
PROGRAM GUIDE:

EXPLORING CANNABIS-BASED MEDICINES AND TOOLS (*mCannabis*)

PROGRAM OVERVIEW

Background

Pain is the most common reason for Canadians engaging the health system and accounts for up to 78% of emergency department visits.¹ The Alberta Pain Society (APS) characterizes multiple types of pain, including acute, chronic, transitional, cancer-related, and neuropathic.² Among the different types, chronic pain is the leading cause of morbidity and disability on a global scale.³ Approximately 1 in 5 adults (i.e., six million people) in Canada experience chronic pain.⁴ The economic burden of chronic pain management in Canada is estimated at \$7.2 billion annually in direct costs; comparable to the cost of some other top-ranked costly diseases in Canada.⁴ Prevalence of chronic pain and other pain types is rising due to an aging population, increasing prevalence of disease conditions (e.g., diabetes, obesity), and more complex disease states.⁴

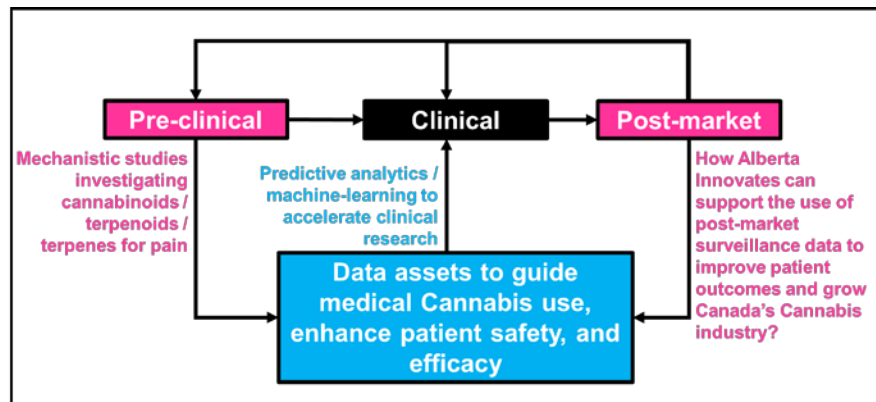
Management of pain often relies on opioids. Opioids can play a role in pain management, however misuse can lead to harms, including addiction, poisoning, and mortality.⁵ Since 2000, Canada has been facing a rise in opioid-related harms resulting in the current crisis state. Between January 2016 and March 2019, more than 12,800 Canadians died from apparent opioid-related harms.⁶ Though not all deaths can be linked to misuse in context of pain management, there is an urgent unmet need for the development or identification of novel pain management strategies for the treatment of pain. A burgeoning body of literature and several anecdotal sources suggests that *Cannabis* may have analgesic properties, however evidence to demonstrate such properties is limited. In parallel, Canada's legalization of *Cannabis* has triggered a post-market setting wherein patients are using *Cannabis* for a several different conditions with limited scientific evidence. Urgent attention is needed to understand post-market data to improve patient outcomes and responsibly grow Canada's *Cannabis* industry.

Cannabis has been reported to contain greater than 560 metabolic constituents with more than 220 different cannabinoids and over 262 different terpenoids / terpenes.⁷⁻¹¹ Very few of these phytochemicals have been extensively studied. There is evidence to suggest that cannabinoids and terpenoids or terpenes may have analgesic or anti-inflammatory properties,¹²⁻¹⁶ however more research is needed to understand their underlying mechanisms of action.

In parallel, urgent attention must be directed towards patients currently using medical *Cannabis* without rigorous pre-clinical mechanistic studies or robust clinical evidence for a variety of conditions. Consequently, there is an urgent need to optimally collect, analyze, link, and / or predict post-market surveillance data on *Cannabis* use.

Program Details

Scheme illustrating a typical drug development process with Alberta Innovates' approach to addressing evidence gaps for medical *Cannabis* use. Boxes that are addressed in the m*Cannabis* Program are shown in pink. Future data assets to guide medical *Cannabis* use, optimize clinical design, enhance patient safety and efficacy is shown in blue. This competition does not support human clinical trials (black box).



The scheme above illustrates a typical drug development process with Alberta Innovates' vision for the medical *Cannabis* research Program. The Pre-clinical Research ("Stream 1") of the Exploring *Cannabis*-Based Medicines and Tools Program (the "m*Cannabis* Program") builds on a recent National Institute of Health (NIH) funding opportunity announcement in 2019¹⁷ and aims to support Applicants in improving our understanding of *Cannabis* phytochemicals for putative pain or analgesic properties and realize economic value for Alberta citizens. Projects will be supported for up to \$300,000 for a maximum term of 24 months. Applications will be accepted until **4:00 pm MST January 29, 2020**.

Step 1 of the Post-market component ("Stream 2") of the m*Cannabis* Program seeks big ideas on how Alberta Innovates can support the use of post-market surveillance data to improve patient outcomes and responsibly grow Canada's *Cannabis* industry through a Request for Information (RFI). Responses to these RFIs will be used to inform a possible future program call. Applications will be accepted until **4:00 pm MST February 12, 2020**.

More information about this RFI process can be found on page 9 of this Guide.

The m*Cannabis* Program provides a platform of engagement among medical *Cannabis* stakeholders to coordinate and collaborate to generate knowledge and evidence for more informed *Cannabis* use.

The mCannabis Program is a two-year, \$1.5 million program, comprised of two independent streams. Stream 1 has available funding of up to \$300,000 per Project for up to a 24-month term.

How the Program Works

Stream 1 - Preclinical / Pain

Investigation of phytocannabinoids and terpenoids / terpenes, either alone or in combination, for their effects on pain perception (i.e., nociception) and analgesia. The *mCannabis* Program will support highly innovative basic and / or mechanistic studies in appropriate model systems or organisms (except humans) to identify, describe, and determine whether cannabinoids and terpenoids / terpenes can help treat pain. Innovative analytical techniques / methods to study the effects of cannabinoids and terpenoids / terpenes for pain will be supported. Proposals incorporating computational approaches in artificial intelligence or machine learning are encouraged. The *mCannabis* Program encourages combinational studies involving phytocannabinoid(s) / terpenoids or terpenes to expand the therapeutic potential. Phytocannabinoids and terpenoids / terpenes of interest include but are not limited to: cannabidiol (CBD), cannabigerol (CBG), cannabinol (CBN), cannabichromene (CBC), myrcene, caryophyllene, limonene, terpineol, linalool, phellandrene, pinene, terpinene, and humulene. The *mCannabis* Program will not support studies that solely investigate tetrahydrocannabinol (THC) alone with the exception that THC is used to validate single versus combined treatments. For more suggested research topics and other resources, refer to the *mCannabis* Frequently Asked Questions (FAQ) document on our [website](#).

Eligibility

(a) Applicant Eligibility Criteria - To qualify as an Applicant, an entity must be one of the following:

- an Alberta-based post-secondary institution;
- a government entity or health delivery agent or
- a not-for-profit organization, that is:
 - incorporated in Alberta, or
 - incorporated in another jurisdiction and extra-provincially registered in Alberta, or
 - a General Partnership, Limited Partnership, or Limited Liability Partnership and registered in Alberta; and
 - have a legal and physical presence in Alberta; and

AND

- be in good financial standing with Alberta Innovates and its subsidiaries InnoTech Alberta and C-Fer Technologies.

(b) Project Eligibility Criteria - To qualify for funding all Projects must:

- identify critical “go / no go” milestones;
- have appropriate Health Canada *Cannabis* licensing or exemptions (if required) to deliver on Project milestones. Refer to Health Canada Guidance Documents on the Cannabis Act and Regulations.
- be completed within the term;
- be able to provide a non-confidential graphical abstract; and

- submit to other criteria that Alberta Innovates may develop from time to time

Program Objectives and Performance Measurement

The mCannabis Program aims to deliver meaningful return on investment to Albertans by investigating Cannabis-based chemicals for effective pain management. In addition, provide an engagement platform for medical Cannabis stakeholders to improve patient care as well as responsibly grow Canada's Cannabis industry.

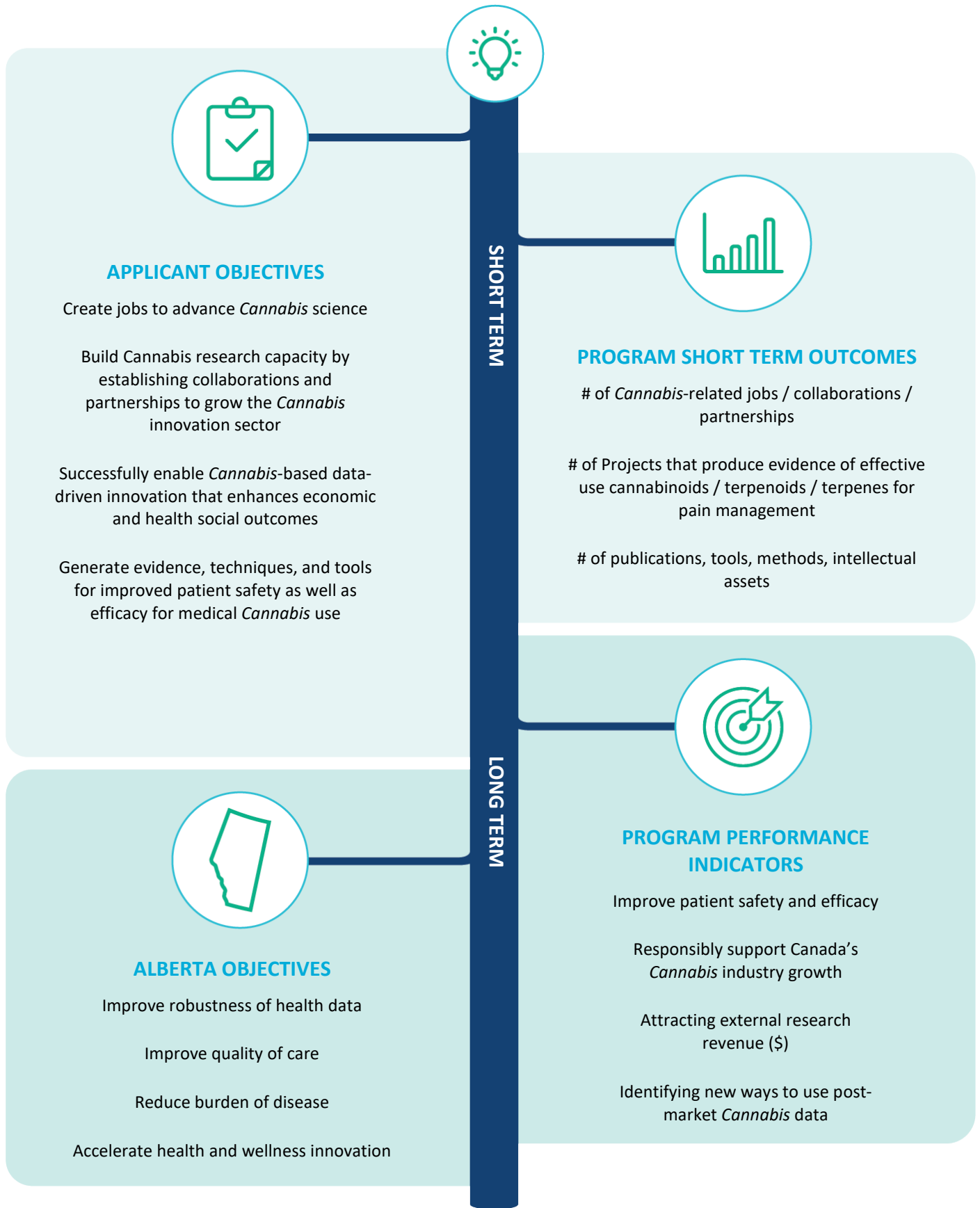
Over the life of a Project, Alberta Innovates employs an active Project management philosophy, regularly monitoring performance and supporting the Applicant to reach their objectives. Funding is tied to outcomes and achievement of results.

Once Projects are completed, Alberta Innovates continues to monitor performance for five (5) years to accurately evaluate the economic, social and health benefits realized for the province.

All Investment Agreements outline performance indicators tracked over the course of the Project and the responsibilities of the Applicant to report on outcomes subsequent to the completion of the Project.

Alberta Innovates has a common set of performance metrics it monitors, both at the individual Project level and for the aggregate mCannabis Program. These are highlighted on the next page.

Objectives and Performance Metrics



How Stream 1 Funding Works

(a) Project Funding

Alberta Innovates' Investment to a successful Applicant is up to \$300,000 for a term not to exceed 24 months. Industry partnerships are encouraged. Funded projects will be required to provide a graphical abstract.

(b) Eligible and ineligible expenses

Alberta Innovates only funds reasonable costs incurred subsequent to a signed Investment Agreement between Alberta Innovates and the Applicant. Any costs incurred prior to the signing of the Investment Agreement or costs greater than market prices are deemed ineligible. Costs must be incurred between arm's length entities. Please refer to our standard form Investment Agreement found on our [website](#) to get an in-depth understanding of eligible and ineligible costs. The chart below provides a high-level summary of eligible and ineligible expenses.

Summary of Eligible and Ineligible Expenses

| Category | Eligible Expenses | Ineligible Expenses |
|--|--|--|
| Salaries and benefits | <ul style="list-style-type: none"> ✓ Salary and benefits for staff, students, or contractors who are specifically working on the Project | <ul style="list-style-type: none"> ✗ Salary, consulting fees, or honoraria support for academic faculty members, physicians, or company executives / senior management involved ✗ Salary and costs of administration and / or indirect support staff ✗ Salary and costs associated with Application development |
| Equipment, materials, and supplies | <ul style="list-style-type: none"> ✓ Cost of equipment, materials, and supplies needed to support Project. | <ul style="list-style-type: none"> ✗ Cost or rental equivalents exceeding accepted values had the equipment been sold or donated ✗ Development costs incurred prior to the start of the Project ✗ Depreciation costs associated with the equipment donated to the Project |
| Software, new technologies, and databases | <ul style="list-style-type: none"> ✓ Costs of purchasing licenses needed for the Project ✓ Costs of collecting, de-identifying, and archiving data that is critical to | <ul style="list-style-type: none"> ✗ Cost of new software and technologies the go outside the scope and / or duration of the Project |

| | | |
|---|--|--|
| | the success of the Project and accessible to the public domain. | <ul style="list-style-type: none"> ✗ Development cost of new technologies related to the Project |
| Use of facilities | <ul style="list-style-type: none"> ✓ Costs for specialized equipment or services needed directly related to the Project | <ul style="list-style-type: none"> ✗ Indirect or overhead costs associated with facilities (utilities, repair of office furniture, administrative fees, insurance, telephones, etc.) that do not contribute directly to the Project |
| Travel (up to 5% of total Project costs) | <ul style="list-style-type: none"> ✓ Cost for mileage, lowest economy class airfare, and accommodation for field work and dissemination activities directly related to the Project. | <ul style="list-style-type: none"> ✗ Costs to cover conference fees, travel, hotels, and food to attend events or meeting unrelated to Project ✗ Entertainment expenses, gifts, awards, and alcoholic beverages ✗ Reimbursement for airfare purchased with personal loyalty reward programs (i.e., frequent flyer points programs) ✗ Commuting costs between residence and place of employment |
| Other expenditures | <ul style="list-style-type: none"> ✓ Costs which Alberta Innovates pre-approves in writing as an eligible expense ✓ Patent filing costs specific to the project. | <ul style="list-style-type: none"> ✗ Expenditures that are not directly associated with meeting the deliverables and milestones in the Project ✗ Expenditures that are incurred outside the scope and / or duration of the Project ✗ Indirect or overhead costs ✗ Costs Alberta Innovates deems ineligible at its sole discretion |

HOW TO APPLY



STEP 1 Application

Application form and supporting information for Stream 1 of the *mCannabis* Program are accessible on our website.

Alberta Innovates will not accept partial or incomplete submissions.

Deadline for Application submission is 4:00 pm MST January 29, 2020.

Applications received after the deadline will not be considered.



STEP 2 Evaluation Process

Applications will undergo scientific review scheduled for the week of **February 17-21, 2020**, and Alberta Innovates will provide the results no later than **February 28, 2020**.



STEP 3 Successful applicants

For approved Applications, the Applicant will execute an Investment Agreement with Alberta Innovates.

All Agreements must be fully executed by March 31, 2020.

Agreement expectations will include a graphical abstract, participation in performance management activities, and reporting on progress and budget during the term of the Agreement as well as up to five years post Investment.

Payments of the Investment are tied to progress and performance reporting.

EVALUATION PROCESS

Alberta Innovates leverages internal staff and external expert reviewers to evaluate the Applications submitted. Alberta Innovates evaluates promising research and technologies for scientific and technical merit based on **innovation opportunity** (problem specificity, understanding of previous research, research goals specificity, and innovation potential), **impact potential** (economic, health, sustainability), and **project design and implementation plan** (hypothesis, approach and deliverables, knowledge translation, project timeline and milestones, risks and mitigation, team structure, governance, scientific environment, budget justification, and regulatory and ethical considerations).

Alberta Innovates retains sole right to determine the evaluation process and does not disclose the names of its external reviewers to ensure their objectivity and impartiality. All external parties are subject to both confidentiality and conflict of interest policies set by Alberta Innovates.

The assessment criteria and all investment decisions are at the sole discretion of Alberta Innovates.

ABOUT THE REQUEST FOR INFORMATION

There is an urgent need to optimally collect, analyze, link, and / or predict post-market surveillance data. Such data can originate from several sources such as patient-reported outcomes, clinical records, administrative records, or consumer behaviour.

This Request for Information (RFI) seeks big ideas on how Alberta Innovates can support the use of post-market surveillance data to improve patient outcomes and grow Canada's *Cannabis* industry. Ideas are encouraged to go beyond the scope of Stream 1, address the challenge, have the potential to leverage partnerships between academics and industry, be suitable for future research, and should have a high probability of resulting in deliverables that will benefit patients and industry within a fixed term.

The collection of these RFIs is for planning purposes only and should not be construed as solicitation for applications or proposals. The intent is to inform a future program call by reviewing all RFIs received and then inviting RFI participants to attend a workshop to seek feedback and set priorities. Any identifiers (e.g., names, institutions, contact information) will be removed before sharing any information publicly and with working groups convened by Alberta Innovates as appropriate. Proprietary, classified, confidential, or sensitive information should not be included.

HOW DOES THE REQUEST FOR INFORMATION WORK?



STEP 1 Request for Information for Big Ideas

Request For Information (RFI) form for Stream 2 of the mCannabis Program is accessible on our [website](#).

This step runs concurrent with Stream 1 Application intake.

Alberta Innovates invites all Cannabis-related stakeholders to contribute.

Deadline for RFI's is 4:00 pm MST February 12, 2020. RFI's received after the deadline will not be considered.



STEP 2 Stakeholder consultations and workshop

Information will be collected and reviewed with intent to hold stakeholder consultations for priority setting. Respondents to Alberta Innovates' Request for Information will have an option to participate at an anticipated workshop.

Expected workshop date is the week of March 30 – April 3, 2020.



STEP 3 Development of a funding call for using post-market surveillance data to improve patient outcomes and grow Canada's Cannabis industry

Alberta Innovates anticipates creating a Stream 2 program call encouraging partnerships with industry sometime in 2020/2021.

TERMS AND CONDITIONS

This program guide is intended as a high-level overview of the program. It provides interested Applicants with a roadmap of what to expect over the lifecycle of an *mCannabis* Program Project, from the announcement of the *mCannabis* Program, through the Application stage, during the Project and post-completion. Should you have any questions about this guide or what is expected, please contact Alberta Innovates. Please be aware Alberta Innovates may modify this guide from time to time in keeping with any changes to the program.

Alberta Innovates will only correspond in writing and provide copies of the Application to the person named in the Application form as the one authorized to speak for the Applicant.

Once we have evaluated and approved an Application for funding, Alberta Innovates will require the Applicant to sign our standard form Investment Agreement. A copy of the Investment Agreement is available on the Alberta Innovates [website](#). The Investment Agreement sets out in detail the roles, responsibilities, and obligations of the various parties to ensure a successful Project. Alberta Innovates will not provide any funding until the Investment Agreement has been signed by all parties.

Alberta Innovates will only fund Applicants who have satisfied all eligibility criteria. Meeting the eligibility criteria does not guarantee access to funding, and all funding decisions will be made by Alberta Innovates at its sole discretion.

DIVERSITY, EQUITY, AND INCLUSION (DEI)

We believe the Alberta research and innovation (R&I) ecosystem is stronger and more sustainable when it is broadly reflective of the overall diversity of our community. Alberta Innovates strives to ensure all interested and qualified parties have an equitable opportunity to participate and contribute. Historically, there have been several groups/populations that have been under-represented in the

Alberta R&I landscape including:

- Women entrepreneurs/researchers;
- Indigenous entrepreneurs/researchers;
- Remote/small community entrepreneurs/researchers; and
- New immigrant entrepreneurs/researchers.

We are guided by the principles of:

- Diversity – both internal and external participants to our processes are comprised of a varied composition of demographics;
- Equity – our processes support equal access across all demographics; and
- Inclusivity – our processes proactively work to include underrepresented segments of the R&I landscape.

Accordingly, as part of its commitment to Diversity, Equity and Inclusion (DEI), Alberta Innovates will request Applicants' permission to:

- Collect data in the Application on a voluntary basis to better understand diversity;
- Provide Application navigation support to Applicants from under-represented groups; and

- Integrate a DEI focus into its due diligence processes including striving to have diverse review committees to foster unbiased decision making.

CONTACT INFORMATION

Sunil Rajput, BSc MSc PhD

Senior Business Partner

Health Innovation

Phone: 780-306-3090

Email: Sunil.Rajput@albertainnovates.ca

References

1. Todd, K. H.; Ducharme, J.; Choiniere, M.; Crandall, C. S.; Fosnocht, D. E.; Homel, P.; Tanabe, P., Pain in the emergency department: results of the Pain and Emergency Medicine Initiative (PEMI) multicenter study. *Journal of Pain* **2007**, *8* (6), 460-466.
2. Alberta Pain Society. Alberta Pain Strategy 2019 - 2024. https://www.painab.ca/uploads/1/0/8/0/108066059/alberta_pain_strategy_october_2019_final.pdf (accessed 14 November 2019).
3. Rice, A. S. C.; Smith, B. H.; Blyth, F. M., Pain and the global burden of disease. *Pain* **2016**, *157* (4), 791-796.
4. Hogan, M.-E.; Taddio, A.; Katz, J.; Shah, V.; Krahn, M., Incremental health care costs for chronic pain in Ontario, Canada: a population-based matched cohort study of adolescents and adults using administrative data. *Pain* **2016**, *157* (8), 1626-1633.
5. Canadian Institute of Health Information. Opioid Prescribing in Canada. <https://www.cihi.ca/sites/default/files/document/opioid-prescribing-canada-trends-en-web.pdf>. (accessed 14 November 2019).
6. Special Advisory Committee on the Epidemic of Opioid Overdoses. National report: Apparent opioid-related deaths in Canada (January 2016 to March 2019). Web Based Report. Ottawa: Public Health Agency of Canada; September 2019. <https://health-infobase.canada.ca/datalab/national-surveillance-opioid-mortality.html> [accessed 14 November 2019].
7. Berman, P.; Futoran, K.; Lewitus, G. M.; Mukha, D.; Benami, M.; Shlomi, T.; Meiri, D., A new ESI-LC/MS approach for comprehensive metabolic profiling of phytocannabinoids in Cannabis. *Scientific Reports* **2018**, *8* (1), 14280.
8. Bonn-Miller, M. O.; Pollack, C. V., Jr.; Casarett, D.; Dart, R.; ElSohly, M.; Good, L.; Guzman, M.; Hanus, L.; Hill, K. P.; Huestis, M. A.; Marsh, E.; Sisley, S.; Skinner, N.; Spahr, J.; Vandrey, R.; Viscusi, E.; Ware, M. A.; Abrams, D., Priority Considerations for Medicinal Cannabis-Related Research. *Cannabis Cannabinoid Res* **2019**, *4* (3), 139-157.
9. ElSohly, M. A.; Slade, D., Chemical constituents of marijuana: The complex mixture of natural cannabinoids. *Life Sci* **2005**, *78* (5), 539-548.
10. ElSohly, M. A.; Radwan, M. M.; Gul, W.; Chandra, S.; Galal, A., Phytochemistry of Cannabis sativa L. In *Phytocannabinoids: Unraveling the Complex Chemistry and Pharmacology of Cannabis sativa*, Kinghorn, A. D.; Falk, H.; Gibbons, S.; Kobayashi, J. i., Eds. Springer International Publishing: Cham, 2017; pp 1-36.
11. Radwan, M. M.; ElSohly, M. A.; Slade, D.; Ahmed, S. A.; Wilson, L.; El-Alfy, A. T.; Khan, I. A.; Ross, S. A., Non-cannabinoid constituents from a high potency Cannabis sativa variety. *Phytochemistry* **2008**, *69* (14), 2627-2633.
12. Hill, K. P.; Palastro, M. D.; Johnson, B.; Ditre, J. W., Cannabis and Pain: A Clinical Review. *Cannabis and Cannabinoid Research* **2017**, *2* (1), 96-104.
13. Carvalho, A. M. S.; Heimfarth, L.; Santos, K. A.; Guimarães, A. G.; Picot, L.; Almeida, J. R. G. S.; Quintans, J. S. S.; Quintans-Júnior, L. J., Terpenes as possible drugs for the mitigation of arthritic symptoms – A systematic review. *Phytomedicine* **2019**, *57*, 137-147.
14. Ware, M. A.; Wang, T.; Shapiro, S.; Collet, J.-P.; Boulanger, A.; Esdaile, J. M.; Gordon, A.; Lynch, M.; Moulin, D. E.; O'Connell, C., Cannabis for the Management of Pain: Assessment of Safety Study (COMPASS). *The Journal of Pain* **2015**, *16* (12), 1233-1242.
15. Stockings, E.; Campbell, G.; Hall, W. D.; Nielsen, S.; Zagic, D.; Rahman, R.; Murnion, B.; Farrell, M.; Weier, M.; Degenhardt, L., Cannabis and cannabinoids for the treatment of people with chronic noncancer pain conditions: a systematic review and meta-analysis of controlled and observational studies. *Pain* **2018**, *159* (10), 1932-1954.
16. Urits, I.; Borchart, M.; Hasegawa, M.; Kochanski, J.; Orhurhu, V.; Viswanath, O., An Update of Current Cannabis-Based Pharmaceuticals in Pain Medicine. *Pain and Therapy* **2019**, *8* (1), 41-51.
17. National Institutes of Health; National Center for Complementary and Integrative Health Exploring the Mechanisms Underlying Analgesic Properties of Minor Cannabinoids and Terpenes. <https://grants.nih.gov/grants/guide/rfa-files/rfa-at-19-008.html> and <https://grants.nih.gov/grants/guide/rfa-files/rfa-at-19-009.html> (accessed 21 October 2019).