveillance programs could underestimate the actual distribution of the prion on the landscape (Miller and Fischer 2016). It is unclear if all events originated from one source (e.g. the Colorado research herd) or if there have been multiple 'origin' events (Williams and Young 1992; Williams and Miller 2003). Spontaneous origin of atypical forms of BSE and scrapie has been documented (Baron et al. 2011) and is suspected to be the cause of an atypical form of CWD in aged Norwegian moose. There is long-standing speculation that CWD originated from scrapie in domestic sheep, but this has not been proven and other mechanisms of origin have not been completely ruled out (Gossert et al. 2005; Greenlee et al. 2011).

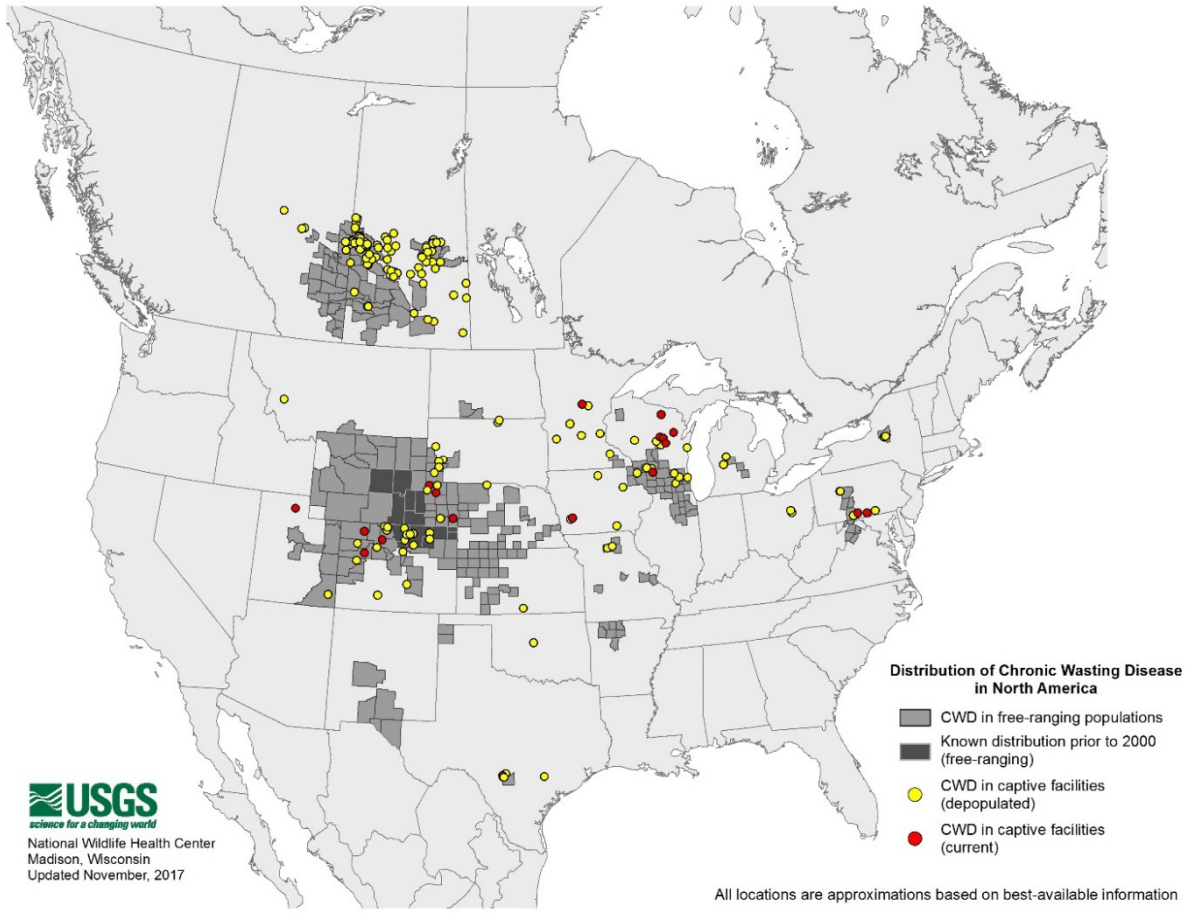
**Affected Hosts**

Chronic wasting disease causes natural disease in members of the Cervidae family and has been detected in free-ranging Rocky Mountain elk, mule deer, white-tailed deer, moose, and reindeer (Miller and Fischer 2016). Species from farmed commercial collections have included elk, mule deer, and white-tailed deer (U. S. Geological Survey 2016). Experimental infections have resulted in infection and disease (development of clinical signs and pathologic lesions consistent with CWD) in elk (Hamir et al. 2006a), muntjac (Napier et al. 2009), red deer (Balachandran et al. 2010), and other relatives. Fallow deer were not able to develop disease after being co-housed with infected mule deer in a contaminated paddock for 6 years (Rhyan et al. 2011). Reindeer have been experimentally infected with CWD prion and there are active research projects investigating potential genetic-based resistance to the development of disease, but this remains an area of uncertainty as the experimental animals could have been euthanized prior to the development of disease (Mitchell et al. 2012). The concept of multiple "passages" has increased complexity in attempts to understand species barriers (i.e. when a prion is fed to transgenic laboratory mice and then infectious material from those mice is fed to subsequent mice), the disease-causing properties of the prion could be altered (Telling 2011). Experimental studies attempting to understand species barriers with CWD in non-cervids have had mixed results. The following species appear to be resistant to the development of disease: ferrets, mink, and non-transgenic mice (Bartz et al., 1998; Browning et al., 2004; Marsh et al., 2005; Sigurdson, 2008). Species that developed disease in an experimental setting included: voles, white-footed mice, deer mice, cats, raccoons, squirrel monkeys, and swine (Heisey et al. 2010; Di Bari et al., 2013; Mathiason et al., 2013; Race et al., 2014; Moore et al., 2017). Many of the studies on experimental infections included methods of infection that are not considered to be natural modes of infection (e.g. direct injection into the brain or abdomen) so in many cases, interpretation of the implications of the results of these studies can be challenging. Experimental infections that attempted to inoculate cattle and sheep were variably effective (Hamir et al. 2005; 2006b) and implications for natural infections are unknown. Cattle that have been co-grazed with CWD-infected cervids have not developed disease (Sigurdson, C. J. 2008).

**Current Distribution of Detected Cases**

A recent map is provided as Figure 1. Additional regional maps of cases in wild deer in Alberta can be found at: http://aep.alberta.ca/fish-wildlife/fishing-hunting-trapping/hunting-alberta/chronic-wasting-disease.aspx and in wild deer from Saskatchewan can be found at: http://www.cwhc-rcsf.ca/surveillance_data_cwd.php. The disease has been found in 24 American states (Arkansas, Colorado, Wyoming, South Dakota, Oklahoma, Nebraska, Montana, Wisconsin, New Mexico, Minnesota, Illinois, Utah, New York, West Virginia, Kansas, Michigan, Virginia, Missouri, North Dakota, Maryland, Texas, Iowa, Pennsylvania and Ohio) and three Canadian provinces (Alberta, Saskatchewan, and Ontario). The disease in Ontario was found in a retrospective study of cases from the Toronto Zoo, with the last animal detected in 1981 and no additional cases diagnosed since (Dubé et al. 2006). Farmed elk infected with CWD were exported from Canada to South Korea (Kim et al. 2005) where the disease has since been detected in additional species including sika deer. More recently, the disease has been detected in 2016 in a free-ranging herd of reindeer and two free-ranging moose in Norway (EFSA Panel on Biological Hazards 2017).

**Figure 1. Distribution of Chronic Wasting Disease in North America (USGS 2017).**




**For an updated map see: https://www.usgs.gov/centers/nwhc/maps**

**Risk Factors for Environmental Persistence and Spread**

Both natural and anthropogenic (human-induced) factors have been identified as contributing to the spread of CWD to new areas; these factors would be the logical target for future mitigation strategies. The primary anthropogenic factor associated with spread of CWD has been the movement of live cervids, which has been documented in a number of epidemiological investigations (Williams et al. 2002; Kim et al. 2005; Bollinger et al. 2004; Argue et al. 2007). In some regions, the natural movement of infected wild cervids to new areas puts commercial facilities and other wildlife populations at risk. Other implicated methods of transmission include escapes of infected farmed cervids, intrusions of infected wild cervids into farmed facilities, high-fence enclosures that allow farmed and wild animals to co-graze, contaminated environments, and fence-line contact between domestic and wild cervids (Miller and Fischer 2016). Additional concerns have been raised regarding the movement of carcasses, biological materials associated with propagation of wildlife in captivity (e.g. urine-based scents and lures), and plant crops or feed materials contaminated with CWD prion. Artificial management activities (e.g. baiting and feeding) and natural behaviors that increase the density of wild cervids in any location are thought to increase opportunities for transmission and enhance local environmental contamination (Fischer and Davidson 2005). Due to the environmental persistence of the pathogen, re-stocking of animals on known positive enclosures is identified as a risk to farmed animals.

**Summary of Recent Research Findings**

Prion diseases are an area of active research in veterinary and human medicine. The following is a targeted summary of recent findings:

*CWD Prion Uptake in Plants and Soil*

Experimental research has found that prions can bind to soil, remain infectious, and upon exposure to certain soil types (e.g. clay), have enhanced persistence and infectivity (Johnson et al. 2007). Additional lab-based research has demonstrated that grass plants can bind prions from exposure on the surface and uptake prion from contaminated soil. Hamsters that were fed the prion-contaminated plant samples developed prion disease (Pritzkow et al. 2015). The implications of this finding are unknown, but highlight reasons to minimize environmental contamination.

*Human Health*

As variant Cruetzfeldt Jacob disease has been shown to be linked with consumption of BSE-positive meat (Aguzzi and Heikenwalder 2006), concerns about the potential human health impacts of consumption of CWD-positive meat have been raised for many years.

Since 1997, the World Health Organization has recommended that it is important to keep the agents of all known prion diseases from entering the human food chain. (Centers for Disease Control (CDC) website; accessed Dec 5, 2017; https://www.cdc.gov/prions/cwd/index.html); however, prion diseases can have extremely long incubation periods and surveillance in humans is fairly limited. The possibility for CWD to cause disease in humans cannot be ruled out. The CDC, state wildlife health agencies and some provincial wildlife health agencies (e.g. Saskatchewan, Manitoba, Ontario, and British Columbia) provide recommendations that hunters use gloves, wash their hands, avoid hunting animals that appear sick, disinfect field dressing equipment, minimize handling of nervous tissue, and do not consume CWD-positive meat.

Although there are no confirmed human cases of CWD infection, the CDC recently posted the following information: “To date, there have been no reported cases of CWD infection in people. However, animal studies suggest CWD poses a risk to some types of non-human primates, like monkeys, that eat meat

from CWD-infected animals or come in contact with brain or body fluids from infected deer or elk." Although Race et al. (2009 and 2018) saw no evidence of transmission of CWD to cynomolgus macaques, preliminary results from a study in which cynomolgus macaques were fed CWD-positive meat developed disease that is clinically similar to prion disease (S. Czub, personal communication). However, the latter study has not yet been published and subjected to peer review.

A small number of studies have investigated humans that were known to consume CWD-positive meat and were unable to establish any links to human disease (Mawhinney et al., 2006; Anderson et al., 2007). A recent systematic review of information on the potential transmissibility of CWD to humans had the following conclusion: "Future discovery of CWD transmission to humans cannot be entirely ruled out on the basis of current studies, particularly in light of possibly decades-long incubation periods for CWD prions in humans. It would be prudent to continue CWD research and epidemiologic surveillance, exercise caution when handling potentially contaminated material and explore CWD management opportunities." (Waddell et al 2017)

*Potential Role of Scavengers in Transmission*

Due to the stability of prions in the environment, the potential role of scavengers in facilitating transmission of prion to new areas has been discussed and investigated. Infective prions can be passed through the digestive tract of coyotes (Nichols et al. 2015) and crows (Fischer et al. 2013). Fischer et al. also suggest that crows could therefore play a role in translocating infectious prion to disease free areas.

A recent experimental study was able to infect swine with disease-associated prion protein through direct injections of CWD prion into the brain (intracerebral injection) and orally by feeding CWD-positive material (Moore et al. 2017). Although the amount of detectable prion in the infected pigs appeared to be low, the authors indicate that "it may be possible for swine to serve as a reservoir for prion disease under natural conditions." This raises concerns regarding the potential for feral swine in endemic areas to play a role in transmission of the disease to new areas.

*Genetics and Strains of CWD*

Variation in the *PRNP* gene that encodes for the normal host protein ($PrP^C$) is a conserved gene amongst cervids with 16 documented polymorphisms (slight alterations in the gene).

Some of these polymorphisms have been associated with prolonged incubation periods (slower progression of the disease), which has driven research questions surrounding the possibility of genetic resistance to the disease (Robinson et al. 2012). More specifically, mule deer with the amino acid phenylalanine (F) as opposed to serine (S) at codon 225 respond differently to CWD, with thoughts that the allele F may be somewhat protective. However complete resistance has not been documented (Wolfe et al. 2014). Similar findings have been found with a number of other amino acid substitutions in Rocky Mountain elk, red deer, sika deer, fallow deer, white-tailed deer, moose, reindeer, caribou, and Chinese water deer (EFSA Panel on Biological Hazards 2017). Polymorphisms associated with suggested "resistance" in codon 138 were found to be less prominent in boreal caribou from Alberta (Cheng 2017).

There also seems to be increasing evidence that there may be at least two strains of CWD in North America. Additional experimental research has raised concerns that there may be differences in zoonotic potential from different CWD strains (Herbst et al. 2017).

*New Technologies*

The lack of a test approved for use in live animals has limited efforts to control disease spread from the movement of live animals. The gold standard remains immunohistochemical (IHC) testing of brainstem (obex) and specific head lymph nodes (medial retropharyngeal lymph nodes). In the United States, the Enzyme-Linked Immunosorbent Assay (ELISA) can be used as a screening tool, but any consistent reactors are confirmed by IHC at the national reference laboratory in the US (USDA-APHIS https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/cervid/cervids-cwd/cervid-cws-specifics).

In Canada, any sample that is positive by any two of the CFIA-approved testing methodologies (IHC, ELISA, Western Blot, and histopathology), one of which would be done by the CFIA laboratory as a confirmatory test, is considered positive.

A number of new technologies have emerged that are currently in use for research that could be examined for potential use as live animal tests. Tonsillar and rectal biopsies have been used in some cervid species but these can be invasive, require immobilization or restraint, are logistically challenging, and demonstrate low to variable sensitivities (Keane et al. 2009; Wild et al. 2002). These tests are not currently considered as "official tests" for CWD in the USA, but have been used in research and management programs. In Canada, samples obtained from these methods would be considered to be "official tests" for detection of disease, but are not used in the national program and are rarely used in practice. Concerns regarding spread from use of shared equipment would occur with the use of these tests.

Additional research lab-based tests include the protein misfolding cyclic amplification (PMCA) and real time quaking-induced conversion (RT-QuIC) that are specialized procedures for detection of small amounts of prion in bodily fluids (e.g. urine, blood, saliva, and feces) and tissues that could potentially be used in live animals (Hayley et al. 2017). The CFIA and the United States Department of Agriculture are not yet utilizing these testing techniques for use in live animals or testing biological products (e.g. urine-based products) outside of research programs, but are investigating the potential use of these testing techniques in the future.

## Scope:

**The activities that are considered to be within the scope of this white paper include:**

- Developing **science-based** CWD disease response options for farmed cervids that reduce the risk of spread of the disease to non-endemic regions and controlling the disease and on-farm contamination as much as possible within endemic regions.
- To include both regulatory and non-regulatory options for CWD response options.
- To develop options that will be adaptable to the changing prevalence and spread of CWD within Canada.
- To include both federal and provincial/territorial activities related to management in farmed cervids in the CWD response options.
- To take into account the pros and cons for each option.
- To make recommendations to the Regulatory ADMs, including potential changes to the current regulatory and policy framework.

**Activities that are considered to be outside of the scope of this white paper include:**

- The continuation of the current CFIA response including depopulation and compensation.

- Review and analysis of political implications of options.
- Review of legal provisions, challenges, or restrictions.
- Detailed review of trade implications.
- Consultation with other government departments including federal and provincial/territorial wildlife, indigenous, and health groups.
- Industry acceptance.
- Control of the spread in wildlife.

It is also important to note that any options requiring provincial/territorial involvement or augmentation to federal response mechanisms carry an inherent challenge associated with varying provincial/ territorial legislation that may or may not support a recommendation as well as identifying resources for new work at the provincial/territorial level. A jurisdictional scan was completed to identify provincial/territorial legislation and program variability. This information is contained in Appendix 1, but due to the short timelines was developed at the same time as the writing of this paper. As such, detailed assessment of the impact of differences in legislation could not be incorporated into the feasibility of each option presented in this document.

In addition, a short timeline of less than two months prohibited any ability to engage with other stakeholders on the development of this document whereas previous work may have had a broader involvement of stakeholders. Engagement of other stakeholders is considered to be extremely important in developing a comprehensive path forward for management of CWD in Canada.

## Context:

The working group tasked with development of this paper feels it is extremely important to point out that, as they worked through the development of this paper, the imposition of associated timelines for completion of this work became a greater and greater hindrance on the range of options available and the quality of the work. These timelines made it impossible to fully explore each option and ensure that assumptions were correct.

There was also much discussion amongst the group regarding terminology. The group felt it important to note that certain terms carry certain legal implications or limitations and therefore, care must be taken when interpreting certain words. As an example, the use of the term “quarantine” within this paper is used with the intent of ensuring movement controls. With that said, there are different tools to impose movement controls in federal and provincial/territorial legislation and they are prescribed via different terms.

Some of the options also refer to adherence to standards or measures. It is recognized that these standards or measures would need to be developed into a robust program which would include a third party audit component.

## Considered Options and Analysis

## Option 1: Short Term Augmentation of the current CFIA Program

One of the primary concerns with CFIA's planned approach for CWD control to be implemented on April 1, 2018 is the lack of any proposed response to CWD detection in non-VHCP herds. Failure to control CWD on an infected cervid farm, or at least restriction of movements off farm, risks potential introduction and establishment of the disease in previously unaffected areas as a result of the movement of infected farmed cervids.

In Option 1, we recommend that in situations where CWD is detected in cervids on farms located in regions, provinces or territories not previously known to have CWD, the CFIA and provincial/territorial wildlife agencies undertake joint response activities. This would include an epidemiological investigation, movement controls, depopulation and compensation of farmed cervids, cleaning and disinfection of the infected premises, combined with an intensive wild cervid harvest and testing in the surrounding area.

This option has the potential to be implemented prior to April 1, 2018 and seemed well supported within the working group. The challenge with this approach is that provincial/territorial wildlife groups were not engaged to measure their level of support or capacity to implement this approach. The working group agreed that the joint farmed/wild activities were essential for the greatest chance of success with this option.

| Pros | Cons |
|---|---|
| Farmed cervid component can be achieved in the time frame allowed and under the existing federal authorities. | Provincial/territorial wildlife groups have not been consulted to determine their level of engagement of capacity to support. |
| Similar approaches have been used in some jurisdictions to prove the absence of spread to wild populations (New York) or slow the progression in wild populations(Illinois, Alberta). | Does not proactively prevent the establishment of the disease in unaffected areas through movement restrictions of infected animals from non-VHCP herds. |
| Provides a comprehensive response to try to control the disease when it occurs in an unaffected area. | Is highly resource intensive and requires strong multiagency coordination, cooperation and communication. |
| Existing provincial restrictions on interprovincial movement, where they exist, can prevent the disease from crossing provincial boundaries via farmed cervids. | |

## Option 2: Zoning with various additions

Zoning and compartmentalization are internationally recognized and scientifically credible approaches to controlling disease and enabling trade from areas without disease. Option 2 introduces the concept of zoning along with a variety of additional measures that may be added to augment this approach. Zoning is highly dependent on effective surveillance as a measure to provide assurance related to the

different status inside and outside the zone and the effectiveness of the zone with respect to containment of the disease within the zone boundaries.

For the purposes of this option, three zones will be considered in accordance with the federal approach to zoning. This is due to the fact that CWD has spread without regard for provincial or territorial boundaries. Provincial/territorial ability to support this zoning framework will vary in accordance with respective legislation. The three zones would be defined based upon the known or believed distribution of Chronic Wasting Disease (CWD) in farmed and wild cervids and the notion of a compartment along with zoning will also be discussed.

The primary control zone is defined as the area where the disease is believed or known to exist in wild cervids, farmed cervids or highly contaminated premises. A secondary control zone is defined as the area that surrounds the primary control zone and provides a reasonable perimeter based on knowledge of deer movement and geography to act as a buffer. The remaining area outside of these two zones would be designated as the free zone and represents an area where the disease is not known to exist. Consideration is needed to develop options in order to maintain business continuity within the primary control zone.

Although significant work is still required to analyze and further develop details around the potential actions that could be taken in each zone, the items below would provide a basis upon which to develop that work:

## Potential actions taken within the Primary Control Zone

**Goal is to contain CWD within the primary control zone**

In the case of new detections of CWD within the zone, the following actions could be taken to control the disease in all herds regardless of VHCP status?

- Movement restrictions placed on newly infected farms and trace-out farms. In order to maintain the viability of farms within the zone, consideration could be given to allow movements to terminal options (slaughter, hunt farms). Consideration may also be given to not applying movement restrictions and treat all farms within the zone as equivalent status but this would not achieve the goal of reducing spread between farms and would likely result in higher prevalence of disease over a shorter period of time within the zone.
- Complete a risk assessment to estimate an on-farm prevalence level. This may incorporate some of the live animal testing techniques and provide a prediction on the potential to manage the herd back to disease freedom.
- Work with owner(s) to develop a biosecurity plan as part of their disease management plan.
- Engage a herd veterinarian to assist with the disease management plan.
- Mandatory disease surveillance in order to understand disease trends in the zone, risks to the secondary control zone, assess the effectiveness of the disease management plans, and determine the need for different response actions. It is important that surveillance is performed by wildlife and agriculture organizations as these outcomes apply equally to wild and farmed cervid populations.
- Restricted movements of live animals to prohibit them from exiting the primary control zone with exception of going to inspected slaughter. This may require certain measures to be taken to prevent or deal with accidental escape during transport.
- Restricted movements of hunted carcasses and parts between primary zone and other zones and possibly within the primary zone.

- Previous efforts in this regard have identified feed or feed components as potential vectors for disease transmission. While this is recognized as a potential risk, further examination of this element would need to be undertaken.

## Potential actions taken with a Secondary Control Zone

**Goal is to monitor, rapidly detect and quickly respond to any new case to try to contain the disease in the primary control zone.**

- A key activity in this zone is surveillance to monitor the effectiveness of containment of the diseases inside the primary control zone. This would include an agreed upon level of surveillance in wild and farmed cervids by their respective agencies. .
- Detections of disease in both wild and farmed cervids (all farms, not only VHCP) should be dealt with aggressively with a stamping out mindset, with the objective of keeping the secondary control zone free of CWD.
- If the number of cases detected in the secondary control zone begins to increase, a transition to extend the boundary of the primary control zone would be taken. Criteria would need to be developed to identify the point that this decision is made.
- Movement between the secondary control zone and free zone should be less restrictive than movement from the primary control zone to other zones. This could include a risk based approach that considers on-farm biosecurity, surveillance levels, or other factors.

## Potential actions taken within the Disease Free Zone

**Goal is to prevent CWD from establishing in an uninfected region**

- Federal disease response on farms coupled with provincial/territorial wildlife disease management actions and surveillance to prevent CWD from establishing in a previously unaffected area of the country. This would occur whenever CWD is detected in farmed cervids, regardless of any participation in any voluntary herd certification programs.
- Prohibitions on repopulation of infected/previously infected premises would be another element of a control program that could be included within the disease free zone
- A base level of wildlife and farmed cervid surveillance to enable early detection of CWD in the free zone and demonstrate the required level of freedom to facilitate trade is required. Evaluation of current surveillance programs would need to be undertaken to see if additional resources or new approaches are required.

## Additional considerations for Zoning

Several other suggestions were raised for consideration in a zoning option. One action that could be added to the list above would include restriction on establishing new cervid farms in areas determined to be of higher risk; parameters defining what constitutes “higher risk” will need to be defined. Prohibition on restocking of previously infected farms would also be an important consideration in this discussion. Implementation of these ideas would require collaboration between the CFIA and the provinces/territories to define when or where these restrictions should be applied, but would likely include the primary control zone and possibly the secondary control zone.

Another idea that was suggested was to allow the continuation of the CFIA’s planned approach in conjunction with a zoning option; in other words, overlaying a zoning approach over top of the VHCP compartment including the allowance for the compartment to exist within the secondary control zone and the primary control zone (PCZ).

Within this combined approach, those producers who employ additional efforts to reduce the risk to their farm and minimize the likelihood of infection within their herds would be allowed to move animals freely across zone boundaries. This would have the overall effect of incentivizing producers to take biosecurity precautions, reduce the chances of disease entering their herds and contribute to slowing the spread of CWD. It may also increase the chances of the industry acceptance of the zoning concept by having a way to maintain the viability of their business operation.

This approach would maintain the federal disease response on any of these farms that fall within the defined compartment, as is currently planned, while adding the list of actions identified in the bullets above. Currently, the VHCP provides the requirements to be included within the compartment and to be eligible for CFIA response, but a review of this would be needed to determine whether any changes should be made for additional control of the disease or enablement of the industry to operate without compromising disease control.

Zones and compartments that extend across provincial/territorial boundaries allow potential for movement within that zone or compartment including across that provincial/territorial boundary. This option would therefore require examination of any interprovincial/territorial movement restrictions that have been established based on the historical risk assessments. It is important, however, to consider that some of those movement restrictions may be in response to diseases other than CWD.

Risk-based decision making was also considered under this option. Criteria related to the proximity to known infected herds or wild populations, levels of surveillance in farmed and wild populations, epidemiological assessments, and adherence to biosecurity measures would be applied. These factors are common to all the approaches in this option.

| Pros | Cons |
|---|---|
| Risk-based control of CWD by preventing high risk movements of farmed cervids. | Challenge and/or controversy could arise when defining the boundaries of the primary control zone. |
| Provide a predictable framework based on internationally recognized and scientifically valid principles of OIE that can be adapted to the situation as the disease spreads. | Enforcing movement controls would be challenging and resource intensive since there are currently no federally mandatory traceability requirements in cervids; however, this is expected to change in the near future. |
| Framework can be adapted should disease containment not be successful and CWD spreads beyond the primary control zone. | Potential loss of markets and future business opportunities for producers in the primary control zone. |
| Adding the compartment approach provides incentive to producers to participate in the VHCP and improves the viability of their business. | Restrictions on movement of hunted carcasses or parts might result in loss of hunting and wildlife tourism as well as food security and cultural impacts. This could create a socio-economic impact in the PCZ |
| Nationally consistent program that is compatible with CFIA regulatory amendments to support zoning. | Acceptance of CWD diseased animals within the primary control zone results in ongoing infections. This could lead to increased infection pressure with the zone with subsequent disease spread outside of the primary control zone. |
| | Requires development and implementation of a |

| | |
|---|---|
| | permit system. |

## Option 3: Maintain fulsome CFIA program response to CWD, with modifications

In this option, the CFIA would continue to respond to all cases of CWD as per the federal legislation and the CWD program policy (prior to December 31, 2017) but changes to compensation and repopulation would be pursued, through legislative changes. In addition, more stringent movement controls could be added.

**Some alterations to the current compensation approach to consider and which could be combined:**

1. Reduce maximum compensation to a lower amount, similar to that used for EIA (maximum $2000 per horse, regardless of value).
2. Limit compensation to any one producer to a one-time event - no subsequent depopulation with compensation for the same producer/premises - "One Strike rule".
    a. Work with provinces/territories to prevent repopulation of any previously depopulated premises through a prohibition on a second round of compensation federally and through licencing changes provincially/territorially. This would require regulatory changes both provincially/territorially and federally.
    b. Currently repopulation is prevented on high risk premises through federal restrictions, but this could be extended to prohibition of repopulation of ANY infected premises using provincial/territorial licencing restrictions rather than federal restrictions.
3. Tie compensation to biosecurity through a biosecurity assessment, with compensation pro-rated based on a biosecurity score. If biosecurity is considered excellent, the farm could qualify for full compensation. If biosecurity is rated as poor, compensation could be reduced accordingly. This would require more work to develop criteria and a third party audit program, but it could be based on the national biosecurity standard or VHCP biosecurity requirements.

**Additional changes to consider to existing response program, other than changes to compensation:**

1. Cost share provision between federal and provincial/territorial governments or even industry funding - provincial/territorial governments will bear cost of CWD surveillance (like industry does for EIA surveillance) and federal government funds a maximum compensation amount. Some provinces/territories already support surveillance.
2. Provinces/territories and CFIA collaborate on defining areas of higher risk where new game cervid? farms could not be established.
    a. Criteria developed nationally.
    b. Will need adequate surveillance of wild populations to adequately demonstrate areas where the risk of infection of game farms is high enough that new farms should not be established.
3. Restrict movement of live animals from farms located in known enzootic areas.
    a. Allow movement of farmed cervids only to slaughter (and possibly terminal hunt farms in known hot spots) unless they have reached a certain level (certified, level A or B) on the VHCP or equivalent (i.e. if herd is on a provincial/territorial mandatory program and meets the testing and inventory requirements equivalent to VHCP Level A or B, as is

used currently for import into Saskatchewan and for Alberta slaughter import requirements). A review of past cases of CWD on herds enrolled in the VHCP would need to be undertaken to evaluate the level of risk associated with this.

| Pro | Con |
|---|---|
| A rapid, consistent federal response would ensure consistency in approach across Canada to hopefully ensure CWD is handled promptly, and positive animals are removed. | The current response policy has not prevented the spread of CWD in farmed cervids in Alberta and Saskatchewan. |
| Mitigate some costs of implementation with money obtained from salvage value from slaughter of affected herds. | The current response policy is costly and costs aside from compensation would continue to be incurred. |
| Animals on infected premises would be ordered destroyed, reducing risk of new infections and ongoing contamination of premises with CWD prions. | Affected producers would expect compensation for depopulation of affected animals. |
| Additional industry/provincial/territorial cost-share for compensation could increase industry prevention efforts. Provincial/territorial share could be in surveillance/early detection. | Industry will be opposed to reduced compensation. Provinces/territories are unlikely to contribute to direct compensation costs. |
| Adjustments to compensation program would save tax payer dollars. | Regulatory/legislative changes would be required so this would take a number of years to design and implement |
| Program changes to limit repopulation of infected farms would reduce risk of paying compensation to same producers multiple times. | Requires federal-provincial/territorial cooperation and regulatory changes. |
| Adding increased movement controls in CWD enzootic areas would help limit spread of CWD in farmed populations. | There will be administrative costs and wild cervid surveillance costs related to the confirmation/creation of enzootic areas. |
| | The development of biosecurity requirements / scales would be extremely challenging. Third party audits for documentation of compliance with biosecurity requirements would be necessary and the infrastructure for that would have to be developed. Audits would add more cost for the producers. |

## Option 4: Transition all cervid producers to the VHCP

This option entails a requirement for all licensed or registered farmed cervid producers to be successfully enrolled in the VHCP or meeting the standards outlined in the VHCP through some other regulatory means by December 2018.

Given that licensing of cervid farms is regulated, for the most part, at the provincial or territorial level, this requirement would presumably best fit with provinces and territories to implement. There could be

mechanisms to link it to federal programming or incentives such as compensation but a scenario such as that would likely only entice some. As a voluntary requirement, regardless of incentives, there may still be some farms that would not find it attractive enough and hence, this would be a key difference between this mandatory proposal and the current voluntary approach of compartmentalization. This option would also require significant investment in regulatory oversight which experience has shown is not palatable to industry, as past attempts to do this have faced legal challenges/litigation.

At a provincial/territorial level, this option could be implemented through one of three mechanisms, the third being one that may promote enrolment rather than make it mandatory:

1. Mandatory enrolment and compliance with the VHCP as part of cervid farming regulations whereby each province or territory develops regulations that require this in order to farm cervids.
2. Implementation of relevant portions of the VHCP into provincial/territorial cervid farm licensing regulations as minimum requirements. This could include mandatory traceability, surveillance, and biosecurity elements that would aid in prevention, detection, and control of CWD.
3. Implementation of a tiered licensing structure which affects fees or access to funding program.

Some provinces/territories might require regulatory changes to enable any of these options and may not be able to provide sufficient oversight.

This option would result in implementation of risk mitigation measures to prevent introduction of CWD into a farmed cervid herd. Once applied in all jurisdictions that allow cervid farming, this would result in a nationally consistent standard of operation that could be promoted to foreign trading partners.

Although this option does mitigate the risk of disease incursion to farmed cervid herds, it does not eliminate it. Risk still exists and given the longer incubation period associated with prion diseases, trading countries may also not see it as sufficient to allow trade based solely on this. In addition, some farms, depending on their business model, will not be able to absorb the additional costs, see sufficient cost benefit, or be able to meet the program requirements. This raises the ultimate question in terms of how to approach farms that become non-compliant. Down-grading a farm's status may not provide sufficient incentive to comply and ultimately, the only tool that could be effective would be revocation of their cervid farm license.

| Pros | Cons |
|---|---|
| Enrollment in and complying with the VHCP would increase adoption of many of the risk mitigation measures for CWD (enhanced biosecurity, surveillance, veterinary care). | Enrollment in the VHCP does not ensure a farm will not become infected with CWD. |
| The CFIA would continue to have responsibility for the control and containment of CWD on a national level. | The costs associated with meeting the criteria of the VHCP are prohibitive for many producers. |
| Trade benefits due to nationally consistent standard. | The cost –benefit of the VHCP does not make sense for some producers or provide value to their business model (the VHCP is not required for |

| | |
|---|---|
| | access to all markets). |
| | Not all provinces/territories have the legislative authority to make the VHCP mandatory for cervid producers. |
| | License removal may be the only compliance tool available. |
| | Past experience shows that enforcement would be very difficult and that compartments only work in voluntary situations and self-motivation. |

## Other Considerations:

It is worth restating that the management or control of chronic wasting disease is a complex issue involving many stakeholders. As with most diseases, it does not recognize provincial/territorial or national borders and the regulation of the cervid industry is accomplished through a range of federal and provincial/territorial legislation involving both agriculture and wildlife jurisdictions.

While other diseases that cross species barriers provide examples of wildlife reservoirs in Canada, these situations also result in variations in species susceptibility that affect the epidemiology of the disease. However, in the case of cervid farming, the farmed cervids are the same species of animals as those present in free ranging populations resulting in an ongoing potential source of infection.

In addition, the presence of the disease in wild populations immediately south of the Canadian border, in many states, results in a constant potential source of prion that is difficult or impossible to mitigate. While spread through wildlife migration in the western provinces and territories may be a likely outcome, spread of the disease to northeastern states means that eastern provinces face the real possibility of introduction through wildlife migration from jurisdictions beyond the control of Canada or its provinces. Importation of potentially infected materials (e.g. urine, meat, carcasses, and other products) is also a possible pathway for exposure.

The reality is that decisions around management or control of this disease require collaborative thought and input from a wide range of stakeholders. As indicated previously, previous efforts have done this to varying degrees but this is something that was not achievable by this working group in the timelines provided for this paper.

As discussed previously in the paper, the work of this group also did not consider political implications or delve deeply into trade ramifications. At a broad level, it is recognized that certain options such as those that carry international credibility such as zoning should result in improved trade opportunities for the industry that exists in the disease free zone. It is also recognized that the opposite occurs for farms located inside the primary control zone. Theory aside, international trade is a highly complex issue in itself with individual countries able to establish import requirements that may not align with these concepts and the acceptability of a compartment within a primary control zone presents further unknowns. In addition to this, time also did not permit a full review of legal implications. A jurisdictional scan of agriculture legislation/policies was completed as a parallel activity and this will be useful in future work on this issue.

## Recommendations:

In the discussions that fed the development and refining of options, the group found several recurring themes and elements occurring in each iteration. Many of these themes and elements are, not surprisingly, well known and used disease control principles including:

- movement restrictions for live animals (off of infected farms and permitted movements between farms) and animal products,
- requirements for biosecurity and veterinary care,
- surveillance,
- depopulation, and
- restrictions on repopulation.

Aside from one exception, the group found that with the imposed timelines, a new, alternative option or recommendations to augment the current CFIA decision which could be applied federally were not attainable. The exception to that was Option 1 which includes the planned CFIA approach along with a federal disease response on all farms located in a disease-free zone or province/territory, regardless of VHCP status. An essential concurrent element of this option was an intensive wildlife response including harvesting and testing wild cervids in the area around the affected farm. This might require the overlay of a zoning approach on the proposed compartmentalization to define the area where this approach would be taken. It is our belief that the legislation is in place to accomplish this and this option would allow a fulsome federal disease response on premises where the disease is detected in a previously unaffected zone or province/territory.

Option 4, requiring participation in a herd certification program, is a concept that seems to be repeatedly presented in any discussions around management of CWD. For this reason, it was included in this paper, but it was not supported by the group due to the cons listed in the table below that option including most notably, challenges with enforcement and previous attempts that have resulted in legal challenges and litigation.

In the absence of any further change prior to April 1, the provinces/territories will inevitably be charged with taking individual responses based on their current disease situation and capabilities to implement actions based on current regulatory frameworks and resources. However, variability in legislative authority or lack of resources could make this a challenge for some jurisdictions.

In addition, while there was general agreement amongst the group in recommending longer term options based on zoning, inclusion of other elements from other options was also seen to be highly beneficial. The working group of the CCVO sees value in continuing work in this area, and has requested approval to do so.

## Reference Material:

Southeastern Cooperative Wildlife Disease Reports

http://vet.uga.edu/population_health_files/briefs/2017_OCT_SCWDS_Briefs_Newsletter.pdf

http://vet.uga.edu/population_health_files/briefs/2016_APR_SCWDS_Briefs_FINAL.pdf


Aguzzi, A., and Heikenwalder, M. 2006. Pathogenesis of prion diseases: current status and future outlook. *Nature Reviews* 4:765-775.

Anderson CA, Bosque P, Filley CM, Arciniegas DB, Kleinschmidt-DeMasters BK, Pape WJ and Tyler KL, 2007. Colorado surveillance program for chronic wasting disease transmission to humans. Lessons from 2 highly suspicious but negative cases. *Archives of Neurology*, 64, 439–441.

Angers, R. C., Browning, S. R., Seward, T. S., Sigurdson, C. J., Miller, M. W., Hoover, E. A., Telling G. C., 2006. Prions in skeletal muscles of deer with chronic wasting disease, *Science*, 311: 1117.

Argue, C. K., Ribble, C., Lees, V. W., McLane, J., and Balachandran, A. 2007. Epidemiology of an Outbreak of Chronic Wasting Disease on Elk Farms in Saskatchewan. *Canadian Veterinary Journal* 48: 1241-1248.

Balachandran A, Harrington NP, Algire J, Soutyrine A, Spraker TR, et al. (2010) Experimental oral transmission of chronic wasting disease to red deer (*Cervus elaphus elaphus*): early detection and late stage distribution of protease resistant prion protein. *Canadian Veterinary Journal* 51: 169–178.

Baron T, Vulin J, Biacabe A-G, Lakhdar L, Verchere J, Torres J-M and Bencsik A, 2011. Emergence of classical BSE strain properties during serial passages of H-BSE in wild-type mice. *PLoS ONE*, 6, e15839.

Bartz JC, Marsh RF, McKenzie DI and Aiken JM, 1998. The host range of chronic wasting disease is altered on passage in ferrets. *Virology*, 251, 297–301.

Bollinger, T. Caley, P., Merrill, E., Messier, F., Miller, M. W., Samuel, M. D., and Vanopdenbosch, E. 2004. Chronic Wasting Disease in Canadian Wildlife: An Expert Opinion on the Epidemiology and Risks to Wild Deer. *Perpared by* Expert Scientific Panel on Chronic Wasting Disease, July 2004. Canadian Cooperative Wildlife Health Centre, Western College of Veterinary Medicine, Saskatoon, SK.

Browning SR, Mason GL, Seward T, Green M, Eliason GAJ, Mathiason C, Miller MW, Williams ES, Hoover E and Telling GC, 2004. Transmission of prions from mule deer and Elk with chronic wasting disease to transgenic mice expressing cervid PrP. *Journal of Virology*, 78: 13345–13350.

Canadian Cooperative Wildlife Health Centre, 2011. A Proposal for Canada's National Chronic Wasting Disease Control Strategy. http://www.cwhc-rcsf.ca/docs/technical_reports/A_Proposal_for_a_National_CWD_Control_Strategy_2011_final.pdf

Cheng YC, Musiani M, Cavedon M, Gilch S. 2017. High prevalence of prion protein genotype associated with resistance to chronic wasting disease in one Alberta woodland caribou population. *Prion*.;11:136-142.

Di Bari MA, Nonno R, Castilla J, D'Agostino C, Pirisinu L, Riccardi G, Conte M, Richt J, Kunkle R, Langeveld J, Vaccari G and Agrimi U, 2013. Chronic wasting disease in bank voles: characterisation of the shortest incubation time model for prion diseases. *PLoS Pathogens*, 9: e1003219. doi: 10.1371/journal.ppat.1003219

Dubé, C., Mehren, K. G., Barker, I. K., Peart, B. L., and Balachandran, A. 2006. Retrospective investigation of chronic wasting disease of cervids at the Toronto Zoo, 1973-2003. *Canadian Veterinary Journal*, 47: 1185-1193.

EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), Ricci A, Allende A, Bolton D, Chemaly M, Davies R, Fernández Escámez PS, Gironés R, Herman L, Koutsoumanis K, Lindqvist R, Nørrung B, Robertson L, Sanaa M, Skandamis P, Snary E, Speybroeck N, Kuile BT, Threlfall J, Wahlström H, Benestad S, Gavier-Widen D, Miller MW, Ru G, Telling GC, Tryland M, Ortiz Pelaez A and Simmons M, 2017. Scientific opinion on chronic wasting disease (CWD) in cervids. EFSA Journal 2017;15:4667, 62 pp.

Evans TS, Schuler KL, Walter WD. 2014. Surveillance and monitoring of white-tailed deer for chronic wasting disease in the northeastern United States. *Journal of Fish and Wildlife Management* 5:387–393.

Fischer JW, Phillips GE, Nichols TA, VerCauteren KC. 2013. Could avian scavengers translocate infectious prions to disease-free areas initiating new foci of chronic wasting disease? *Prion*, 7:263-266.

Fischer, J., W. R. Davidson. 2005. Reducing Risk Factors for Disease Problems Involving Wildlife. *Transactions of the North American Wildlife and Natural Resources Conference*, 70: 289-309.

Greenlee JJ, Smith JD and Kunkle RA, 2011. White-tailed deer are susceptible to the agent of sheep scrapie by intracerebral inoculation. *Veterinary Research*, 42:107.

Gossert AD, Bonjour S, Lysek DA, Fiorito F and Wuthrich K, 2005. Prion protein NMR structures of elk and of mouse/elk hybrids. *Proceedings of the National Academy of Sciences of the United States America*, 102: 646–650.

Gough KC and Maddison BC, 2010. Prion transmission. *Prion*, 4: 275–282.

Haley NJ, Mathiason CK, Zabel MD, Telling GC and Hoover EA, 2009b. Detection of sub-clinical CWD infection in conventional test-negative deer long after oral exposure to urine and feces from CWD+ deer. *PLoS ONE*, 4, e7990.

Haley NJ, Richt .JA. 2017 Evolution of Diagnostic Tests for Chronic Wasting Disease, a Naturally Occurring Prion Disease of Cervids. *Pathogens*, *6*, 35.

Hamir AN, Kunkle RA, Cutlip RC, Miller JM, O'Rourke KI, Williams ES, Miller MW, Stack MJ, Chaplin MJ and Richt JA, 2005. Experimental transmission of chronic wasting disease agent from mule deer to cattle by the intracerebral route. *Journal of Veterinary Diagnostic Investigation*, 2005: 276–281.

Hamir, A. N., Gidlewski, T., Spraker, T. R., Miller, J. M., Creekmore, L., Crocheck, M., Cline, T., O'Rourke, K. I. 2006a. Preliminary observations of genetic susceptibility of elk (*Cervus elaphus nelsoni*) to chronic wasting disease by experimental oral inoculation. *Journal of Veterinary Diagnostic Investigation*, 18: 110-114.

Hamir AN, Kunkle RA, Cutlip RC, Miller JM, Williams ES and Richt JA, 2006b. Transmission of chronic wasting disease of mule deer to Suffolk sheep following intracerebral inoculation. *Journal of Veterinary Diagnostic Investigation*, 18: 558–565.

Heisey DM, Mickelsen NA, Schneider JR, Johnson CJ, Johnson CJ, Langenberg JA, Bochsler PN, Keane DP and Barr DJ, 2010. Chronic wasting disease (CWD) susceptibility of several North American rodents that are sympatric with cervid CWD epidemics. *Journal of Virology*, 84: 210–215.

Herbst A, Velásquez C, Triscott E, Aiken JM, McKenzie D. Chronic Wasting Disease Prion Strain Emergence and Host Range Expansion. Emerg Infect Dis. 2017;23(9):1598-1600. https://dx.doi.org/10.3201/eid2309.161474

Johnson CJ, Pedersen JA, Chappell RJ, McKenzie Dand Aiken JM, 2007. Oral transmissibility of prion disease is enhanced by binding to soil particles. *PLoS Pathogens*, 3, e93.

Keane, D., Barr, D., Osborn, R., Langenberg, J., O'Rourke, K., Schneider, D., and Bochsler, P.. 2009. Validation of Use of Rectoanal Mucosa-Associated Lymphoid Tissue for Immunohistochemical Diagnosis of Chronic Wasting Disease in White-Tailed Deer (*Odocoileus virginianus*). *Journal of Clinical Microbiology* 47: 1412-1417.

Kim, T.-Y., Shon, H.-J., Joo, Y.-S., Mun, U.-K., Kang, K.-S., and Lee, Y.-S. 2005. Additional cases of chronic wasting disease in imported deer in Korea. *Journal of Veterinary Medical Science* 67: 753-759.

Llewelyn, C. A. et al. 2004. Possible transmission of variant Creutzfeldt-Jakob disease by blood transfusion. *Lancet* 363: 417-421.

Marsh RF, Kincaid AE, Bessen RA and Bartz JC, 2005. Interspecies transmission of chronic wasting disease prions to squirrel monkeys (*Saimiri sciureus*). *Journal of Virology*, 79: 13794–13796.

Mathiason CK, Powers JG, Dahmes SJ, Osborn DA, Miller KV, Warren RJ, Mason GL, Hays SA, Hayes-Klug J, Seelig DM, Wild MA, Wolfe LL, Spraker TR, Miller MW, Sigurdson CJ, Telling GC and Hoover EA, 2006. Infectious prions in the saliva and blood of deer with chronic wasting disease. *Science*, 314, 133–136.

Mathiason CK, Nalls AV, Seelig DM, Kraft SL, Carnes K, Anderson KR, Hayes-Klug J and Hoover EA, 2013.Susceptibility of domestic cats to chronic wasting disease. Journal of Virology, 87, 1947–1956.

Mawhinney S, Pape WJ, Forster JE, Anderson CA, Bosque P and Miller MW, 2006. Human prion disease and relative risk associated with chronic wasting disease. *Emerging Infectious Diseases*, 12, 1527–1535.

Miller M, Williams E, Hobbs N and Wolfe L, 2004. Environmental sources of prion transmission in mule deer. *Emerging Infectious Diseases*, 10, 1003–1006.

Miller, M. W., and J. R. Fischer. 2016. The First Five (or More) Decades of Chronic Wasting Disease: Lessons for the Five Decades to Come. *Transactions of the North American Wildlife and Natural Resources Conference* 81: In press

Mitchell GB, Sigurdson CJ, O'Rourke KI, Algire J, Harrington NP, et al. (2012) Experimental Oral Transmission of Chronic Wasting Disease to Reindeer (*Rangifer tarandus tarandus*). *PLoS ONE*, 7, e39055. doi:10.1371/journal.pone.0039055

Moore SJ, West Greenlee MH, Kondru N, Manne S, Smith JD, Kunkle RA, Kanthasamy A, Greenlee JJ. 2017. Experimental transmission of the chronic wasting disease agent to swine after oral or intracranial inoculation. *Journal of* Virology, 91:e00926-17

Nalls AV, McNulty E, Powers J, Seelig DM, Hoover C, Haley NJ, Hayes-Klug J, Anderson K, Stewart P, Goldmann W, Hoover EA and Mathiason CK, 2013. Mother to offspring transmission of chronic wasting disease in reeves' muntjac deer. *PLoS ONE*, 8, e71844.

Napier D, Green M, Hoover E, Spraker T, O'Rourke K, Balachandran A and Telling GC, 2009. Chronic wasting disease prions in elk antler velvet. *Emerging Infectious Diseases*, 15, 696–703.

Nichols TA, Fischer JW, Spraker TR, Kong Q, VerCauteren KC. 2015. CWD prions remain infectious after passage through the digestive system of coyotes (*Canis latrans*). *Prion*, 9:367-375.

Ortiz-Pelaez A, Arnold MEand Vidal-Diez A, 2016. Epidemiological investigations on the potential transmissibility of a rare disease: the case of atypical scrapie in Great Britain. *Epidemiology and Infection*, 144, 2107–2116.

Pritzkow, S., Morales, R., Moda, F., Khan, U., Telling, G. C., Hoover, E., and Soto, C. 2015. Grass plants bind, retain, uptake, and transport infectious prions. *Cell Reports,* 11: 1168-1175.

Race B, Meade-White K, Phillips K, Striebel J, Race R and Chesebro B, 2014. Disease agents in nonhuman primates. *Emerging Infectious Diseases*, 20: 833–837.

Race, B., Williams, K., Orru, C. D., Hughson, A. G., Lubke, L., and Chesebro, B. 2018. Lack of transmission of chronic wasting disease by cynomolgus macaques. J. Virol. doi:10.1128/JVI.00550-18

Robinson SJ, Samuel MD, O'Rourke KI and Johnson CJ, 2012. The role of genetics in chronic wasting disease of North American cervids. *Prion*, 6, 153–162. doi: 10.4161/pri.19640

Rhyan, J. C., Miller, M. W., Spraker, T. R., McCollum, M., Nol, P., Wolfe, L. L., Davis, T. R., Creekmore, L., and O'Rourke, K. I. 2011. Failure of Fallow Deer (*Dama dama*) to Develop Chronic Wasting Disease When Exposed to a Contaminated Environment and Infected Mule Deer (*Odocoileus hemionus*) *J Wildl Dis* 47: 739- 744

Rubenstein R, Bulgin M, Chang B, Sorensen-Melson S, Petersen R, ad LaFauci G. 2012. $PrP^{Sc}$ detection and infectivity in semen from scrapie-infected sheep *J. Gen Virol* 93:1375-1383.

Saunders SE, Bartelt-Hunt SL and Bartz JC, 2012. Occurrence, transmission, and zoonotic potential of chronic wasting disease. *Emerging Infectious Diseases*, 18, 369–376.

Sigurdson, C. J., 2008. A prion disease of cervids: Chronic wasting disease. *Veterinary Research* 39:41.

Tamgüney G, Miller MW, Wolfe LL, Sirochman TM, Glidden DV, Palmer C, Lemus A, DeArmond SJand Prusiner SB, 2009. Asymptomatic deer excrete infectious prions in faeces. *Nature*, 461, 529–532.

Telling GC, 2011. Transgenic mouse models and prion strains. *Topics in Current Chemistry* 305, 79–100.

United States Geological Survey. 2016. Chronic Wasting Disease (CWD). National Wildlife Health Center. Web 1 April 2016. (http://www.nwhc.usgs.gov/disease_information/chronic_wasting_disease/)

Waddell L, Greig J, Mascarenhas M, Otten A, Corrin T, and Hierlihy K. 2017. Current evidence on the transmissibility of chronic wasting disease prions to humans—A systematic review. *Transboundary and Emerging Diseases*, 00,1–13.

Wild, MA, TR Spraker, CJ Sigurdso, K. I. O'Rourke, and MW Miller 2002. Pre-clinical diagnosis of chronic wasting disease in captive mule deer (*Odocoileus hemionus*) and whitetailed deer (Odocoileus virginianus) using tonsillar biopsy. *Journal of General Virology* 83: 2629– 2634

Williams ES and Young S, 1980. Chronic wasting disease of captive mule deer: a spongiform encephalopathy. *Journal of Wildlife Diseases*, 16, 89–98.

Williams ES and Young S, 1992. Spongiform encephalopathies in Cervidae. *Revenue Scientific Technical Review of The Office International Epizooties*, 11, 551–567.

Williams ES and Young S, 1993. Neuropathology of chronic wasting disease of mule deer (*Odocoileus hemionus*) and Elk (*Cervus elaphus nelsoni*). *Veterinary Pathology*, 30, 36–45.

Williams, E. S., Miller, M. W., and Thorne, E. T. 2002. Chronic Wasting Disease: Implications and Challenges for Wildlife Managers. *Transactions of the North American Wildlife and Natural Resources Conference* 67: 87-103.

Williams ES and Miller MW, 2003. Transmissible spongiform encephalopathies in non-domestic animals: origin, transmission and risk factors. *Revue Scientifique et Technique (International Office of Epizootics)* 22:145-156.

Wolfe LL, Fox KA and Miller MW, 2014. "Atypical" chronic wasting disease in PRNP genotype 225FF mule deer. *Journal of Wildlife Diseases*, 50, 660–665.