Evaluation of the Alberta Prion Research Institute

Final Report

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Table of Contents

Acronyms ii

Acknowledgements ii

Executive Summary iii

1.0 Introduction 1

1.1 Overview of the Alberta Prion Research Institute 1

1.2 Objectives of the Evaluation 3

1.3 Evaluation Methodology 4

1.4 Limitations 5

2.0 Findings 7

2.1 Is APRI Answering a Current and Continuing Need? 7

2.2 Has APRI been Responsive to Shifts in the Disease and Scientific Landscape? 10

2.3 What is APRI's Role in the Research Ecosystem? 11

2.4 What is the Alignment between APRI and Provincial Priorities? 12

2.4 Has APRI Achieved its Expected/mandated Outcomes? 14

2.5 What are the Barriers/facilitators to Achieving APRI's Goals? 29

2.6 How can APRI be more Efficient? 30

3.0 Conclusions 33

Appendix A: Logic Model 35

Appendix B: Evaluation Matrix 36

Appendix C: APRI Performance Metrics 41

Acronyms

AARP	Alberta Alzheimer Research Program
ALMA	Alberta Livestock and Meat Agency
APRI	Alberta Prion Research Institute
ARC	Alzheimer's Research Committee
ARIF	Average of Relative Impact Factors
BSE	Bovine Spongiform Encephalopathy
CJD	Creutzfeldt-Jakob Disease
CWD	Chronic Wasting Disease
EDTT	Economic Development, Trade and Tourism
HCPs	Highly Cited Publications
IRAC	International Research Advisory Council
SI	Specialization Index
TSEs	Transmissible Spongiform Encephalopathies
WAFWA	Western Association of Fish & Wildlife Agencies

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Executive Summary

This report presents the results of the Evaluation of the Alberta Prion Research Institute (APRI) which was conducted in 2019 for Alberta Innovates. Funded by Economic Development, Trade and Tourism (EDTT), APRI supports research that is meant to generate new knowledge and innovations to minimize risk and the impacts of potential outbreaks related to prion diseases. APRI funds research to advance the prevention, mitigation and treatment of prion and prion-like protein misfolding neurodegenerative diseases.

The evaluation of APRI has three main areas of focus: relevance; effectiveness; and efficiency. The period under study is 2005 to the present, with a focus on the Institute's most recent years (from 2015 to 2019) where relevant. The evaluation is based on multiple lines of evidence, including a review of documents/data, key informant interviews, a survey of APRI-funded lead researchers, survey of trainees and case studies of three APRI initiatives (the Alberta Alzheimers Research Partnership (AARP), APRI funding for core research infrastructure; and APRI-funded research on chronic wasting disease, including the impact on management practices).

Relevance

The evaluation evidence confirms the ongoing need for research on prions. Animal prion diseases, particularly CWD, are recognized as a threat to the agricultural sector, with the potential to impact human health. Human neurodegenerative diseases such as Alzheimer's disease have a known prion component and the public health concern associated with this disease is expected to increase with an aging population. Yet, there is much that is still unknown about prions and the evaluation founds that APRI's areas of research focus have been appropriate to respond to knowledge gaps related to CWD, and research contributing to advancing new or improved diagnostics for Alzheimer's. APRI's sustained funding of prion research has also led to the development of an Alberta-based specialization in prions has drawn the attention of other countries experiencing incidences of CWD.

APRI is well-aligned with Alberta's overarching framework for research and innovation in the province – the Alberta Research and Innovation Framework. APRI's research focus and broad mandate covering animal, ecosystem and human health are difficult to align with a single ministry funder, however, and decision-makers are not well-aware of the potential indirect benefits of addressing CWD in protecting the agricultural industry from the negative economic impacts of potential trade restrictions.

Performance

During the period under study, APRI reported annually on targets related to capacity building, and knowledge generation and mobilization. APRI achieved or surpassed all performance metrics identified in its 2015 funding agreement, indicating that Alberta realized or exceeded the

expected return on this investment. With an almost 1:1 ratio of leveraged funding, APRI has funded, co-funded or leveraged almost $130M in prion research in the province. There are examples where APRI's funding has laid the foundation for successful applications to national, international and philanthropic research granting agencies.

The dedicated research and infrastructure funding has built research capacity, including attracting researchers to Alberta that form a multidisciplinary centre of excellence for research on prions. According to researchers, the infrastructure supports have expanded the nature and accuracy of experimentation into prion diseases. There has been significant training of new researchers in the field, as well as diverse career enrichment activities. Trainees confirm that APRI grants have supported a high quality training and research experience that has impacted their subsequent research and career decisions.

APRI research is generating new knowledge in prions and protein misfolding. Researchers and the bibliometric analysis confirm that Alberta is a strong contributor to Canada's overall research output related to prions and protein misfolding. APRI and funded researchers have established diverse partnerships with stakeholders including other researchers internationally, as well as the end users of research (government policy makers and local health and industry organizations). These partnerships were noted as important contributors to the success of funded research.

There are efforts to proactively disseminate research findings through partnerships and more broadly to scientific and lay audiences through various means such as patents, workshops, publications and public lectures. Among APRI's funded research projects, there are many examples of high quality and transformative research (e.g., transmission across species, vaccination), as well as examples of applied research projects informing the development of policy and regulations (e.g., CWD management practices).

Over time, the bibliometric analysis shows a trend toward decreasing impact in terms of citation indicators, although these data also show that APRI funds leading researchers with citation indicators well above world levels. Citation indicators, while indicative, may not be capturing research impact of APRI's spectrum of projects, including translational research and the work related to Alzheimer's.

Design and Efficiency

The evaluation found that APRI is an effectively-managed and responsive organization with strong scientific and organizational leadership. At 11% on average, the operational expenditures for the Institute have decreased over time. The suite of funding opportunities are similar to other research entities and the application and review processes are well-regarded and reflect the practices of other research granting entities. Advisory committees for APRI and AARP have been assets in ensuring research excellence and improving the quality of grant applications. There were suggestions for APRI to improve its communications function and streamline reporting requirements.

Recommendations

Based on the evaluation findings and conclusions, recommendations include:

1. APRI should consider increasing attention to the communications function, including developing a strategy to more effectively convey messages to provincial officials, media and industry regarding:
   - The threat of prion and prion-like misfolding diseases and the potential economic and human costs of these diseases; and
   - APRI's early impacts on CWD management policy and practices.

2. Maintain the dual focus on prion and prion-like human neurodegenerative diseases (the latter being dependent on the partnership with the Alzheimer Society)

3. Continue to pool resources, seek co-funding from industry organizations and jurisdictions impacted by prion diseases (especially CWD)

4. Ensure that there are resources and referrals available to transition researchers to other forms of support to capture the benefits of discovery (patent, pre-commercialization)

1.0 Introduction

This report presents the results of the Evaluation of the Alberta Prion Research Institute for Alberta Innovates. The evaluation was designed to provide comprehensive and reliable evidence to support decisions regarding continued funding and delivery of APRI.

1.1 Overview of the Alberta Prion Research Institute

Context

Prions are misfolded proteins which are infectious and self-replicate in tissue (especially brain tissue), causing fatal neurodegenerative diseases including transmissible spongiform encephalopathies (TSEs), for which there are no known treatments. Prions are associated with bovine spongiform encephalopathy (BSE) in cattle, which gravely impacted Alberta's agricultural sector during the 2003 BSE crisis and chronic wasting disease (CWD) in cervids which is becoming an increasing threat in Alberta. In humans, prions are associated with Creutzfeldt-Jakob disease (CJD), and misfolded proteins are also involved in neurodegenerative diseases such as Alzheimer's, Parkinson's and Huntington's that present similarities to prion diseases.

In April 2005, the Government of Alberta created the Alberta Prion Research Institute (APRI or the Institute) in response to the BSE crisis. Prion proteins are complex to study and APRI supports research that is meant to generate new knowledge and innovations to minimize risk and the impacts of potential outbreaks.

Alberta Prion Research Institute Programs

APRI is committed to the prevention, mitigation and treatment of prion and prion-like protein misfolding neurodegenerative diseases. The Institute achieves its mandate by supporting top researchers and innovation through:

- investing in the development of fundamental and applied research on BSE, CWD and other prion and protein misfolding diseases;
- increasing research capacity and expertise in Alberta through providing funding for facilities, equipment and collaborations;
- developing highly qualified people who are able to tackle complex issues like prions and other challenges in Alberta; and,
- facilitating knowledge mobilization by organizing events for Albertans, industry, and the research community, both domestic and international, to discuss latest research being done in Alberta and possible opportunities for collaboration.

The pathway to impact for the Institute is included in Appendix A.

APRI focuses its funding opportunities in the four following areas of research:

- Protein folding and misfolding;
- Pathobiology of TSEs;
- Surveillance and control; and
- TSEs and society.

The Institute offers direct research funding through its programs including its Explorations and Specified Risk Materials Program, and it also supports partnerships and cross-sectoral collaborations, namely through its New Collaborations, Research Team, IDeal and Research and Policy Fellowship Programs. The Institute also offers funding programs for knowledge transfer and career development activities, with its Guest Speaker Support and Mobility Programs for researchers and highly qualified people.

APRI has participated in two co-funding partnerships. In 2009, APRI and the Alberta Livestock and Meat Agency (ALMA) established a partnership, including PrioNet Canada to co-fund research in a number of areas relevant to the livestock industry.

In 2012, APRI entered into a partnership with the Alzheimer Society of Alberta and Northwest Territories to enhance research funding of prion-like protein misfolding neurodegenerative diseases through the Alberta Alzheimer Research Program (AARP). The AARP provides funding to investigators conducting Alzheimer's disease research in areas related to understanding the fundamental mechanisms related to the prion-like characteristics of the disease and controlled intervention trials to improve the quality of life for those with Alzheimer's disease.

Organization and Resources

APRI is situated within Alberta Innovates (AI) which is an agency of Alberta Economic Development, Trade and Tourism (EDTT). APRI has a small staff of three positions responsible for the administration of research funding opportunities and knowledge mobilization programs. The APRI Executive Director reports to the lead Executive Director of AI Biosolutions who in turn reports to the Chief Executive Officer of AI.

Application to APRI's research funding opportunities are submitted through a call for applications process. Applications are assembled by APRI staff and reviewed by the volunteer International Research Advisory Council (IRAC) which is composed of experts in the prion research field from around the world. Based on their review of the scientific merit of the applications, the IRAC makes recommendations for funding. The IRAC also regularly reviews and monitors the status of research projects. Applications for funding that are submitted to the AARP are reviewed by an independent AARP Review Committee (ARC). ARC members bring the highest level of expertise in Alzheimer's disease and other dementias. There is overlap in membership between IRAP and ARC to ensure consistency in the quality of reviews across all competitions. While the research

approaches that were eligible for funding under the AARP included both Fundamental mechanisms[1] and Quality of life[2], only projects related to the former were funded.

For the period 2014-2015 to 2019-2021, AI received a grant of $27.5M from the then Ministry of Innovation and Advanced Education for APRI (**Table 1**). As mentioned above, additional resources for prion research have been secured from co-funders ALMA (now Alberta Agriculture and Forestry), Alzheimer Society of Alberta and Northwest Territories (AS AB NT), Genome Canada and Genome Alberta. Before 2014-15, the former Networks of Centres of Excellence PrioNet was also a co-funder. The vast majority of funds are dedicated to APRI's research funding opportunities.

Table 1: APRI Expenditures: 2014-15 to 2018-19

Expenditure	2014-15	2015-16	2016-17	2017-18	2018-19
Operating Expenditures	$680,390	$709,527	$653,323	$702,341	$523,358
Peer Review, committee	$28,711	$104,732	$230,029	$260,887	$82,932
Communications, education, outreach, conference	$270,442	$118,039	$85,124	$111,652	$110,160
Total research funding	$4,604,837	$4,203,912	$3,993,193	$4,199,206	$5,667,761
APRI Funding Opportunities	$3,699,031	$2,528,127	$3,034,557	$3,116,933	$5,389,112
Research co-funding (AARP)	$286,888	$815,065	$804,378	$830,727	$278,649
Research co-funding (ALMA)	$618,918	$860,720	$154,258	$251,547	$0
Infrastructure funding	$100,000	$849,860	$1,443,417	$2,251,031	$1,499,410
Total Prion Expenditures	$5,684,381	$5,292,810	$5,654,928	$6,774,654	$6,384,210

Source: APRI Financial Records

1.2 Objectives of the Evaluation

All APRI research and related programs funded by EDTT are included within the scope of this evaluation. The scope of the evaluation is 2005 to the present, with a focus on the Institute's most recent years (from 2015 to 2019) where relevant.

The evaluation of APRI has three main areas of focus: relevance; performance; and design and efficiency. Four evaluation questions guided the evaluation.

[1] Fundamental studies of molecular and cellular mechanisms in Alzheimer's disease that take into account the protein misfolding and prion-like properties of Alzheimer's disease pathobiology

[2] Controlled trials to determine the effectiveness of specific interventions to improve the quality of life of persons with Alzheimer's disease. Only one proposal focusing on quality of life was received, and it did not meet review quality standards

Relevance

1. Is APRI answering a current and continuing need?
2. Has APRI been responsive to changes in the disease and scientific landscape?
3. What is APRI's role in the research ecosystem?
4. What is the alignment between APRI and provincial priorities?

Performance

5. Has APRI achieved its expected/mandated outcomes?

   Immediate Outcome: Increased Research Capacity

   Immediate Outcome: Increased research collaboration and partnerships

   Immediate Outcome: Increased knowledge generation and dissemination

   Intermediate Outcome: Mobilization of knowledge through adoption, application, implementation

   Ultimate Outcome: Prevention, risk management and treatment of prion diseases in humans and animals

Design and Efficiency

6. What are the barriers/facilitators to achieving APRI's goals?
7. How can APRI be more efficient?

1.3 Evaluation Methodology

To ensure a valid assessment of APRI, the evaluation used multiple lines of evidence, including both qualitative and quantitative methods, and gathered input from various perspectives (e.g., APRI management and staff, IRAC, partners, researchers and trainees). The evaluation was guided by an Evaluation Advisory Committee comprised of representatives from the funders and APRI. The lines of evidence for the evaluation included:

- ***Document review/environmental scan***: A review of Institute (e.g., annual reports, funding agreement, financial data) and Ministry documents was conducted to understand the objectives and delivery of APRI and contribute to assessing the relevance and performance of the Institute. Grey literature (i.e., government, industry commentary) related to prion diseases was also reviewed to help address questions related to relevance. A focused environmental scan examined other research centres/institutes similar to APRI to consider opportunities for improvement.

- ***Interviews with key informants*:** Interviews with 26 key informants were conducted to gather in-depth views related to the evaluation issues and questions. Respondents included AI/APRI representatives, IRAC members, experts, and APRI-funded researchers.
- ***Survey of lead researchers*:** An online survey of APRI-funded lead researchers was conducted to gather views related to their satisfaction with APRI funding mechanisms and research outputs and impacts. A total of 36 funded researchers completed the survey for a response rate of 51%.
- ***Survey of trainees:*** An online survey was conducted of trainees who had been funded directly or indirectly by APRI. In total, 58 trainees completed the survey for a response rate of 24%.
- ***Case studies*:** Three case studies were completed to examine selected aspects of APRI's funding activities in more detail: AARP, funding for core infrastructure; and APRI-funded CWD research, including the impact on management practices. Case studies involved a review of documentation, as well as interviews of researchers and stakeholders, where relevant.
- ***Bibliometric analysis***: A bibliometric analysis was commissioned from Science-Metrix to assess the research productivity and impact of scientific publications by APRI-funded researchers. The publications were extracted from the Scopus database and include articles, reviews and conference papers covering the core research on prion and protein misfolding, as well as publications in all fields and subfields of research. The impact of APRI-funded researchers, Alberta universities and the province in prion and protein misfolding research was examined in comparison to other provinces, other countries and over time. The analysis focused on five indicators: number of papers; average of relative citations (ARC); average of relative impact factors (ARIF); Highly Cited Publications (HCPs); and Specialization index (SI).

1.4 Limitations

The evaluation is based on a strong evidence base drawing from performance data maintained by APRI and primary data collection with stakeholders. However, the following limitations of the evaluation and mitigation strategies should be noted:

- ***Research impact may materialize only over a long period of time:*** As a research funding agency, the impacts of APRI's investment may be realized only in the longer-term and fall outside the time period for the study. Discovery or bench research investments can reach the translation phase over decades. This limitation was mitigated by including interim measures of success such as publications and ensuring applied research projects were examined in the evaluation which have a shorter time horizon for achieving impacts.
- ***Potential for positive response bias in key informant interviews as most respondents were invested in the Institute or in prion research***: The prion research community is relatively small – those who are knowledgeable about APRI are also likely to have been funded by or collaborated with APRI or have been a member of the APRI review process. This limitation

was mitigated by the use of bibliometrics which provides a more objective assessment of research productivity and impact.

- ***Volatility in the survey and bibliometrics measures due to the focused nature of the prion research field***: The survey sample size is too small to disaggregate responses by research area. Where differences are noted for AARP researchers, these should be treated with caution. For the bibliometric analysis, indicators are more open to variations across time periods compared to assessing output and impact of a larger funding program or broader field of study. In addition, bibliometrics is a more appropriate measure of discovery research projects and less so for projects funded by APRI that focus on applied or field research. The bibliometric data, therefore, has been triangulated with other lines of evidence where appropriate.

2.0 Findings

2.1 Is APRI Answering a Current and Continuing Need?

SUMMARY: A thriving Canadian and Albertan agricultural sector depends on the confidence of the export market. Lessons from the BSE crisis in the early 2000's show that trade restrictions can have a devastating effect on industry and experts now see the potential for CWD – a more virulent prion disease – as posing similar risks to animal health. CWD also has the potential to impact human health. Human neurodegenerative diseases that have a prion-like component such as Alzheimer's disease are a current health concern, which is expected to increase as the population ages. The evaluation evidence suggests that APRI is responding to a need to address knowledge gaps related to CWD, and advance understanding of the prion component of Alzheimer's, contributing to new or improved diagnostics. Early diagnosis leads to timely access to therapies and practical mitigation tools and supports.

While BSE has been controlled, prion and prion-like diseases remain a risk to the agricultural sector and potential human health.

APRI was established in 2005 in response to the BSE crisis which severely and negatively impacted the Canadian and Albertan beef industry. Since that time, BSE is now controlled and the industry has largely recovered. Today, agriculture is a key and growing sector in Canada and in Alberta, accounting for 6.7% of GDP in Canada in 2016, with exports of $56B. [3] The sector represents 1.4% of Alberta GDP[4] and Alberta's agriculture industry increased 13.6 per cent to $3.7 billion in 2016[5]. In a recent report on the future growth prospects for the Canadian economy, agriculture was identified as key sector and export improvement opportunity for Canada to become the 'trusted global leader in safe, nutritious, and sustainable food in the 21st century'.[6] The report recommended continued investment in the agriculture sector as part of a new approach to focused sectoral development.

At the same time, research suggests that there continues to be risks associated with prion diseases, specifically CWD, yet the causes and mechanisms of prion diseases such as CWD remain

[3] Agriculture and Agri-food Canada, An Overview of the Canadian Agriculture and AgriFood System, November 2016. http://www.agr.gc.ca/eng/about-us/publications/economic-publications/an-overview-of-the-canadian-agriculture-and-agri-food-system-2017/?id=1510326669269#a3
[4] Government of Alberta, Industry Profiles 2018, Agricultural Industry. https://work.alberta.ca/documents/industry-profile-agriculture.pdf
[5] Agri-food statistics update, issue no: GDP17-1
[6] Advisory Council on Economic Growth, Unleashing the growth potential of key sectors. (2017, February 6). Retrieved from https://www.budget.gc.ca/aceg-ccce/pdf/key-sectors-secteurs-cles-eng.pdf

largely unknown.[7] A research priority for APRI for many years, CWD is becoming an increasing concern given the contagious nature of the disease, wide-ranging migration of infected wild animals, and the persistence of CWD when prions are shed in the environment.[8] The incidence and prevalence of CWD are increasing; as of 2018, CWD was detected in farmed and wild herds in Alberta, Saskatchewan and Quebec, and internationally in the US, Scandinavia and Korea. Troubling new research (funded by APRI) has demonstrated that there can be transmission of CWD between species and that there is at least the potential for CWD to infect humans, particularly as there is human consumption of cervids such as deer and elk.

To date, there is no effective treatment or preventative interventions for CWD. With the increasing threat of the disease, the Ontario Federation of Anglers and Hunters organized a conference in March 2019 focused on CWD. The conference brought together over 50 CWD interested organizations from various sectors and over 200 attendees "to raise awareness and to build a strong coalition that can push for CWD action".[9] The increased prevalence and spread of CWD also led a coalition of 30 organizations and researchers to submit an open letter to the Prime Minister and Cabinet Ministers in June, 2019 urging funding and action to mitigate the spread of this prion disease.[10] In the letter, the signatories warn that "CWD presents profound threats to wildlife and the environment, to agriculture and international trade, to Indigenous rights, traditions, treaties, food security, and, potentially, to human health".

During the BSE crisis in early 2000's, the incidence of BSE led more than 40 countries to close their borders to imports of Canadian beef. Borders did not begin to open until 2007 with devastating impacts to the industry. The more immediate economic losses of the crisis were estimated to be between $4 and $11B, Governments spent almost $2 billion in farm assistance and recovery of the industry in Alberta was slow.

There are some early indicators of the potential for economic impacts of CWD.

The BSE crisis, which led to trade restrictions on Canadian beef, offers lessons on industry vulnerability when export markets lose trust in the commodities and, motivated by competitive advantage, exercise 'an abundance of caution' in re-opening markets.[11] Threats to livestock and crop exports from CWD have already occurred; in 2018, Norway adopted regulations requiring feed hay and straw crop from Canada and the US to be certified as harvested in a province or state where no CWD has been detected. In response, jurisdictions (e.g., Manitoba) are taking steps

[7] T Onodera, T Nishimura, K Sugiura - Prions, 2019 - Future Perspectives on Prior Diseases nature, Caister Academic Press, 2019
[8] Geist, V., Clausen, D., Crichton, V. and Rowledge, D. (2017). The Challenge of CWD: Insidious and Dire. Manitoba Wildlife Federation. Retrieved from https://mwf.mb.ca/wp- content/uploads/2017/03/CWD-Comprehensive-Analysis-LR-14March.single-page-versionpdf.pdf.
[9] https://www.ofah.org/2019/03/ofah-focuses-2019-conference-saving-deer-cwd/
[10] Cashman, N., Lucas, A., Schaetzl, H., Sockett, P., Gilch, S., Osterholm,… Bouzan, A. Open Letter to the Rt. Hon. Prime Minister Trudeau and Cabinet Ministers, June 17,2019, June 17Retrieved from https://mwf.mb.ca/wp-content/uploads/2019/06/CWD-Ltr-to-PM-Ministers-CWD-June-2019-1.pdf
[11] Gregory Mason, Mad Cow crisis holds surprising lessons, Winnipeg Free Press, January 6, 2017; Canadian Agricultural Trade Policy Research Network, The Losses in the Beef Sector in Canada from BSE, September 2006. http://www.uoguelph.ca/catprn/PDF-CP/Commissioned_Paper_2006-5_LeRoy.pdf

through regulations and management practices to stay CWD-free. In order to avoid dire economic consequences seen during the BSE crisis, the coalition of experts argue for precautionary policies, an emergency response plan and additional research investments.

From a human health perspective, neurodegenerative disease with a prion link – Alzheimer's, Parkinson's, CJD – cause public health concern and a significant human and economic burden.

A number of neurodegenerative diseases have been found to have a prion link; Dr. Stanley Prusiner, the researcher who originally identified the prion protein as the cause of Creutzfeldt Jakob Disease, now categorizes Alzheimer's disease as a prion disorder in which two proteins work together to "destroy the brain"[12]. Diseases such as Alzheimer's and Parkinson's and CJD are devastating diseases that are expected to have an increasing prevalence due to Canada's aging population. According to the Alberta Dementia Strategy and Action Plan, 42,000 Albertans were living with dementia as of 2016, and the number of diagnosed cases is expected to increase to over 155,000 within the next 30 years. The human and economic burden associated with these diseases is significant. Recent research confirms that considering direct and indirect costs, as well as intangible costs related to quality of life, Alzheimer's disease and related dementias is one of the costliest diseases at a societal level and predicted to be unsustainable over time without risk factor reduction, early detection, novel therapeutics, and integrated care and support paradigms.[13]

At present, there is limited understanding on why misfolded proteins occur and spread, and why the impact on humans can vary greatly. Research funded by AARP (Fundamental Mechanisms stream) is exploring these issues at the molecular and cellular level for new or improved diagnostics. Early diagnosis has been identified as important for people with dementia in order to receive timely access therapies that may improve cognition, as well as practical information, advice and support. Early detection also reduces other safety risks associated with dementia and can delay institutionalization.[14]

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[12] University of California San Francisco. *Alzheimer's Disease is a 'Double-Prion Disorder', Study Shows.* May 1, 2019.

[13] El-Hayek, Y. E., Wiley, R. P., Khoury, C., Daya, R., Ballard, C., Evans, A., … Alireza, A. (2019, July 23). Tip of the Iceberg: Assessing the Global Socioeconomic Costs of Alzheimer's Disease and Related Dementias and Strategic Implications for Stakeholders. *Journal of Alzheimer's Disease*, *70*(2), 323-341. doi: 10.3233/JAD-190426

[14] https://alzheimer.ca/sites/default/files/files/national/core-lit-brochures/importance_early_diagnosis_e.pdf

2.2 Has APRI been Responsive to Shifts in the Disease and Scientific Landscape?

SUMMARY: The evaluation evidence suggests that APRI has funded research in areas of importance in the field, including a focus on CWD and diverse projects that range from fundamental to applied research and engage a variety of disciplines. There is broad approval for the Institute's focus on prion and prion-like protein misfolding diseases related to human health. The potential to manage CWD in wild and farmed cervids remains uncertain and a question requiring engagement of industry and communities.

APRI is addressing research questions/knowledge gaps related to CWD and prion-like human neurodegenerative diseases through diverse research projects that leverage Alberta researchers' strengths in the field.

APRI's research funding during the period under study has focused on four themes as noted above. While the Institute was established to address research questions related to BSE, over time funding opportunities have increasingly focused on CWD where many knowledge gaps remain and where the potential economic, ecosystem and health impacts are significant.

There was broad agreement among key informants that APRI has funded high quality research across a broad spectrum of research areas (bench/fundamental research, as well as field studies that are more applied/translational). Research projects have also funded scientists in the natural, health and social sciences. Interviewees with expertise in the field commended APRI's funding of novel and cutting edge research in prion disease, especially CWD transmission, therapeutic approaches such as vaccination and new detection methods. APRI's Explorations Program – a specific funding opportunity for higher risk or exploratory research – was praised by several key informants as highly valuable. Some researchers used this grant to propel research in novel concepts and theories and a springboard to securing larger grants from other sources.

With respect to the co-funded AARP program with the Alzheimer Society of Albert/NWT, although a few researchers noted that APRI should not depart from its focus on 'genuine' prion research, most key informants viewed research related to prion-like human neurodegenerative diseases as a promising line of inquiry. Alzheimer's is the most prevalent human disease with a prion-like component and key informants noted the important synergies between the prion research tools, methods and techniques and investigation into early detection of the disease. These interviewees observed that AARP has funded research in areas of importance in the field, including projects in both basic research and applied translational research such as understanding mechanisms of the disease for new or improved diagnostics. Key informants indicate that the distinguishing focus of AARP is that grants are provided to focus on the prion-like component of the disease, whereas other health research funding agencies may focus on neuro inflammation and other aspects of Alzheimer's diseases.

There continue to be knowledge gaps related to prion and prion-like diseases and many potential future research priorities.

The secondary sources and interviews with experts confirm that while progress has been made in advancing research on prions, many questions remain. These include both fundamental research questions such as the properties of different CWD prion strains and the zoonotic potential of strains of CWD prions to applied questions related to the management of CWD given its highly contagious nature.

There was no evident consensus on the views of surveyed researchers on future priorities for the Institute. Surveyed researchers identified a number of future research priorities, with comments supporting both sustained attention on CWD as well as prion-like neurodegenerative diseases. In addition to understanding the biochemical processes related to prions, a number of researchers echoed the importance identified above of translational research to advance strategies to manage CWD, including greater partnership with industry and engagement at the community level (e.g., with Indigenous communities).

The relatively smaller AARP funding envelope and shorter timelines was noted by some key informants as supporting "high risk" early research that is necessary as researchers endeavour to understand the cause and effect of protein misfolding on humans. A few key informants stated that AARP funding complements other funding sources as it has served as a facilitator of early research that has allowed researchers to successfully apply for other grants such as from the Canadian Institutes of Health Research (CIHR) and other international and philanthropic granting agencies, bringing in funding from these highly competitive and larger funding envelope organizations for greater capacity to further advance prion-like neurodegenerative disease research.

2.3 What is APRI's Role in the Research Ecosystem?

SUMMARY: As funding for prion and prion-like research has reportedly declined or shifted in Canada and internationally, APRI has helped to sustain scientific attention on prions, including prion-like protein misfolding human degenerative diseases. The development of Alberta-based specialization in prions has drawn the attention of other countries experiencing incidences of CWD.

In Canada and internationally, prion research funding and output is declining or has shifted focus to prion-like or health related prion research. APRI provides a dedicated source of funding for Alberta-based researchers working in the prion and prion-like disease fields that have supported a specialization in the field that is recognized internationally.

The evaluation evidence indicates that APRI is a valued and dedicated source of research funding in a field where, according to some key informants, other countries have reportedly reduced or shifted the focus of prion research funding. The bibliometrics data show an international decline in prion research output (with some exceptions – China, Korea, India, Brazil).

In Canada, there is some federal funding available for prion and prion-like disease research through the federal research granting councils and Genome Canada and there is prion research being conducted in other provinces (Ontario and BC particularly). This funding is typically focused on discovery and less so on applied or translation field studies that are also funded by APRI. Among surveyed researchers, however, all said their research program would not have been carried out without APRI funding with the same scope and timeframe (75% said their research program would not have been carried out at all). The AARP case study found that this funding opportunity provided important resources for foundational data supporting researchers' subsequent applications for larger grants from other funders such as CIHR.

APRI's funding opportunities have contributed to a recognized specialization in the field. The bibliometrics data indicate that Canada is a leading country in terms of specialization in prion research and Alberta is leading within Canada as a focal point for prion and protein misfolding research. Canada currently produces about twice the number of prion publications that would be expected given its share of the world scientific production across all research fields (Specialization Index of 2.1). Alberta's Specialization Index in relation to world scientific production is 6.85, surpassing all other provinces. This specialization has translated into European nations that have detected CWD looking to Canada and Alberta for expertise to inform their response.

Leveraging prion research tools, techniques and methods for prion-like neurodegenerative diseases is a distinctive approach in this important but vast research field.

APRI's partnership with the Alzheimer Society of Alberta/NWT has reinforced APRI's mandate in the area of investigating prion-like protein misfolding. Strengths in the prion research field have been found to be transferable to the study of Alzheimer's, particularly in the area of early diagnosis. According to interviewees, targeted funding opportunities under the AARP build on research strengths in the province that have developed by APRI since its inception.

2.4 What is the Alignment between APRI and Provincial Priorities?

SUMMARY: APRI's investments in discovery research are aligned with Alberta's framework guiding research and innovation. However, a mandate that supports the priorities of several ministries (i.e., those concerned with animal, ecosystem and human health) creates challenges in alignment with the priorities of its current funder.

APRI is broadly aligned with the Alberta Research and Innovation Framework, however, because of its cross ministry focus and benefits related to mitigation of economic risk rather than economic benefits, APRI's link to EDTT's agenda related to diversification and economic benefits is less clear.

Since 2005 when APRI was established, the organizational home of the Institute has shifted several times. The prion science initiative was initiated under the Ingenuity Centre Program. In January 2010, with the creation of Alberta Innovates, APRI was included within the Bio Solutions business line, and prion and prion-like neurological diseases were identified as a priority area under the Alberta Innovates Bio Solutions 2012-15 Business Plan. In October 2015, the new Ministry of EDTT was established[15], subsuming Alberta Innovates and entities such as APRI.

The mandate of EDTT with respect to research is focused heavily on innovation and bringing technologies to market. Ministry responsibilities in this sphere are stated as "coordinating and leveraging research and innovation to increase the commercialization of Alberta ideas and meet the needs of Albertans". Alberta Innovates, as a key service area of EDTT, is mandated to "deliver 21st-century solutions for the most compelling challenges facing Albertans" and the 2018-21 Business Plan vision is to be "recognized provincially, nationally, and internationally as a leader in catalyzing research and innovation in Alberta".

APRI resides within Alberta Innovates' Bio Sector core area of focus and while the Institute has not focused to a great extent on commercialization, it does have an alignment with the 2017 Alberta Research and Innovation Framework (ARIF). This document articulates the strategic direction for research and innovation for the Government of Alberta. The ARIF Action Plan lays out the shared outcomes for achieving a healthy innovation eco-system in the province, identifying a target to become a top ten location for health and wellness innovations. APRI is among the multi-year, strategic investments to achieve this target. APRI's mandate was confirmed and renewed in 2015 with the six-year funding agreement. Also relevant, the Action Plan establishes an agriculture sector target to strengthen public trust for expanded markets by meeting or exceeding public expectations.

While clearly aligned with the ARIF document, the province's current focus is noted by some interviewees to be moving increasingly toward an emphasis on investments in applied research that can be leveraged toward commercial outcomes, and for EDTT, the focus is on diversification of Alberta's economy and jobs. This trend has been reinforced in the 2019 provincial Speech from the Throne and 2019 Budget. There was some feeling that APRI's scientific research mandate lacks obvious alignment with this evolving economic benefits focus. Others, however, noted that APRI's link to economic benefits for the province is through *mitigation* of economic risks; that is, addressing the risks of a crippled agricultural sector with the spread of CWD and associated trade

[15] Established in 2015 as Economic Development and Trade and subsequently restructured in 2019 to become Economic Development, Trade and Tourism.

restrictions. As well, APRI's development of highly qualified people and attraction of leading scientists to the province can be viewed as providing a spark to innovation.

By virtue of its focus on prions which have impacts on animal, ecosystem and human health, APRI straddles a number of different Alberta ministry domains making it difficult to establish a clear mandate alignment with any single ministry. This is a challenge endemic to other zoonotic and infectious disease areas. New frameworks such as One Health highlight the interconnections between the health of people, the ecosystem and animals. However, funders are often lagging in responding to this more integrated and holistic paradigm.

2.4 Has APRI Achieved its Expected/mandated Outcomes?

Overall, APRI has achieved the outcomes that it was mandated to complete in its agreement with EDTT. The funding proposal commits to a number of performance measures to be achieved by the end of funding in 2021. These outcomes are explored in more detail below, however, with respect of research capacity building, knowledge generation and knowledge mobilization, the Institute is on the way to meeting or exceeding their targets (Appendix C).

2.4.1 Immediate Outcome: Increased Research Capacity

SUMMARY: APRI has been successful in building prion research capacity in Alberta. APRI funding has attracted researchers to Alberta and created a leading multidisciplinary community of over 60 prion experts based in the province. APRI's investments in infrastructure, facility operations and research have created a world-class environment for prion research. APRI has further supported 461 postdoctoral fellow and student positions through research grants/career enrichment activities. The survey of trainees indicates that the quality of the training and research experience is high and confirms that participating in APRI projects has had an impact of trainees' subsequent research undertakings and careers.

APRI funding has helped to attract and retain researchers specializing in prions in Alberta.

APRI continues to be the primary contributor to increased capacity in prion and misfolding protein research in Alberta. Upon the creation of the Institute, there were very few, if any, academic researchers specializing in prions in Alberta. As a direct result of APRI's funding, over 60 leading prion researchers are now based in Alberta investigating CWD, the prion component in Alzheimer's among others. Seven in ten APRI-supported researchers surveyed for the evaluation confirmed that APRI resources influenced them to work on prion research, and half said it played a role in them choosing to locate their research in Alberta (higher among AARP-funded researchers).

Interviewees observed that APRI funding created a world-class centre of excellence and research hub in the province. APRI is described as unique in that it provides funding to support long-term

research endeavors, supports a spectrum of research, and encourages novel research and cross-fertilization between disciplines within the field.

APRI's support for the infrastructure for prion research has been important in building capacity and attracting and retaining world class researchers.

As of 2017-2018, APRI invested about $6.14M in core facilities and their operations at the University of Alberta and University of Calgary. The investment has varied year to year depending on the needs of institutions. In the early years of APRI, infrastructure funding was reportedly focused on investments in facilities and equipment. Later investments have supported costs associated with the continued operations of the facilities. Interviewees noted that APRI's investments in infrastructure have been leveraged to create world class facilities and that this represents one of the major successes of APRI.

- APRI's investment of $1.9 million for a Biosafety Level 2 laboratory space at the University of Calgary was part of a total $4.3 million investment.
- The initial $2 million invested to help establish the Centre for Prions and Protein Folding Diseases (CPPFD) at the University of Alberta was leveraged to $22.9 million for the facility.
- In April 2010, CPPFD at the University of Alberta was certified with the Canadian Food Inspection Agencies certification for contaminant lab handling prion disease agents. The Centre houses more than 23,000 square feet of lab space and provide facilities for 60 researchers and lab technicians.

Funding to the University of Alberta and the University of Calgary to sustain core facilities and technical personnel (e.g., animal care specialists, lab technicians) is reportedly central in attracting expert talent and high-quality research, including the feasibility of more accurate experimentation into prion diseases. Interviewees commended APRI for a funding model that supports both the research and research infrastructure in a coherent way. According to several stakeholders, without dedicated APRI infrastructure funding, the research environment would be impossible to maintain. The facilities that are required to conduct prion research are expensive to establish, and require expertise and sustainable funds to keep them operational. Key informants felt that this would be untenable on a research grant basis. The majority of surveyed lead researchers (75%) indicated that APRI's suite of research funding and other activities meet the needs of researchers for infrastructure and operational capacity (higher among researchers funded under the AARP).

A few stakeholders noted that the facilities that APRI funding has created would also be useful in the event of a new BSE-like crisis, such as is currently evolving with CWD. The facilities offer containment and adequate installations for the study of infectious prions. Overall, key informants interviewed for the evaluation argued that APRI is vital to maintain prion research capacity and that other sources of funding would not be sufficient to support the research ecosystem that has developed in Alberta. The majority of respondents indicated that the research capacity would be

depleted in the absence of APRI funding, and would be difficult to rebuilt once diminished, given the complexity of the subject matter.

APRI has increased research capacity through support for early investigators and trainees. Trainees are exposed to diverse opportunities and most feel that the quality of the training and research experience was high. Two-thirds indicate an impact on their career and research interests.

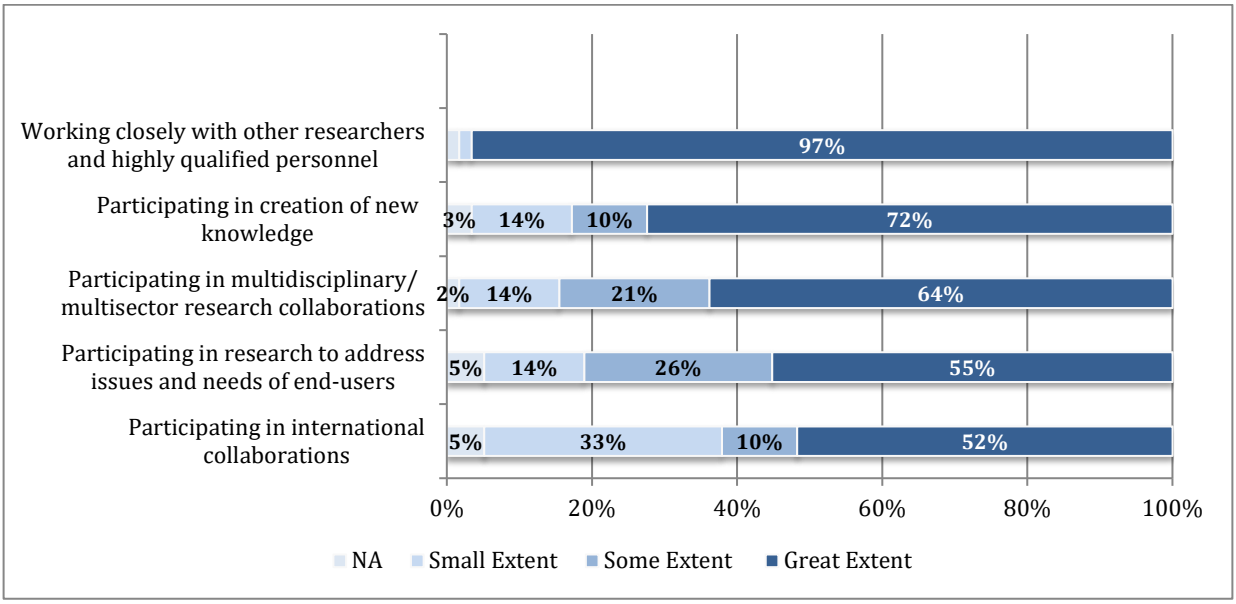
Under the AARP funding opportunity, APRI and the Alzheimer Society have provided grants to the Young Investigator program. This funding stream was noted by key informants to be crucial in building research capacity by helping new investigators to explore creative or high risk concepts that may be transferrable to the field.

As of 2017-2018, APRI has supported 461 postdoctoral fellow and student positions through research grants/career enrichment activities (e.g., networking, conference participation, etc.). All surveyed lead researchers confirmed that their research program involved training of researchers and HQP (i.e., undergraduate students, Masters students, PhD students, post-doctoral fellows, as well as technicians/research associates). Interviewees reported that many grant research applications submitted to APRI prioritize training to build technical and problem solving skills.

Surveyed trainees and personnel broadly indicated that they were exposed to a variety of technical and professional opportunities. Those who participated in APRI-supported opportunities reported that they acquired knowledge on protein folding and misfolding in animal prion diseases (83%), as well regarding protein folding and misfolding in prion-like human neurodegenerative diseases (76%). About two thirds of respondents reported acquiring knowledge on the pathobiology of TSEs, diagnostic technologies, surveillance and control of prion diseases.

Practically all trainees and personnel surveyed reported working collaboratively with other researchers and highly qualified personnel and seven in ten participated in the creation of new knowledge (**Figure 1**). About two-thirds engaged in multidisciplinary collaboration and half took part in international collaboration. Just over half of trainees were involved in research that more directly addressed the needs of end-users. In another question, fewer still indicated that they participated in post-research developments involving changes in end-user practices and protocols (25%) or policy/regulatory changes (20%). Overall, three-quarters or more of trainees were satisfied with the quality of their research and training experience.

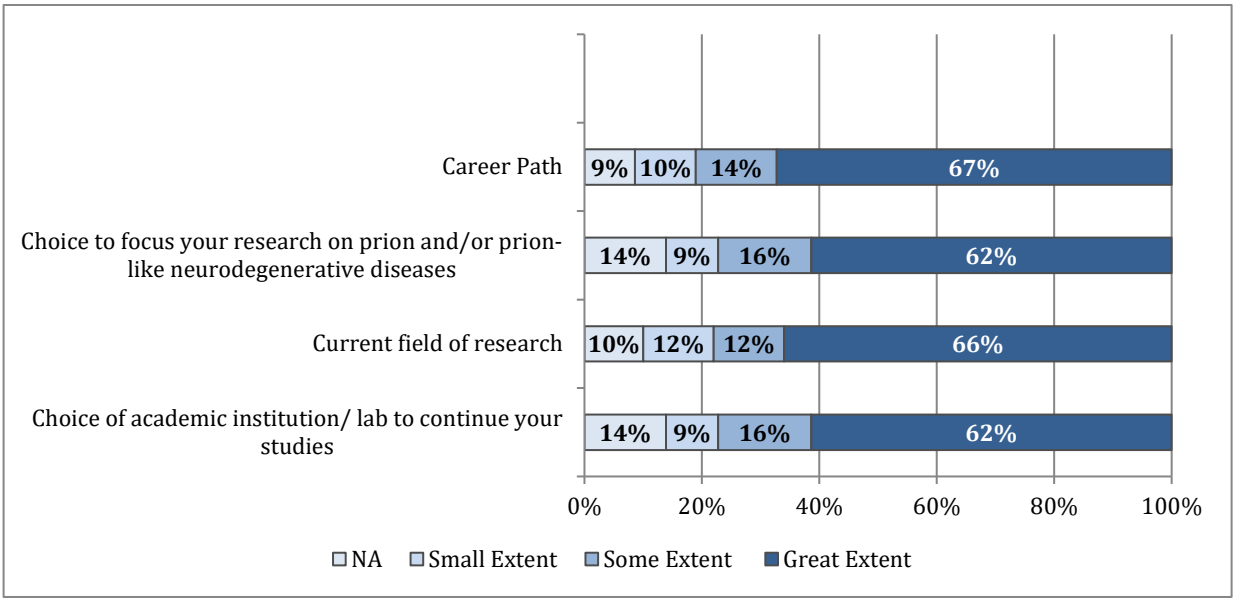
Figure 1: % of Trainees that Participated in APRI-supported Opportunity(ies) Indicating Extent to which they were Involved in…..



Source: Survey of APRI trainees, 2019, n=58

Two in three trainees surveyed indicated that their participation in APRI-supported opportunities influenced their career path and/or their choice to focus their research on prions (**Figure 2**).

Figure 2: % of Trainee Respondents whose Participation in APRI-supported Opportunity(ies) had or is having an Influence on Decisions Regarding their…



Source: Survey of APRI-supported trainees, 2019 n=58

Among those trainees that are currently employed (n=43), 67% indicate that they work in an area related to prions, and the same proportion confirm that they use skills acquired through their participation in APRI-funded research opportunities in their current position. Of respondents who confirmed a connection between their current position and the APRI supported opportunities they participated in (n=41), over half indicate that their participation in APRI-supported activities assisted them in obtaining their position.

2.4.2 Immediate Outcome: Increased Research Collaboration and Partnerships

SUMMARY: Key to APRI's success has been establishing a variety of partnerships with diverse stakeholders including government agencies at the provincial and federal level, other research institutes worldwide and local health and industry organizations. The vast majority of the research funded by APRI is collaborative and interdisciplinary. APRI undertakes efforts to facilitate these partnerships which have led to an almost 1:1 ratio of leveraged funding.

APRI has established diverse partnerships to co-fund research and extend APRI's reach and connections with policy-makers, industry and international research entities.

At the Institute level, APRI has established many partnerships. Importantly, and mentioned previously, APRI has undertaken three co-funding partnerships with ALMA, Genome Canada and the Alzheimer Society of Alberta and NWT. In addition, the most recent APRI Annual Report indicates that since the creation of the institute, 40 partnerships have been established between researchers, industry and policy makers in connection to APRI's activities. APRI's partners during the period 2005 to 2018 included provincial players such as Alberta Agriculture & Forestry, Alberta Innovates, Campus Alberta Neuroscience, Genome Alberta, the University of Alberta, the University of Calgary, and the University of Lethbridge. APRI's federal partners included: Genome Canada, the Canadian Food Inspection Agency (CFIA), CIHR, the Canadian Consortium on Neurodegeneration in Aging (which includes 16 public and private funding agencies), and Agriculture and Agri-food Canada. Internationally, APRI has ongoing partnerships with various institutions, including several in Germany (e.g., University of Göttingen, the Technical University of Munich, and the Robert-Koch-Institut).

APRI-funded researchers collaborated extensively with other prion researchers in Canada and internationally.

Between March 2005 and April 2018, APRI has also supported over 210 partnerships and collaborations within Alberta and internationally through its research funding. APRI and AARP application guidelines encourage partnerships and the funding mechanism allows for international collaborations. APRI's hosted scientific events and the IRAC were also mentioned by several key informants as being helpful in identifying and facilitating partnerships.

Almost all surveyed researchers indicated that their research program involved collaborations (**Table 2**). Eight in ten researchers engaged in interdisciplinary partnerships and researchers partnered with others in Alberta, in Canada and internationally. Researcher interviewees described a number of collaborations in the context of their research projects with researchers in the UK, Italy, Germany, Scandinavia, Japan and the US. Researchers also collaborated with public sector partners (e.g., ministries related to the environment and parks) and end users (private sector and non-governmental organizations).

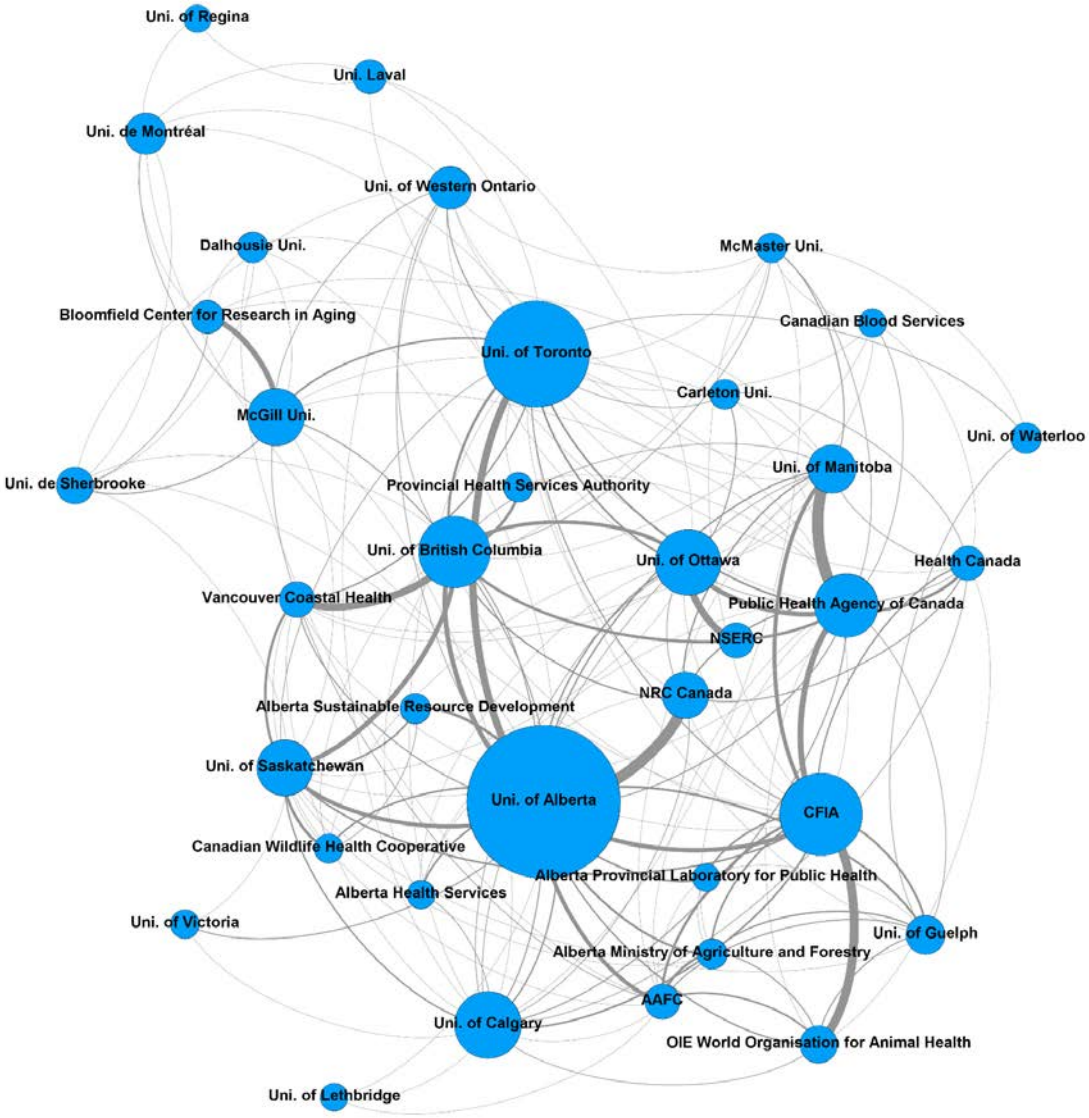
Table 2: Types of Collaborations or Partnerships

Which of the following types of collaborations or partnerships have been involved in your APRI-funded research program?	**% (n=36)**
Interdisciplinary academic collaboration and partnerships	81%
Collaboration between academic institutions in Alberta	53%
Collaboration with academic institutions elsewhere in Canada	42%
Collaboration with academic institutions outside Canada	42%
Collaboration with private sector partner(s)	19%
Collaboration with public sector partner(s)	22%
Collaboration with non-profit/ non-governmental partner(s)	8%
Research program does not involve a collaboration/ partnership	3%

Source: Survey of APRI Researchers, 2019

The bibliometric analysis shows connections between APRI-funded researchers and other scientists: collaborations at the researcher/project level are multi-sectoral and international. In term of scientific collaborations, during the most recent period (2014-2018), 44% of papers from the Institute were co-published with at least one author from another country. However, most of the papers (88%) involved collaborations with other research institutes within Canada. These collaboration rates have evolved relative to the previous 5-year period (2009-2013), where they equalled 39% and 83%, at the international and national level, respectively. A network analysis based on the bibliometric data depicts the prominence of University Alberta researchers, in particular, in terms of collaborations with other Canadian institutions (**Figure 3**).

Figure 3: Network of Collaboration between leading Canadian Institutions in Prion and Protein Misfolding Research (1999–2018)



Source*:* Prepared by Science-Metrix using Scopus database (Elsevier) and information from the Alberta Prion Institute

APRI and APRI-funded researchers have leveraged significant funding from other organizations in a ratio of almost 1:1.

APRI funding has played a role in attracting other research funding to Alberta from the Alzheimer Society, Canadian Consortium on Neurodegeneration in Aging (CCNA), NSERC, Canada Research Chair, Genome Canada, CIHR, Canadian Foundation for Innovation, and CFIA. In the survey of lead researchers, all but one respondent indicated that they used other sources of funding to support

their research program, and over half used more than one additional source of funding besides APRI. A majority indicated they benefitted from federal funding (67%). As of 2017-2018[16], in the period from March 2005 to April 2018, $66.2M in APRI funding for prion research resulted in $61.8M in cash co-funding by partners, in addition to leveraging almost $27M in in-kind support.

2.4.3 Immediate Outcome: Increased Knowledge Generation and Dissemination

SUMMARY: Metrics that were established for APRI's research and dissemination activities were exceeded during the period under study. APRI researchers have generated new knowledge in prions and protein misfolding. Overall, the prion research output worldwide has declined and while Canada's output has declined overall, Alberta's contribution to Canadian prion research output is considerable. Evidence of research impact is mixed. While there are many examples of high quality and transformative research funded by APRI, bibliometric measures of impact show declining impact of publications compared to worldwide measures. These data also show, however, that APRI funds leading researchers with citation indicators well above world levels. Citation indicators, while indicative, may not be capturing research impact of APRI's spectrum of projects, including translational research and the work related to Alzheimer's.

APRI has met or exceeded targets with respect to research investments and dissemination. APRI-funded research projects are creating new knowledge which is published and shared. As a result of APRI funding, Alberta contributes significantly to Canada's overall research in prion and protein misfolding research.

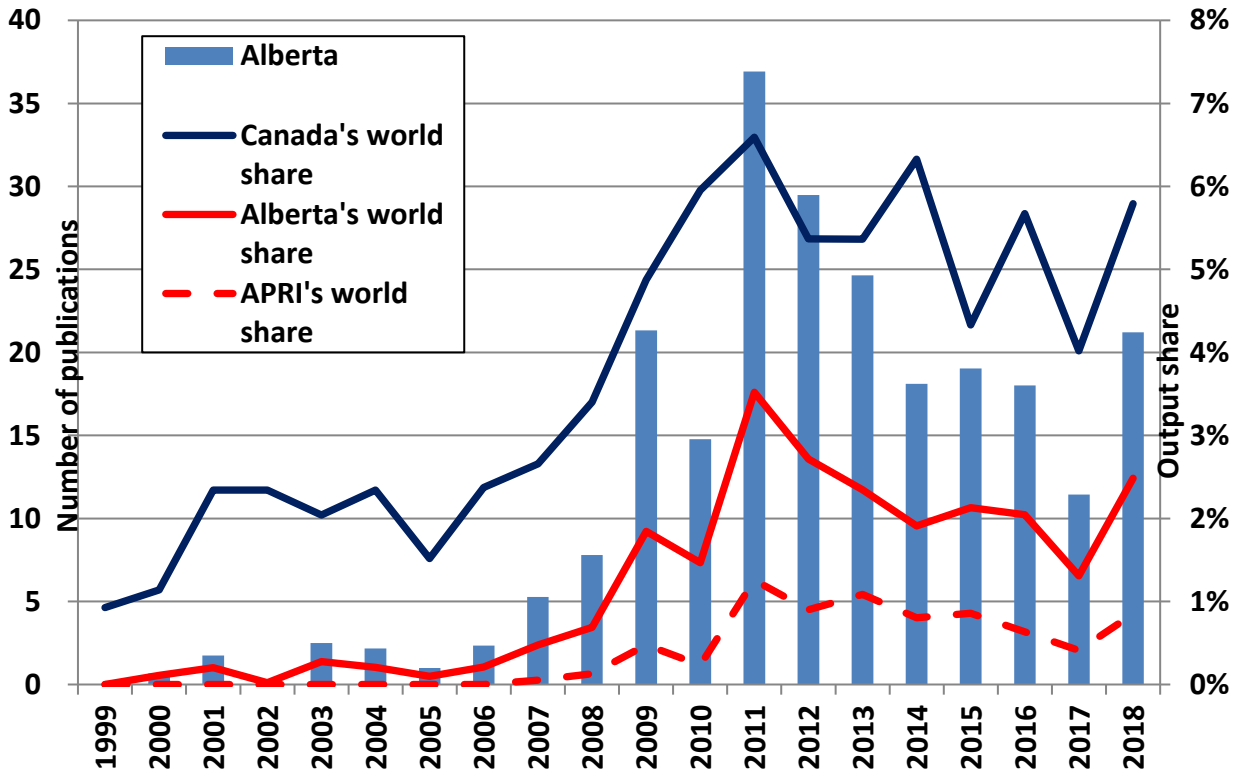
Since 2005, APRI has funded 169 projects in fundamental research and 40 projects in targeted and applied areas (exceeding targets). The APRI 2017-18 Annual Report indicates that since inception, APRI has generated 346 refereed publications and 882 articles, presentations, posters and thesis. Based on the bibliometric analysis, APRI[17] researchers' peak output occurred during the period 2009-2013, where the number of publications and share of world output more than doubled compared to the preceding period. In recent years (2014-2018), however, most countries including Canada have experienced a decline in their output, with notable exceptions to this general decline being India, Russia, the Republic of Korea and Brazil. However, Canada's share of world output in prion and protein misfolding research has remained fairly stable at around 5% and APRI researchers are responsible for 1% of prion research output worldwide (**Figure 4**). Canada is ranked 8 out of the top 20 publishing countries and Alberta contributed 43% of the Canadian output in 2018. At the institution level, the University of Alberta is among the top 5

[16] APRI Annual Report 2017-2018

[17] The output of APRI is estimated based on the share of work contributed by APRI-supported researchers. This includes the sum of contribution to papers in Prion and Protein Misfolding research published one year after the start of support until 2018. Therefore, in the early years of inception, fewer researchers contributed to APRI's output compared to more recent years.

publishing institutions in the world in prion and protein misfolding research (in the period 2004-2008, the University of Alberta was outside the top 100).

Figure 4: Trend in Publication Output of Alberta and Canada, Alberta and APRI's Share of World Publication Output in Prion and Protein Misfolding Research, 1999–2018



Source: Prepared by Science-Metrix using Scopus database (Elsevier) and information from the Alberta Prion Institute

Evidence of research impact is mixed. Researchers and interviewees highlighted many examples of high quality and transformative research funded by APRI. The bibliometric data, however, indicate that citation indicators measuring the impact of publications are declining for a variety of reasons.

There is mixed evidence on the quality and impact of APRI-funded research depending on the measures used. For instance, most surveyed APRI lead researchers (64%) reported that their research program is contributing to major scientific advances. (**Table 3**)

Table 3: Supported Research or Activities that Resulted in New Knowledge

To date, has your APRI funded research program supported research or activities that resulted in new knowledge regarding:	**% (n=36)**
Protein folding and misfolding in prion-like human neurodegenerative diseases	39%
Prion-like mechanisms in human neurodegenerative diseases	39%
Protein folding and misfolding in animal prion diseases	33%
Pathobiology of transmissible spongiform encephalopathy (TSEs)	22%
Surveillance and control of prion diseases	22%
TSEs and society	11%
Diagnostic technologies	17%
Innovative disposal and/ or uses of specified risk material	8%
Solutions to enhance market access	3%

Source: Survey of APRI Researchers, 2019

Many areas of research success were further highlighted by interviewees, including: fundamental breakthrough with basic mechanistic work that may lead to an effective CWD vaccine; examining mechanisms of persistence when prions are shed in the environment; work on CWD detection; transmission of CWD to other species; and published work on ground breaking mitigation treatments (going forward look at scaling). Some the projects alluded to in interviews are highlighted as examples in **Table 4** below.

Table 4: Knowledge Generation and Dissemination – Examples of Funded Projects
Dr. Debbie McKenzie's work relates to the susceptibility of cervids to CWD, characterization of CWD strains, and study of CWD host range. Dr. McKenzie's research supports greater understanding of the variations in zoonotic potential between CWD strains, which connects to issues of vulnerabilities and resistance in various species. Results were published in a research Letter Chronic Wasting Disease Prion Strain Emergence and Host Range Expansion (Center for Disease Control and Prevention). As a result of early research funded by APRI, Dr. McKenzie's team applied for and received $25M from Genome Canada to continue this work.
Dr. Stefanie Czub's ongoing study (started in 2009) on CWD transmissibility to non-human primates showed that macaques can be infected with CWD through oral consumption of infected muscle tissue. This finding is prompting authorities and the research community to revisit the possibility that CWD might be transmissible to humans via consumption of game meat. APRI funding is vital to the conduct of this study.
Drs. Hermann Schätzl, Dalia Abdelaziz and Simrika Thapa tested a CWD vaccine in a mouse model and found that the vaccine delayed the onset of the disease, prolonging the time before infected animals develop symptoms. Their research was published in 2018 in the Journal of Biological Chemistry.
Drs. Holger Wille and Michael Woodside received APRI funding to study the structural biology of prions. This work advances understanding of the mechanism underlying the folding of proteins and their infectious nature. This research is important to discovering the conditions that inhibit or protect against misfolding or propagate misfolding.

With respect to the bibliometric analysis, the indicators of impact show, first, that APRI is funding strong researchers. When considering the total output of APRI-funded researchers (i.e., not restricted to prion and protein misfolding research) during the years they were supported by APRI, the performance of those publications in terms of the average of relative citations, HCP1% and ARIF is generally well above world level.

When the impact of APRI-funded researchers' publications related to prion and protein misfolding is compiled, the bibliometric data indicate that the impact of research as measured by publication citations peaked in APRI's early years. However, APRI's citation indicators (ARC and ARIF) between 2009-13 (P3) and 2014-18-(P4) are below world level. Because there are few APRI papers overall given the small number of researchers funded, the proportion of papers falling within the top 10% of highly cited publication (HCP10%) was also examined.[18] However, only 5% of papers in P3 and 2% in P4 fell in the top HCP10%, which is also below world level.

There are a variety of reasons for the apparent decrease in citation indicators (ARC and HCP especially). The indicators may suffer from a lagging effect; that is, the number of citations is

[18] Bibliometric analysis of larger fields or funding agencies often uses the top 1% of highly cited publications.

expected to grow as time elapses and papers accumulate more citations over time. Recent work funded by APRI on a vaccine for CWD or transmission across species would suffer from this lag. As well, the decline in citation indicators may be related to the mix of research projects that APRI funds. Applied/translational research is less likely to be disseminated through academic publications, but rather attain their impact with dissemination through policy making. Finally, APRI's co-funding of work in Alzheimer's since 2012 may account for the decline to the extent that the impact of papers published in this domain could not be adequately captured in the bibliometric methodology without forcing all research on Alzheimer's disease in the benchmarking set of prion research publications, which would have broadened the data set too much for it to be a useful comparator for the much smaller data set of Alberta contributions. (**Table 5**)

Table 5: Trend in Publication Output and Impact Indicators of the Alberta Prion Institute (APRI) in Prion and Protein Misfolding Research, 1999–2018

	Total	P1 1999-2004	P2 2004-08	P3 2009-13	P4 2014-18
			Papers		
World	19,141	3,893	5,448	5,349	4,451
Canada	741	72	135	300	233
Alberta	239	5	19	127	88
APRI	76	0	2	42	32
			ARC		
World	1.00	1.00	1.00	1.00	1.00
Canada	0.88	1.00	1.20	0.77	0.76
Alberta	0.76	N/C	0.91	0.78	0.65
APRI	0.72	N/C	1.15	0.75	0.61
			HCP10%		
World	10.00%	10.00%	10.00%	10.00%	10.00%
Canada	8.88%	11.55%	13.80%	7.45%	6.19%
Alberta	5.76%	N/C	8.07%	7.21%	2.36%
APRI	4.21%	N/C	4.51%	5.18%	2.35%
			ARIF		
World	1.00	1.00	1.00	1.00	1.00
Canada	0.98	0.94	1.05	0.94	1.00
Alberta	0.94	N/C	1.01	0.92	0.94
APRI	0.91	N/C	1.05	0.89	0.93

Source: Prepared by Science-Metrix using Scopus database (Elsevier) and information from the Alberta Prion Institute [19]

[19] The output from APRI consists of publications by APRI-funded researchers in Prion and Protein Misfolding research, spanning from one year after the start of funding until 2018. The number of papers and indicators are based on fractional counting. The indicators (ARC, HCP, ARIF) are also to the world level.

In addition to academic publications, APRI supports other channels for knowledge dissemination, including for academic audiences, as well as other stakeholders and end-users of the research.

Knowledge dissemination is a key priority for the Institute and key informant respondents across all categories agreed that APRI has been effective in this regard. It was noted that APRI hosts/supports conferences and scientific meetings and APRI-funded researchers are frequent presenters at these conferences. APRI has hosted the annual international prion conference on multiple occasions (according to APRI's reporting, they are the only prion research organization that has been asked to host the international meeting three times, in 2011, 2013 and 2019). The conference affords an opportunity for both prion and prion-like protein misfolding human neurodegenerative disease researchers to gather. The last Prion 2019 conference held in Edmonton attracted more than 350 participants, half of which were researchers, and a quarter were students. Seven in ten attendees were from outside of Canada.

APRI's Guest Speaker Support Program supports knowledge dissemination to the scientific community by funding researchers in prion and protein misfolding science to present lectures and to participate in panel discussions. The APRI 2017-18 Annual Report quantifies 78 instances where Alberta's "international capacity and stature" was recognized, including special Invitations to present addressed to APRI Researchers. Many researchers who were interviewed or surveyed for the evaluation noted APRI's important contribution to knowledge exchange and, through these venues, creating opportunities for facilitating further scientific collaborations and partnerships across institutions

APRI has also taken a leadership role in sponsoring communications events targeted to the general public and engagement with industry audiences and has supported training for students on communicating scientific results. While the number of attendees cannot be tracked for all events, APRI's records indicate that conservatively, over 7,500 participants have attended these events. Events included:

- 63 processes that engage stakeholders in knowledge exchange
- 22 industry/government/academia workshops and similar meetings
- 24 public awareness activities such as lectures and updates for media
- 24 presentations to stakeholder groups; and
- 33 print and web-based publications.

Greyed-out italic scores indicate that there are less than 30 papers with a relative score. Such a low score means that the reliability of the indicators is not robust and more subject to change as papers are published. Scores for cases with less than 10 counts are not computed. The data is coloured from red (below index level) to white (at index level) to green (above index level).

This type of dissemination beyond the academic community includes, for example, free public lectures series on prions and, recently, on Alzheimer's. These events take place in rural areas as well as large centres, and are focussed on the aspects a given audience is likely to be most interested or concerned about. APRI-supported researchers (e.g., Stefanie Czub, Sabine Gilch, Debbie McKenzie, Evelyn Merrill and Hermann Schätzl) spoke with media at various times throughout the 2017-2018 fiscal year, to provide research updates and context to developing stories related to chronic wasting disease. Between 2005 and 2018, APRI has held multiple public awareness activities, produced updates for the media, and generated print and web-based publications for general conception.

2.4.4 Intermediate Outcome: Mobilization of Knowledge through Adoption, Application, Implementation

SUMMARY: The evaluation evidence confirms that APRI's supports for knowledge mobilization have been diverse and that these efforts are leading to tangible examples of adoption and application in policy, practices and regulations. There have been fewer opportunities or examples where research has had commercial outcomes.

At the project level, knowledge exchange is an expectation for APRI-funded projects. There are many examples of knowledge mobilization through influence on regulatory, policy or practice change. There are fewer examples of commercial mobilization of new knowledge.

At the project level, there is an expectation that researchers consider the potential mobilization of their work. At the grant application stage, APRI and AARP researchers are required to articulate a knowledge exchange plan[20] as part of their application. The knowledge exchange plan may include different strategies, but APRI encourages partnerships, particularly with potential end-users of the research.

According to surveyed researchers, the most common type of knowledge mobilization was informing changes to practices, processes, policy and protocols, more frequently related to agricultural/wildlife and less often to human health practices. Almost one in three researchers (31%) indicated their research program as having this type of impact. Commercial-related outcomes are less common, although almost one in five researchers (19%) indicated that their research program results in a patent or licensing. In one instance, AARP-funded researchers have patented compounds that are being considered by pharmaceutical companies for further development as potential therapeutics for the disease. (**Table 6**)

[20] From the Explorations application guidelines: Knowledge Exchange Plan - Provide strategies for exchanging knowledge including a description of partnerships with the public and private sector. The Prion Institute strongly encourages early interaction between researchers and potential end users during the design and throughout the period of the grant and in the utilization of results of the research findings.

Table 6: Results of Supported Research or Activities

To date, has your APRI funded research program supported research or activities that resulted in:	% (n=36)
Practices, processes and protocols	
Informing change to agricultural/wildlife related practices related to detection/ diagnosis	11%
Informing change to agricultural/ wildlife related practices related to prevention or risk management	17%
Informing change to human health practices related to detection/ diagnosis	3%
Informed change to human health practice related to prevention or risk management.	8%
Informing policy/ regulatory change	19%
Commercial-related	
Patenting and licensing	19%
Spin-off company(ies)	8%
Major technological innovations	14%

Source: Survey of APRI Researchers, 2019

The role of APRI in facilitating collaborations among policy makers and the impact of APRI-funded research are evident in agricultural/wildlife practices related to the management of CWD. In September 2016, Alberta researchers attended the APRI-sponsored Northern Plains Ecosystem Chronic Wasting Disease Workshop in Calgary. Discussions, informed by the work of APRI-funded Dr. Evelyn Merrill, resulted in the formation of a self-appointed "Ad hoc Working Group on Chronic Wasting Disease Management in the West" that drafted the original version of *Recommendations for Adaptive Management of Chronic Wasting Disease in the West.* This publication has been widely used by jurisdictions seeking to manage the spread of the disease or remain 'CWD-free'.

In another example, Dr. Sabine Gilch, an APRI-funded researcher and also a Canada Research Chair in Prion Disease Research, was approached by the governments of Alberta and Saskatchewan concerning her work on the early detection of chronic wasting disease prions and opportunities to adopt early detection tests developed in her lab for their CWD surveillance programs.

The 2016, workshop Northern Plains Ecosystem Chronic Wasting Disease Workshop hosted and led by APRI made recommendations that were approved by the Western Association of Fish & Wildlife Agencies (WAFWA) and has been used as a foundation for management plans in other jurisdictions:

- Montana and Colorado have developed management plans to be consistent with the recommendations;
- In Alberta, for the fall 2019 hunting seasons, mule deer hunting regimes were changed to align more closely with the recommendations in the WAFWA documents; and
- In Manitoba, where no known cases of CWD have been found, strategies have been implemented to prevent translocation in farmed cervids and monitor migration along borders where cases exist (e.g., Saskatchewan).

2.4.5 Ultimate Outcome: Prevention, Risk Management and Treatment of Prion Diseases in Humans and Animals

As mentioned in previous sections, the literature and evaluation evidence point to progress in advancing knowledge through prion research. APRI has been an important contributor in uncovering insights that could potentially contribute to the understanding and policy and regulation development for the prevention, management and mitigation or treatment of prion and prion-like protein misfolding diseases in animals and humans.

There remains work to be done in many areas, however, the Institute is generally well-regarded in terms of its selection of research questions to be funded in the animal and human health areas related to prions. Research investments in some of the themes described above – transmission, vaccine-related work, management strategies and early diagnosis of Alzheimer's Disease – are widely considered to be advancing the field and supporting the practical management of neurodegenerative diseases.

2.5 What are the Barriers/facilitators to Achieving APRI's Goals?

SUMMARY: APRI scientific and organizational leadership is cited as a facilitator to achieving the goals of the Institute. The dedicated funding to advance prion research has also been crucial to increasing prion research capacity in Alberta. APRI has been proactive in its outreach to industry and the public, and fostered collaborations among researchers which are further noted as important contributors to the success of funded research.

The uncertainty of continued funding is identified as a barrier, threatening the momentum of prion research in Alberta. The profile of CWD is also noted as not having the same attention as BSE, although containment of the disease is of comparable importance. Finally, prions affect animal, human, and environmental health, so there is no focus that aligns with a specific agency or ministry (i.e. nobody has the responsibility or governance).

APRI's staff and leadership is a strong facilitator of success of the organization.

Key informants across all respondent groups provided were in general agreement about factors that have contributed to or inhibited the achievement of APRI's objectives. Most often, respondents noted that APRI's people are a strength; providing strong leadership and managing APRI as a well-run and lean organization. The IRAC was further noted as facilitating the achievement of APRI's goals. The committee is described as well-respected internationally and providing strong guidance and direction in application review and recommendations. Similar feedback was gathered for AARP's ARC.

The availability of dedicated funding to advance prion research is crucial, according to some key informants. This funding has increased capacity for prion research, attracted research talent and

invested in infrastructure. Similarly, APRI's funding mechanisms were described by key informants as flexible, independent and responsive in the selection of projects.

Key informants further highlight APRI's commitment to translation and outreach, including to industry and to the public. Research has been translated to high profile journals, while outreach has helped to communicate the achievements of the organization. Some respondents noted the importance of infrastructure funding as helping to facilitate the goals of the organization. Some also identified collaborations as important contributors, including international collaborations and supporting good engagement among researchers within Alberta.

Few significant barriers were identified.

Barriers to achieving APRI's goals noted by key informants focused on the uncertainty of funding for the organization as the cycle draws to an end. According to these interviewees, while the funding was important in attracting world leading prion talent, without the funding, the capacity for prion research will regress. In addition, some key informants identify a general lack of awareness within the Government of Alberta of APRI, the research that is supported and its impacts. As noted, BSE was a "high profile" disease, while CWD is not as well-known and difficult to garner political attention for the importance of working towards containing the disease.

2.6 How can APRI be more Efficient?

SUMMARY:

APRI is viewed as a responsive and efficiently managed organization, administering grants with an appropriate balance of fundamental and applied research. Opportunities for improved communication can help build awareness of the need for prion research and sharing of outcomes of grants. IRAC is noted as an asset to APRI, as a well-recognized group of experts in the prion field, contributing to improving the potential of grant applications and involved past the approval phase.

Most researchers are satisfied with the application process, particularly the timeliness of awarded funds and funding decisions, along with the type of information required in the application. The project reporting requirements were viewed somewhat less favourably by researchers and some interviewees urged APRI to improve communications.

There is positive feedback overall from stakeholders about the management of APRI.

Overall, key informants agree that APRI is a responsive and well-managed organization, efficiently managed with few staff, and with the vision and goals of APRI well executed by the Executive Director and Director, Prion Programs. Based on the Institute's financials, operational expenditures represented 11%, on average, of total expenditures during the period (which declined during the period to a low of 8% last year).

The IRAC was noted by most key informants as a well-recognized and cohesive group. The IRAC's role is to review grant applications, solicit expert opinion in the area and make funding recommendations. A few key informants point out that the IRAC has a more robust role than other advisory committees, as they also review progress and end of grant reports. Researcher key informants indicate that feedback by the IRAC on applications was helpful, and in some cases, improvements to the proposal can be made based on feedback prior to funding decisions.

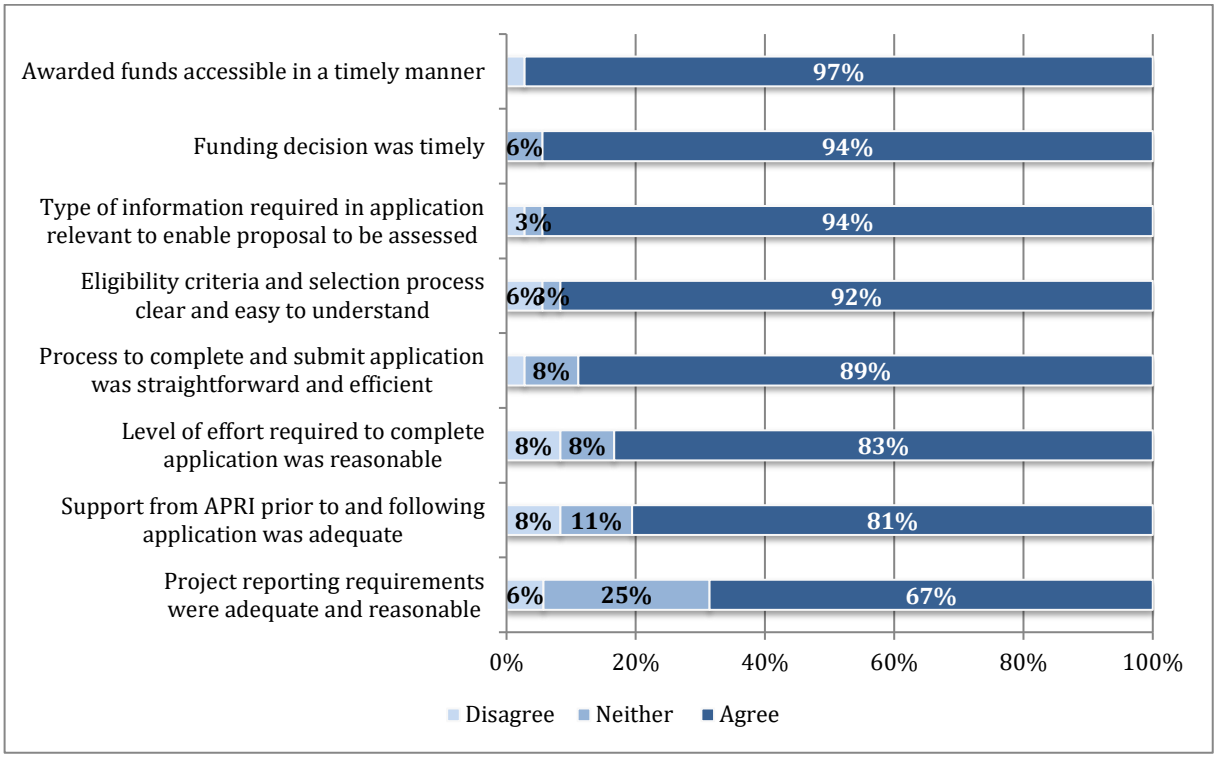
APRI's suite of funding opportunities is viewed as appropriate.

Most key informants stated that APRI is notable for administering a cohesive funding approach that include research, core infrastructure and knowledge mobilization funding across the spectrum of prion related fields. APRI's suite of programs reflects the practices of other small research granting agencies. An environmental scan of a sample CIHR's Institutes found many similar approaches including accompanying basic research with a strong translational component, partnerships and collaborations to leverage funding and pool resources and grants for training and knowledge translation (e.g., Institutes offer Knowledge to Action grants and host Best Brain Exchanges, and Café Scientifiques).

Researchers were satisfied with the funding mechanism overall (flexible, predictable, independent and responsive). There is some interest in streamlining the funding application form/reporting.

Interviewees felt that the funding application process is straightforward, rigorous, and peer reviewed. The calls for proposals every one to two years was cited as beneficial, and the duration of grants adequate, although some would like to see longer durations particularly when the research is in areas such as translational or in structural biology. Surveyed researchers echoed these sentiments, with most being satisfied with the various elements of the application process (**Figure 5**). Nearly all agreed that awarded funds were accessible in a timely manner (97%) (less so among AARP-funded researchers), that the funding decision was timely (94%), or that the type of information required in the application was relevant to enable the proposal to be assessed (94%). Researchers were least likely to agree that project reporting requirements were adequate and reasonable (67%), signaling a potential opportunity for improvement in program delivery.

Figure 5: % of Researchers who Agree with Statements about the Funding Application Process



Source: Survey of APRI Researchers, 2019, n-36

A few key informants mentioned that communication from APRI could be improved, including greater publicity regarding the need for prion research and sharing outcomes of funded projects. Updating the websites with recent highlights and outcomes was also noted as an opportunity for improved communication.

3.0 Conclusions

Following are the conclusions and considerations from the evaluation of APRI.

Relevance

The evaluation evidence points to a continuing need to investigate prions, particularly related to CWD. There are risks associated with prion and prion-like diseases related to animal, ecosystem and human health. At the same time, there continue to be many research questions related to prions.

With the current government's focus on innovation, economic diversification and growth, APRI's research focus could appear mis-aligned. However, research on prions, particularly CWD, has indirect economic benefits in protecting Albertan livestock and crop industries from the potential for trade restrictions although some decision-makers do not appear to be aware of the risks associated with CWD.

Performance

APRI has achieved or exceeded the performance metrics identified in its 2015 funding agreement. Since it was established, APRI has funded many research projects; with 1:1 leveraged funding, often from national, international and philanthropic sources outside the province, almost $130M has been invested. The dedicated research and infrastructure funding has built the capacity for diverse and more accurate research on prions, including training new researchers in the field. The bibliometric data confirm a specialisation in the prion research field, which is also being leveraged to contribute to Alzheimer's research, especially new and improved diagnostics. The APRI 2017-18 Annual Report quantifies 78 instances where Alberta's "international capacity and stature" was recognized, including special invitations to present addressed to APRI Researchers.

APRI research is generating new knowledge. Researchers and the bibliometric analysis indicated that Alberta is a strong contributor to Canada's overall research output related to prions and protein misfolding. APRI-funded research is proactively disseminated to scientific and lay audiences through various mechanisms such as patents, workshops, publications and public lectures.

There are many examples of transformative research conducted by APRI funded researchers (e.g., transmission across species, vaccination), as well as illustrations of practical impacts of research informing CWD management practices. The bibliometric analysis, however, shows a trend toward decreasing impact in terms of citation indicators, although there are some limitations with these indicators in capturing the impact of APRI-funded research (e.g., applied research, Alzheimer's research).

Design and Efficiency

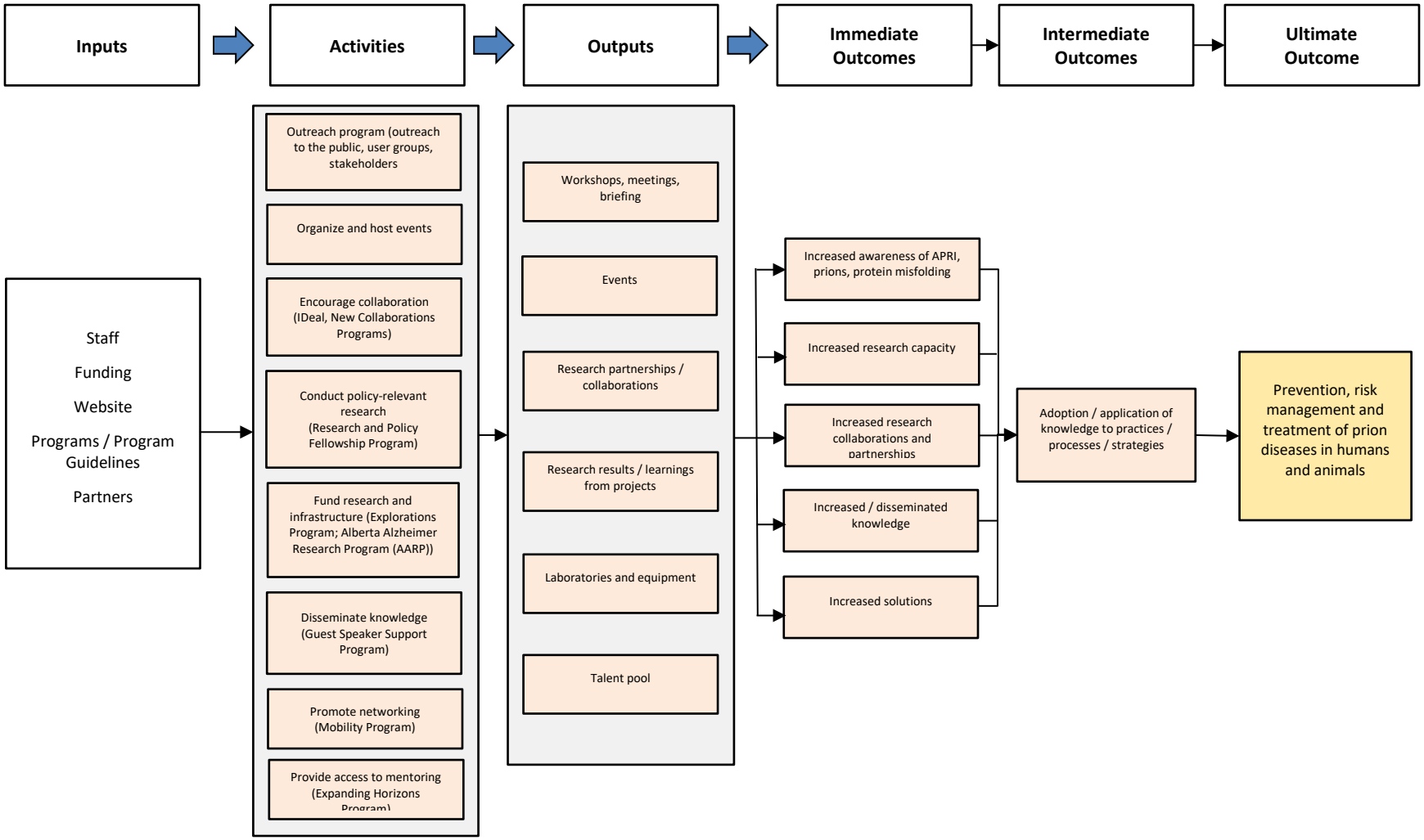
The evaluation found that APRI is an effectively-managed organization. The operational expenditures for the Institute represent 11% of total expenditures. The Institute's suite of funding opportunities and the design and delivery of the funding mechanisms are sound and consistent with practices of other research granting entities. IRAC and ARC have ensured that funded projects exhibit research excellence, while providing advice and support to researchers to improve their research efforts and to APRI to help it shape its programs.

Recommendations

Based on the evaluation findings and conclusions, recommendations include:

1. APRI should consider increasing attention to the communications function, including developing a strategy to more effectively convey messages to provincial officials, media and industry regarding:
   - The threat of prion and prion-like misfolding diseases and the potential economic and human costs of these diseases; and
   - APRI's early impacts on CWD management policy and practices.
2. Maintain the dual focus on prion and prion-like human neurodegenerative diseases (the latter being dependent on the partnership with the Alzheimer Society)
3. Continue to pool resources, seek co-funding from industry organizations and jurisdictions impacted by prion diseases (especially CWD)
4. Ensure that there are resources and referrals available to transition researchers to other forms of support to capture the benefits of discovery (patent, pre-commercialization)

Appendix A: Logic Model



Appendix B: Evaluation Matrix

Evaluation Question	Indicators	Method	Data Sources
Relevance			
Q1. Is the Alberta Prion Research Institute answering a current and continuing need? a. To what extent has the Institute been responsive to changes in the disease and scientific landscape?	Evidence of current/continuing need for prion research in Alberta	Document review	Scientific and grey literature on ongoing and emerging risks/health and economic burden related to prion diseases
	Extent of alignment between APRI and goals and priorities of Alberta Innovates and EDTT/Government of Alberta	Document review	AI/EDTT/Government documentation
	Stakeholder perspectives on the unique value/relevance and responsiveness of APRI	Interviews; Surveys; Case studies	AI/APRI interviewees; Partners; Researchers; case study respondents
	Evidence of/views on extent to which APRI complements/duplicates other programs	Interviews; Surveys	AI/APRI interviewees; Partners; Researchers
Performance			
Q2. Has the Alberta Prion Research Institute achieved its expected/mandated outcomes?	Overall extent to which APRI has met goals/deliverables in contribution agreement	Admin data/document review	Program project database
Immediate outcome: Increased awareness	Participation in outreach program events	Admin/data document review	Program database
Immediate Outcome : Increased Research Capacity	Investment and # of funded projects by program, by research areas, by year (e.g., fundamental/applied, # of individual researchers, average amount allocated, etc.); applicant success rates	Admin data/document review	Program project database

Evaluation Question	Indicators	Method	Data Sources
	Importance of program funding relative to total project value	Admin data/document review; (surveys)	Program funded projects database; final reports; (recipients)
	Funding leveraged by APRI	Admin data/document review; (surveys)	Program funded projects database ; (recipients)
	Extent of researchers/trainees access to/use of other funding programs	Surveys	Recipients
	Investment in core facilities (e.g., infrastructure, operation and use)	Admin data/document review	Program financial information and reports
	Rate of utilization of the equipment, infrastructure, and other resources directly supported by APRI	Admin data/document review;	Program information on use of laboratories, facilities, spaces, equipment, etc.
	Number of Alberta and Canadian researchers in prion and protein misfolding science - trend over time	Document review	Program data or publically available sources
	Number of researchers and students attracted/retained	Admin data/document review; surveys; interviews	Program information on researchers attracted and retained; recipients; trainees; researchers interviewed
	Number of research trainees and research assistants supported and trained	Admin data/document review; surveys	Program information on students/HQP trained; recipients and trainees
	Placement rate of students and trainees	Admin data/document review; surveys	Program information on students/HQP trained; trainees
	Number of students and fellows who have benefited from career enrichment opportunities provided through the Prion Research Institute and partners	Admin data/document review; surveys	Program information on students/HQP participating in activities; recipients and trainees
	Views on ultimate benefits of APRI capacity-building efforts	Interviews	AI/APRI interviewees; Partners; Researchers

Evaluation Question	Indicators	Method	Data Sources
Immediate outcome: Increased research collaboration and partnerships	Researcher, country and organization network analysis describing centrality of APRI-funded researchers, APRI and Alberta/Canada	Network analysis	Bibliometric analysis
	Number and nature of partnerships formed between APRI/APRI researchers and: • Academia (including cross-institution, cross-disciplinary) • Private Sector/Non-profit sector • Government/policy makers Engagement with local, national and international stakeholders	Admin data/document review; surveys	APRI Information on partnerships; recipients;
	Views on the contribution of APRI to enabling/maintaining partnerships and collaborations	Interviews	AI/APRI interviewees; Partners; Researchers; Trainees
Immediate outcome : Increased knowledge generation and dissemination	Evidence of new knowledge/increased understanding of: • the nature of prions, • prion pathogenic processes, the spread of prions	Administrative/data review; surveys; case studies	APRI reports; research project reports; researchers
	Trend analysis of the quantity and quality of research by APRI-funded researchers (bibliometric analysis of peer-reviewed publications and citations)	Biblometric analysis	Biblometric analysis
	Evidence of other research outputs	Administrative data report; project reports; survey	APRI reports; research project reports; researchers
	Number and nature of knowledge dissemination events and activities with various audiences (e.g., workshops, presentations, meetings, networking, etc.)	Administrative/data reviews;	APRI documentation on activities

Evaluation Question	Indicators	Method	Data Sources
	Number and type of attendees for APRI knowledge dissemination activities and events	Administrative/data reviews; surveys	Program data on attendance; question to researchers and trainees on attendance
	Views on APRI knowledge generation and dissemination activities	Surveys; interviews	Researchers and trainees; researchers; partners and collaborators, end-users
	Evidence of use of APRI resources (e.g., number of downloads and visits on the APRI websites, portals and databases)	Administrative/date reviews; surveys; interviews	Analytics on print and web-based APRI publications ; interviews with members of the various communities on utilization; potentially a question for researchers and trainees
Intermediate outcome: Mobilization of knowledge through adoption, application, implementation	# of new processes, practices influenced by APRI research (e.g., testing, diagnostics, preventions protocols, surveillance and containment procedures, deactivation and decontamination approaches) developed / implemented by end-users locally, nationally and internationally	Admin data/document review; surveys	APRI information on project outcomes, recipients;
	# of spin-off companies	Admin data/document review; surveys	APRI information on project outcomes, recipients;
	Number of patents/IP developed or granted	Admin data/document review; surveys	APRI information on project outcomes, recipients; bibliometrics analysis
	#/nature of policies and regulations informed/#/nature of instances of policy and regulation changes	Admin data/document review; surveys	APRI information on project outcomes, recipients;
	Level of public awareness of APRI and APRI supported research results	Admin data/document review; interviews	APRI analytics on public awareness; recipients; interviews with external stakeholders

Evaluation Question	Indicators	Method	Data Sources
Ultimate Outcome: Prevention, risk management and treatment of prion diseases in humans and animals	Evidence of progress towards improved prevention, reduced risk and improved detection for animal diseases	Admin data/document review; interviews; surveys; case studies	
	Evidence of progress towards improved prevention, reduced risk and improved detection for human diseases	Admin data/document review; interviews; surveys; case studies	
	Evidence of progress towards economic impact (e.g., evidence of prion research contributing to maintaining trade standards)	Admin data/document review; interviews; surveys; case studies	

Appendix C: APRI Performance Metrics

Strong Alberta capacity for prion and protein misfolding science	Target Cumulative Expected by 2021	Actual to March 31, 2018
Number of Alberta Researchers in Prion and Protein misfolding science	60	60
Number of young research trainees and research assistants supported and trained	400	461
Students and fellows who have taken advantage of career enrichment opportunities provided through that Prion Institute and its partners	200	362
Partnerships and collaborations within Alberta, in Canada and internationally	170	211
Investments in core facilities and their operations and uses	$13,913,739	$15,217,629

Knowledge generation in fundamental and applied areas that leads to prevention, mitigation and treatment of prion and protein misfolding diseases in animals and humans	Target Cumulative Expected by 2021	Actual to March 31, 2018
Excellent projects in fundamental research funded	168	169
Excellent Projects funded in targeted and applied areas	30	40
Communications in scientific and other literature		
Referred Publications	250	346
Abstracts, Presentations, Posters & Thesis	750	882
Intellectual property and patents generated	17	17
Recognition of Alberta's international capacity and stature	35	78

Mobilization of knowledge generated for use by industry, government and researchers	Cumulative Expected by 2021	Actual to March 31, 2018
Processes that engage stakeholders in knowledge exchange	75	63
Industry/government/academia workshops and similar meetings	10	22
Partnerships established between researchers, industry and policy makers	27	40
Processes, practices, products, patents and policies informed	14	11
Public awareness activities such as lectures and updates for media	15	24
Presentations to stakeholder groups	30	24
Print and web-based publications	32	33

Source: APRI 2017-18 Annual Report