Consultation: Building the future of clinical trials at the Canadian Institutes of Health Research

HealthCare*CAN* submission

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INTRODUCTION

HealthCare*CAN* is the national voice of action for health organizations and hospitals across Canada. We advocate in support of health research and innovation; to enhance access to high-quality health services for Canadians; and we empower health professionals through our best-in-class learning programs. We welcome the opportunity to make this submission to the Canadian Institutes of Health Research (CIHR) as part of their study on building the future of clinical trials at the Canadian Institutes of Health Research. HealthCare*CAN* wishes to acknowledge the extensive input from our Vice Presidents of Health Research Committee in the preparation of this submission.

Clinical trials are an important step in the development of innovative treatments to ensure safety and efficacy as novel medical approaches are brought to market. Canada has historically been a global leader in clinical trials through major leading advancements in science and research, a diverse population of potential participants, and strong clinical trial capabilities.

Overall, the global market for clinical research is estimated to reach a value of US$ 57.46 billion by 2026. Given the benefits of conducting clinical trials for hosting jurisdictions, the global market is becoming increasingly competitive as jurisdictions invest to incentivize and enhance their clinical trial attractiveness.

While all the world's top pharmaceutical companies regularly conduct trials in Canada, the number of clinical trials taking place across the country has declined over the last decade due to several challenges and barriers. Individual provinces and territories have undertaken localized or subject-specific efforts to address these issues, which has resulted in duplication, inconsistency, and different directions across the country. Canada's lack of a focused, targeted approach for clinical trials at a pan-Canadian level has increasingly left Canada lagging behind peer jurisdictions.

It is time for Canada to take a bold approach to clinical trials and create an ecosystem that better supports trainees and researchers in Canada, promotes and facilitates partnerships domestically and internationally, makes Canada an attractive place to invest and conduct trials, and positions Canada for success now and into the future.

The remainder of this submission outlines HealthCare*CAN*'s recommendations to ensure Canada's success in the clinical trials space, based on the seven key areas outlined in CIHR's consultation paper.

RECOMMENDATIONS

CIHR Funding for Clinical Trials

Clinical trials bring safe, innovative, and effective medical approaches to the healthcare system and market, lead to improved patient outcomes, and result in cost savings in healthcare delivery. Eliminating barriers to implementing clinical trials for researchers will position Canada as a world-leading destination for clinical research and ensure that people across Canada can continue to benefit from these innovative treatments, employment opportunities, and economic growth.

CIHR's strength lies in coordinating the financial and administrative aspects of health research grants. CIHR must focus its efforts to this space and continue building its capabilities to ensure that more promising research and researchers are funded, and that Canada remains competitive on the global stage. To achieve this in the clinical trials space, CIHR must:

- Enhance Canada's ability to sustain Phase 1 and Phase 2 trials so that funding is available to test newly developed therapies and medical devices, including made in Canada interventions. This can be achieved through a funding program dedicated specifically to this goal.
- Invest more heavily in Canadian companies with made in Canada therapies and medical devices, as well as better promote Canadian companies as outstanding partners for domestic and international organizations and companies worldwide.
- Develop funding programs focused on fostering innovative collaborations and partnerships between public institutions, private industry and academia. This would include programs concentrated on different stages of the clinical trials process, from design to validation to commercialisation.

For stakeholders and partners to support successful partnerships under CIHR funding programs, the following guidance will be needed:

- Information on the commercialisation of research in Canada, including how IP works in clinical trials.
- Guidelines for data sharing across institutional, provincial/territorial, and international boundaries.
- Support for investigators seeking to conduct joint research projects, including facilitating innovative collaborations and partnerships between the public and private sector.

Innovative Clinical Trials

Innovative clinical trials (iCT) promote the adoption of new methodologies, lead to new discoveries, and encourage collaboration with patients and stakeholders, including the private sector. With adequate investment, oversight, coordination, and integration with the Biomanufacturing and Life Sciences Strategy (BLSS), Canada can strengthen its capabilities in this space and move toward an ecosystem that emphasizes iCT over traditional clinical trials to reap greater health and economic benefits.

One area that Canada must focus on to further develop its innovative clinical trials capabilities is data interconnectivity. Linked data sets that enable comparisons across provinces and territories is necessary as comparisons across jurisdictions is difficult to do presently. Canada needs a data strategy for clinical trials, and it must be tied to the Pan-Canadian Health Data Strategy.

Regarding new areas of innovation in clinical trials, the following should be included in iCT initiatives:

- Decentralized clinical trials: Gaining significant momentum during the COVID-19 pandemic, decentralized clinical trials utilize innovative approaches to conduct clinical trials remotely or using a hybrid approach. The flexibility of decentralized clinical trials benefits patients, improves participant recruitment, and increases diversity in trial participation. Decentralized clinical trials encourage patient participation in clinical trials outside of larger academic centres, including community hospitals and long-term care. When conducting and designing decentralized clinical trials, regional equity must be considered.
- Adaptive design clinical trials: Designed to allow modifications to the trial after its initiation, adaptive clinical trials require expertise in Bayesian and other statistical methods.
- Pragmatic trials: Designed to evaluate the effectiveness of interventions using real-word evidence, pragmatic trials produce results that can be generalized and applied in routine practice settings.
- Implementation trials: A lot of areas where evidence is clear what to/not to do and Canada does not have best practices on integration into practice. There is a need for more implementation and knowledge-based trials to promote the systemic uptake of evidence-based interventions into practice and policy to improve health.

Clinical Trials within Canada's Biomanufacturing and Life Sciences Strategy

While current federal government initiatives, including the BLSS and Clinical Trials Fund (CTF) are steps in the right direction, many gaps still exist in Canada’s clinical trials ecosystem. The COVID-19 pandemic highlighted that Canada needs to be better prepared for pandemics in the clinical trials space, including in the biomanufacturing and testing of therapies, much of which was done outside of Canada during the pandemic due to our lack of capabilities.

Clinical trials infrastructure and configuration

Improving Canada’s clinical trials capabilities, especially as it relates to pandemics, requires improved infrastructure and configuration of clinical trials. Canada lacks strength in early-phase development and innovative clinical trials design, including the development of new and novel therapies. Areas where increased clinical trials support can help build Canada’s biomanufacturing and life sciences sector include:

- The ability to run multi-site trials testing the same treatment and protocols.
- Data collection and sharing across institutions and jurisdictions.
- Streamlined approval of trials that can be implemented within 30 days.
- Appropriate Phase 1 and Phase 2 facilities and monitoring.

- Hospital space for Phase 1 and Phase 2 clinical trials (biologics). This requires dedicated bed space in hospitals adjacent to an ICU to allow 24-hour monitoring in case of an adverse reaction.
- Clinical investigation units and a strategy to establish them across the country. Clinical investigation units are discussed further in the section on "International Models of Clinical Trials Funding".
- Primary and preventative care clinical trials, as much of the current focus is on disease-specific clinical trials.
- Phase 1 and Phase 2 testing to support biomanufacturing in Canada, as this is most often contracted out to pharmaceutical companies or other countries.
- More diversity in clinical trials participation, which will require innovative solutions in clinical trials design.
- Cultural safety training and qualifications for individuals carrying out clinical trials with equity-deserving groups should be mandatory.

Clinical trials for medical devices

Additional support is needed for medical devices clinical trials in Canada, especially for Phase 1 and Phase 3. The areas outlined in the previous section are also needed specifically for medical devices.

Partnerships

Another aspect of Canada's current clinical trials ecosystem, including as it relates to the BLSS and CTF, is the need for increased opportunities for partnership. A better ability to partner with companies that are already doing similar work, as well as to spread and scale successful solutions is critical to strengthening Canada's clinical trial ecosystem and capabilities.

The Canadian Clinical Trials Ecosystem

The environment in which clinical trials are conducted in Canada is complex, often occurring across multiple jurisdictions, involving multiple sites, and with every study needing ethics and governance approvals before commencement. While these approvals safeguard the welfare of study participants, the requirement that each site in the clinical trial receive approvals adds unnecessary duplication, considerable time, resources, and costs that delay the trial's start. This is but one example of the barriers researchers encounter in Canada's clinical trials ecosystem.

Reducing barriers and streamlining operations has been a key focus of peer countries that have increased their desirability as a place to conduct clinical trials. Canada must do the same if we wish to be a premier market for clinical trials globally.

As a starting point, Canada needs a modern pan-Canadian framework for clinical trials and a new arms-length body reporting to Health Canada that is tasked with implementation and ongoing governance of the clinical trials framework in Canada. This current initial consultation is a good starting point for developing such a framework, and additional consultations specifically around a modern clinical trials framework involving all clinical trials stakeholders and all levels of government will help flesh out a modern clinical trials framework for Canada moving ahead.

In addition, a new pan-Canadian arms-length governance body for clinical trials would serve to coordinate and provide governance at the pan-Canadian level of clinical trials across the country, implementation of the clinical trials framework, and ongoing monitoring of the clinical trials ecosystem. Its members would be a representative mix of stakeholders in the clinical trials ecosystem in Canada with expertise in various aspects of the clinical trials system, including researchers from health research institutes, the private sector, academia, and government; patients; and representatives from all levels of government.

This pan-Canadian clinical trials governance body would be complemented by pan-Canadian infrastructure to better support and harmonize clinical trials across Canada, and encourage provinces, territories, and regions across Canada to work together and share learnings. This would include supports to enable greater coordination, collaboration and information sharing across institutions and jurisdictions. Such supports will accelerate clinical trials and encourage knowledge mobilization.

Under pan-Canadian governance for clinical trials, funding initiatives would be better coordinated, ensuring that:

- Funding opportunities better align with provincial/territorial priorities and population needs.
- New initiatives do not become silos, as is currently the case, but rather, resources are better integrated across initiatives.
- The use of current infrastructure across provinces, territories and institutions is maximized, better coordinated, and replication is reduced.
- Opportunities for collaboration are better identified and maximised.

Additional areas where the clinical trials ecosystem in Canada can be improved include:

- Allowing multiple co-principal applicants for grants as the single nominated principal applicant requirement serves as a barrier at the institutional level.
- Covering the full costs of research for clinical trials, understanding that these differ from the full costs of research for other types of health research, either by incorporating it into existing funding opportunities or creating new funding opportunities to address these costs.
- Recognize the importance of clinical trials as an integral component of hospital culture, notably, in community hospitals and rural and remote areas by developing financial and other supports to allow these centres to flourish in the clinical trials space. This produces benefits for researchers and healthcare providers in these institutions, their patients, their communities, and the broader Canadian population, especially since many community, rural and remote healthcare organisation across the continuum of care serve populations that are underrepresented in clinical trials generally.
- Accelerating the ethics review process, limiting delays and expediting progress in clinical trials.
- Exploring non-traditional approaches to clinical trials that can be undertaken at a lower cost and with fewer resources. Examples include Clinical Trials in a Dish (CTiD), which involves testing medical therapies on a sample of human tissue in a laboratory, and N-of-1 clinical trials, in which a single patient is the sole unit of observation in a study.

- Investing in designated clinical investigation units in health research institutes. These are units integrated within hospitals with specialized research nurses and physicians as well as research equipment to conduct clinical trials and monitor both in-patient and out-patient clinical trial participants.

International Models of Clinical Trials Funding

The international models cited in CIHR's consultation paper offer excellent examples for initiatives that Canada should be implementing to strengthen the clinical trials ecosystem and position Canada for long-term success.

Integrating clinical trials into the health system

In a June 2022 report entitled "The Future of Clinical Research Delivery: 2022 to 2025 Implementation Plan", the UK government outlines its approach to integrating clinical research in the health system, which is currently underway, to ensure that health research conducted in the UK is viewed as an integral part of the health care system.

Canada should be doing the same. Embedding clinical research investments directly into the health system and automatically opting patients "in" to research of benefit to them (with an option to "opt out") will allow more patients to benefit from research of relevance to them, provide clinician researchers better access to patient populations (including within primary care, allowing greater focus on prevention), and speed up knowledge translation, converting promising interventions in clinical research into healthcare practice. The translation piece is especially promising as Canada underperforms in investing and realizing translation of health research into practice.

Conducting clinical trials in primary care settings

Many jurisdictions around the world, including Australia and the UK, have the capabilities and funding to conduct clinical trials in primary care settings. Canada currently faces challenges in doing the same, and these international models should be explored to identify approaches that could be replicated in Canada, including the role that community hospitals can play in these types of trials.

Knowledge translation

Another UK example that could be replicated in Canada is the National Institute for Health and Care Research's approach to knowledge translation, which funds the distribution of data and evidence into the health system. CIHR's current funding is not sufficient to both support the generation of research and its dissemination and translation into practice. The health research community has observed that funding from Health Canada/CIHR does not support translation as much as funding received through Innovation, Science and Economic Development (ISED). For example, the Alliance Grants administered by NSERC, which reports to ISED, is a funding program that supports translation. As well, federal innovation programs such as the Strategic Innovation Fund (SIF) and the Strategic Science Fund do not have a dedicated line item for knowledge translation.

Creating a branch or program under Health Canada to facilitate knowledge translation by setting the standards by which health research would move into practice would help increase uptake of best practices and improve health outcomes. This could be achieved by creating a methodology centre and/or assuming the Strategy for Patient-Oriented Research (SPOR) program from CIHR. This approach should be adopted for all health research, including clinical trials.

There are also domestic examples of approaches to ensuring that health research innovations are implemented in the healthcare system, such as Alberta's Health System Research and Innovation approach that outlines a 5-step process for the rigorous and ongoing testing of innovation through different stages of implementation in partnership with researchers, patients and healthcare teams.

Setting research priorities

Another area where Canada could be learning from its international peers is in involving people with lived/living experience, whether they be patients/residents, caregivers, researchers, or healthcare providers, in the setting of research priorities.

The UK's James Lind Alliance (JLA) method is one example that encourages priority setting partnerships in which patients, caregivers, and health professionals collaborate to identify a "Top 10" list of research priorities. There are domestic examples of this approach as well, including Alberta's Partnership for Research and Innovation in the Health System (PRIHS) that strengthens health research capacity by encouraging collaborations between academic institutions, health and clinician researchers, patients, and AHS to align knowledge production efforts of researchers with the evidence needs of the health system.

CIHR Policies to Support Equity, Diversity and Inclusion (EDI), Transparency, and Research Excellence

While Canada has made efforts to promote equity, diversity, and inclusion (EDI), more must be done to improve EDI and raise the bar on research excellence in Canada.

As noted in the previous section related to setting research priorities, there are examples domestically and internationally on ways to support more effective participation of various stakeholders in the development of clinical trials, including the UK's James Lind Alliance (JLA) method and Alberta's Partnership for Research and Innovation in the Health System (PRIHS) approach.

Standards, programs, and funding that improve EDI on research teams and among participants in clinical trials, including individuals from equity seeking groups or lived/living experience, are additional approaches Canada can adopt. Some recommendations include:

- Incorporating a mandatory EDI component in grant applications, similar to the Sex- and Gender-based Analysis (SGBA) component. Consider increasing the length of applications to accommodate these additional components while also ensuring enough space to discuss the science.
- Developing evaluation guidelines or other mechanisms for CIHR reviewers to assist them in effectively analysing genuine EDI efforts in applications.

- Adapting the structure of clinical trials to enable a wider breadth of individuals to participate.
    - For example, the timing/schedule for clinical trials makes it difficult for those who have other commitments, including work or caregiving responsibilities, during regular business hours.
    - Timing/scheduling and the commitment that participating in a clinical trial may entail often limits who can participate in clinical trials to people who can financially afford to do so.
    - Geography and personal mobility can also limit who can participate in clinical trials, so bringing clinical trials to people, rather than bringing the people to the trials should be explored.
- Increasing the salary and dollar amount of awards for trainees, post-doctoral fellows, and early-career investigators. As with participants in clinical trials, this limits who can participate in this work.
- Ensuring that funding calls specify a need for different types of research and knowledge translation efforts that focus on equity-deserving groups and groups that are underrepresented in clinical trials and health research generally.

Development of a Long-Term Clinical Trials Strategy

Canada lacks a bold pan-Canadian vision and overarching governance structure for clinical trials to enable greater coordination, collaboration and information sharing across the ecosystem. As Canada looks to develop a long-term clinical trials strategy, it must consider how it can create a Canadian ecosystem that works well for all stakeholders domestically, while maintaining Canada's attractiveness as a place to invest and conduct clinical trials.

In developing a long-term clinical trials strategy for Canada, important considerations include:

- When developing grants, the federal government and CIHR must take a longer view across the clinical trials continuum and consider how to support research beyond the initial grant period so that research does not languish, can be further studied/tested and, if successful, rolled out to improve patient care and health system delivery.
- Fostering a more research positive culture in clinical and academic settings through better integration between research, clinical, and academic settings. Research is vital to better care, but health research and researchers can be siloed from healthcare delivery and from their clinician and academic colleagues. Greater efforts are needed to cross-train/educate across these groups so there is better understanding of the interdependence of these various aspects of healthcare and the benefits of research to patients and health system innovation.
- Tied to the first point, greater supports are needed for healthcare providers in community hospitals and rural and remote settings to enable them to participate in research endeavours. These institutions often do not have dedicated individuals conducting research and so it becomes even more important that healthcare providers understand the research side of healthcare and the benefits for patients and communities.
- Similarly, there is a need for better support and outreach to community hospitals and rural and remote organizations/health authorities looking to enhance their clinical trials capacity, including assistance in the accrual of patients and recruitment of research staff.

- Dedicating investments and resources to ensure a skilled and sustainable clinical trials workforce across the country, including in urban, rural and remote settings, and that includes more equity-deserving groups and those that continue to face barriers in pursuing a career in research.
- Modernizing clinical trials regulations in Canada to support researchers, attract global pharmaceutical and biotechnology companies, and improve access to innovative therapies for people across Canada. Streamlining regulatory processes for researchers and companies must include improvements to the efficiency of Research Ethics Board (REB) reviews, optimization of contract development and IP protection policies, and statistical and data analysis supports for researchers.

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