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Health Products and Food Branch (HPFB) Risk Advisory Opinion: Potential Human Health Risks from Chronic Wasting Disease

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Issue:

Chronic Wasting Disease (CWD) is a progressive, fatal, transmissible spongiform encephalopathy (TSE), or prion disease, that naturally infects cervids (i.e., deer, elk, moose, and reindeer). To date, there have been no reported cases of CWD infection in humans, and there is no direct evidence to suggest that CWD may be transmitted to humans. However, the continued spread of this disease in farmed and wild cervid populations raises concerns regarding human exposure to CWD. In response, Health Canada's Health Products and Food Branch (HPFB) has reviewed the Branch's position on CWD in health products and food (1) based on a review of the scientific literature published since 2017.

Summary and Recommendation:

HPFB is responsible for assessing risks to human health from diseases of animal origin that may be transmitted through health products and food, and for developing regulations and policies to mitigate risks from products regulated under the *Food and Drugs Act* as well as various associated regulations. While extensive disease surveillance in Canada and elsewhere has not provided any direct evidence that CWD has infected humans, the potential for CWD to be transmitted to humans cannot be excluded.

In exercising precaution, HPFB continues to advocate that the most prudent approach is to consider that CWD could have the potential to infect humans and appropriate measures should be taken to limit exposure to humans. This position has been aligned with that of the World Health Organization (WHO) since the late 1990s, and remains consistent with the WHO's current position (2) that "No tissue that is likely to contain the bovine spongiform encephalopathy (BSE) agent, nor part or product of any animal which has shown signs of a TSE should enter the (human or animal) food chain." This precautionary position on TSEs is also consistent with the conclusions documented by the TSE Secretariat in 2003 (3), a systematic literature review conducted by the Public Health Agency of Canada (PHAC) in 2017 (4), and two comprehensive reviews on CWD published in 2019 by the European Food Safety Authority (5) and Osterholm et al. (6).

HPFB's current position with respect to the safety of food and health products and CWD does not change following a review of the most recent scientific literature (2017–2019). The available information continues to suggest that the risk of CWD transmission to humans remains theoretical. However, recent published and unpublished findings from ongoing research continue to present conflicting evidence on the zoonotic potential of CWD. Therefore, a precautionary approach to the management of CWD which limits human exposure through health products and food continues to be warranted. As part of this precautionary approach, meat, processed meat products, offal and any other products from known CWD-infected cervids should not be consumed or used by humans and animals.

This review has also found that the range and prevalence of CWD has increased geographically in North America and Europe (5, 6). Therefore, HPFB supports disease control policies that minimize the spread of the disease in animals. The efforts of Federal, Provincial and Territorial governments to improve management practices for both farmed and wild cervids in Canada should be continued.

Background:

Chronic Wasting Disease (CWD) is a fatal disease of cervids. To date, the disease has been identified in deer, elk, moose, and reindeer. CWD belongs to a class of diseases known as transmissible spongiform encephalopathies (TSEs), or prion disease. Though CWD shares features with other TSEs, such as bovine spongiform encephalopathy (BSE) in cattle, scrapie in sheep, and Creutzfeldt-Jakob disease (CJD) in humans, it is a distinct disease only known at this time to naturally affect members of the deer (cervid) family (7).

CWD was first recognized as a fatal disease of captive deer in the United States in the late 1960s, and was later identified as a TSE in 1980. In Canada, CWD was first detected in a Saskatchewan farmed elk in 1996 and retrospectively was found in archived cervid samples from the Toronto Zoo dating back to the 1970s. The first Canadian case in a wild cervid was confirmed in a mule deer in Saskatchewan in November 2000. By 2019, the disease is known to be present in free-ranging and/or captive cervids in 26 states and 3 provinces in North America, in captive cervids in the Republic of Korea, and in free-ranging cervids in Norway, Sweden and Finland. In Canada, CWD has been identified in both free-ranging and captive cervids in Alberta and Saskatchewan, and in captive cervids in Quebec (5, 6, 8).

The exact routes and mechanisms of CWD transmission between animals remain unclear. There is evidence that infection is transmitted directly from animal to animal during close contact with saliva, urine and feces, and indirectly through the environment and fomites (5). While incubation periods may be variable, once the disease is contracted, the time to presentation of clinical symptoms is about 16 to 36 months (8). It is only in the later, clinical stages that CWD is typified by clinical signs such as the chronic weight loss and behavioral changes that eventually lead to death.

In 2003, Health Canada's TSE secretariat assessed the potential for CWD to pose a hazard to human health. It was noted at that time that there was no direct evidence to indicate that CWD had ever infected a human. However, given there was existing research to suggest TSEs have the potential to become a human pathogen (e.g., human cases of variant CJD (vCJD) related to consumption of BSE-contaminated beef), it was stated that the most prudent course of action was to consider that CWD could have the potential to infect humans, and thus take a precautionary approach to its management, which was consistent with the position taken by the WHO (2, 3).

The Public Health Agency of Canada (PHAC) published a systematic review summarizing the evidence in the scientific literature on the transmissibility of CWD prions to humans. This review summarized available epidemiological evidence, as well as evidence on CWD infectivity using experimental models, including non-human primates, transgenic mice, and *in vitro* experiments. Two transmission experiments using squirrel monkeys have been able to show prion disease after intracerebral and oral inoculation with CWD prions. The systematic review also summarized two transmission experiments using macaques (a non-human primate species considered genetically closer to humans than squirrel monkeys (9)) which, at the time of review, had not caused prion disease after inoculation with CWD prions by several modes (e.g., intracerebral, oral) up to 10 years of observation since exposure to CWD prions (4).

As the lead Department in managing the potential human health risks related to health products and food, Health Canada's HPFB has conducted a review of published scientific literature related to the zoonotic potential of CWD in order to provide an updated advisory opinion on the risk to human health. This opinion is provided to Health Portfolio partners to inform the assessment of current CWD control policies in Canada as well as the advice communicated to Canadians on the potential risks posed by CWD.

Health Canada's Current Position on TSEs in Health Products and Food:

HPFB has previously addressed concerns regarding human exposure to BSE (10), and remains alert to the possibility that other animal TSEs such as scrapie and CWD may also pose risks to human health. HPFB maintains a precautionary stance in relation to human exposure to TSEs through health products and food.

In 2003, HPFB adopted the position that no material derived from an animal known to be infected with any TSE (including CWD) should be used or consumed by humans or animals. This position was, and continues to be, consistent with the position of the WHO (2, 3).

HPFB requires pre-market review and approval of all human therapeutics, biologics and genetic therapies, veterinary drugs and natural health products intended for sale in Canada. This includes a requirement for license holders of these products to maintain documentation and provide information for any materials of animal origin that may be used within their products, including therapeutic substances, reagents and excipients. This documentation can include letters of attestation, Certificates of Suitability or Veterinary Certificates.

Health Canada also regulates the safety of Canada's blood supply and plasma-derived drug products for human use. Similar to existing precautionary measures for the risk of blood transfusion transmission of the human prion and bovine variant, donor deferral measures would likely be an appropriate risk management measure should transmission of CWD to humans be identified. To date, there are no documented cases of CWD infection in humans and therefore the risk of transfusion-transmitted infection remains theoretical.

While there are no specific federal regulations related to the use(s) of cervids in foods, it is prohibited under Section 4 of the *Food and Drugs Act* to sell food from diseased animals. Current federal animal disease control policies divert known CWD-infected farmed animals away from the food and feed supply.

Outreach, communications, and monitoring programs related to wild cervids, as well as disease surveillance for farmed cervids, fall within the jurisdiction of the Federal, Provincial and/or Territorial governments.

Hazard Characterization

In 2003, Health Canada's TSE secretariat assessed the potential for CWD to pose a hazard to human health (3). Even though there is a lack of direct scientific evidence of the potential for CWD to become a human pathogen, it was stated that the most prudent course of action was to consider that CWD and other TSEs could have the potential to infect humans, and thus concluded that a precautionary approach was warranted to manage exposure to CWD.

Following nearly two decades of ongoing human prion disease surveillance and retrospective review by PHAC and the Centers for Disease Control and Prevention (CDC), there have been no identified cases of human prion disease or any other outcome attributed to CWD in Canada, the USA, or elsewhere. Interspecies transmission of CWD to non-cervids has not been observed under natural conditions. However, CWD can be transmitted experimentally to goats, sheep, rodents, mink, ferrets and squirrel monkeys (11).

In 2017, PHAC published a systematic literature review of the evidence for the transmissibility of CWD to humans, which included evidence of successful transmission of CWD intracranially and orally to squirrel monkeys. From this review, no CWD transmission to humans has been recorded. In five epidemiological studies no association between CWD exposure and human prion disease was identified. Some cases of CJD had a history of exposure to cervids and venison in CWD affected regions, but no definitive link to CWD could be found. The assessment of the evidence captured in this systematic review does not support the hypothesis that CWD is readily transmitted to humans; however, the positive evidence of interspecies transmission from *in vivo* and *in vitro* experiments indicates that the human species barrier is not absolute (4).

Potential Sources of Exposure to Cervids and Cervid-derived Materials:

Canadians may be exposed to cervids, and materials derived from cervids through a variety of sources, and routes of exposure, including food and through the use of health products that contain cervid material. There is also the potential for Canadians to be exposed to cervids through farming, slaughter, antler velvet harvest, as well as through field dressing of hunted animals, preparing trophies, taxidermy and/or the use of cervid-derived materials (e.g., urine) as hunting lures. While monitoring and control programs are in place to reduce the likelihood that cervids known to be infected with CWD reach the marketplace, the possibility cannot be excluded that some of these sources of exposure may be derived from animals with CWD due to limitations in current CWD diagnostic testing capabilities.

Cervid meat is available in many of the same cuts and processed meat products as for other meat products. While consumption survey estimates for the general Canadian population (2015 Canadian Community Health Survey) indicate that overall venison consumption is quite low, there are known subpopulations, including rural and Indigenous populations that have higher dietary exposures to this food. In addition, populations that rely on cervids as an important source of protein and for cultural reasons are more likely to hunt and/or consume wild cervids (12).

There are no human biologics or genetic therapies licensed in Canada that contain ingredients of cervid origin, and it is considered unlikely that cervid materials or cervid derived ingredients would be used in the manufacture of these human therapeutic products, including medical devices. There are approximately 200 licenced natural health products (NHPs) that contain ingredients of cervid origin such as antler velvet.

Impact of Emerging Research on Human Health Risk Assessment:

HPFB continues to review and monitor scientific literature related to CWD, as well as emerging research related to the potential transmissibility of CWD to humans. At this time, there is conflicting evidence on the potential transmissibility of CWD under experimental conditions. In 2017, preliminary findings from a CFIA led research project indicated that CWD can be transmitted to non-human primates via different exposure routes (13). These findings suggest that CWD, under specific experimental conditions, has the potential to cross the species barrier. These experimental results have not yet been published in the scientific literature. In 2018, a study published in the Journal of Virology found no evidence that CWD could be transmitted from cervids to macaque monkeys following a lengthy investigation by National Institutes of Health scientists exploring risks to humans (14). Experiments using transgenic mice that express the human prion protein (humanized) have also been unable to show definitive evidence for zoonotic transmission (15, 16).

Additional studies are currently underway to determine if experimental exposure to CWD prions can result in producing a prion disease in macaque monkeys (17). It is well recognized that research into CWD is a long-term undertaking. For example, it has been postulated that for non-human primates orally exposed to CWD, disease symptoms would be detected or observed between 10 to 18 years post infection.

In the absence of definitive information related to the transmissibility of CWD to humans, and in light of the accepted evidence that BSE has transmitted to humans (vCJD), HPFB is taking a precautionary approach with respect to CWD and other TSEs that is in agreement with the WHO's current recommendation that "No tissue that is likely to contain the BSE agent, nor part or product of any animal which has shown signs of a TSE should enter the (human or animal) food chain." This precautionary approach also aligns with the recommendations from two comprehensive reviews on CWD published in 2019 (5, 6).

HPFB continues to recommend avoiding consumption and use of products from known infected or any diseased animals, and taking precautions when handling and processing cervids (17). In addition, in areas where CWD has been

detected, continued and consistent risk communication messages should be provided to groups who may be exposed to CWD-infected cervids through harvesting, hunting, slaughter and consumption (7, 12, 18, 19).

As the range and prevalence of CWD increases, so does the potential for human exposure to CWD prions. HPFB supports disease control policies that limit the spread of CWD geographically, and thus, limits exposure to humans. The efforts of Federal, Provincial and Territorial governments to improve management practices for both farmed and wild cervids in Canada should be continued.

Current animal disease control policies support the diversion of known CWD-infected animals away from the marketplace. However, there are testing limitations since current CWD tests are surveillance and monitoring tools which are validated only for specific target tissues (e.g., brain and retropharyngeal lymph nodes) (20). While a negative test result does not guarantee that an individual animal is not infected with CWD, it may reduce the risk of exposure to CWD (7). HPFB supports CWD and TSE research that is focussed on transmissibility, zoonotic potential, and the development of rapid and reliable detection methods (Annex 1).

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Annex 1. CWD Research Plans

There remains considerable scientific uncertainty related to the potential risk to humans. Research is needed to address evolving science and emerging findings linking CWD to possible human health outcomes. HPFB's Food Directorate is planning to continue the following targeted research activities that focus on determining the potential transmissibility of CWD to humans:

- Development of a repetitive non-invasive ante-mortem test for detection of CWD in asymptomatic CWD exposed non-human primates (macaques)
- Surveillance of asymptomatic non-human primates (macaques) orally and blood transfusion exposed to various Canadian CWD isolates initiated under Health Canada's CWD research study
- Exposure of specific strains of North American CWD known to have transmitted CWD to humanized mice models to non-human primates (macaques)
- Exposure of specific strains of North American CWD known to have transmitted CWD to porcine to non-human primates (macaques)
- Investigation of potential transmissibility of Canadian BSE with no detectable PrPres to non-human primates (macaques)

Research activities undertaken by Health Canada will support improved risk assessment and diagnosis capacity. Ongoing research efforts related to CWD will also provide the information required to confirm or adjust the current CWD control policies in Canada as well as the advice communicated to Canadians on the potential risks posed by CWD.

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