

Canadian Clinical Trial Summit

Starting the Conversation

Canada's Research-Based
Pharmaceutical Companies



Les compagnies de recherche
pharmaceutique du Canada

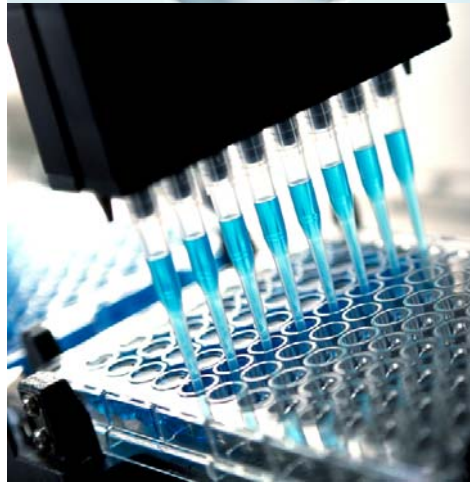


CIHR IRSC

Canadian Institutes of Health Research
Institut de recherche en santé Canada



Cameron Institute



Ottawa, September 15, 2011

A Summary & Message from the Presidents

Canada has enjoyed a reputation for excellence in the area of clinical research. Our participation and leadership in clinical trials has led to many world first medical discoveries and innovations; attracted world leading clinicians and researchers; benefited patients and families; and resulted in important pay-offs for our economy.

However, there are operational barriers that could compromise our future success. We are seeing a decreased number of clinical trial applications in Canada and an increase in the impact of issues related to the cost, quality and time required to conduct clinical trials in our country. These need to be addressed in order to re-establish and secure the future human, social and financial benefits from clinical trials that we currently enjoy.

Other countries face the same issues. To address them, they are using the full force of their unique populations, environments and competitive advantages. Their strategies range from the selection of clinical areas for strategic foci, to the establishment of nation wide infrastructure that facilitates training, recruitment and operations; the standardization or centralization of legal and ethics review environments; streamlining of forms and processes; the funding, licensing or accreditation of clinical sites participating in trials; and collaboration across geographic regions to maximize harmonization of processes and available populations for recruitment into trials.

In Canada, nearly every province has also invested in strategies for strengthening clinical trials; we have formal and informal disease and population based networks; and we are making progress on a variety of individual operational barriers. While many of these initiatives may not yet be fully coordinated across the country, they are living experiments and resources that can catapult our national progress, especially considering our relatively small population size. Establishing and implementing a plan that can harness these efforts, build on our strengths, and successfully address issues related to cost, quality and speed, will help us to secure and expand Canada's position as a leading environment for clinical research.

The question that must be answered at the summit however, is *"How?"*. On September 15, 2011, our goal is to unite across sectors and from coast to coast, to develop an action plan that can further guide academia and clinical sites, government, and industry on a common path. This document provides a backdrop of some common high level issues and perspectives. But remember – this is just the beginning of the conversation. We look forward to your contributions, and ultimately, to an action plan for a future of excellence in clinical trials - to the health and economic benefit of all.

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Meet the Sponsors

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Rx&D is the association of leading research-based pharmaceutical companies dedicated to improving the health of all Canadians through the discovery and development of new medicines and vaccines. Our community represents over 15,000 men and women working for 50 member companies and is responsible for generating 60,000 jobs across Canada. Member companies come in all sizes and fund 27% of health science research & development in Canada. Our Mission is to advocate for policies that will bring the best innovative medicines and vaccines to Canadians in a timely an appropriate manner; improve Canada's global

competitiveness; and make Canada a world leader in attracting pharmaceutical and biotechnology investments. Our Objectives are to conduct and promote health research in Canada; To strive for full access to innovative medicines for all Canadians ; inform Canadians about the contribution of the research-based pharmaceutical companies in improving their quality of life; communicate the role of Canada's research-based pharmaceutical companies in the advancement of an effective, integrated and accessible health care system; work cooperatively with our partners in Canada's health care system; promote a competitive intellectual property protection and regulatory framework that encourages the discovery and development of new medicines in Canada; communicate high standards of safety and quality of medicines; educate health professionals and consumers in the optimal use of medication. You can read more about Rx&D at <https://www.canadapharma.org>



CIHR IRSC
Canadian Institutes of
Health Research Instituts de recherche
en santé du Canada

The Canadian Institutes of Health Research (CIHR) is the Government of Canada's agency responsible for funding health research in Canada. CIHR was created in 2000 under the authority of the *CIHR Act* and reports to Parliament through the Minister of Health. CIHR's budget for 2008-09 is \$928.6 million, of which \$132 million is allocated to administering the Networks of Centres of Excellence and Canada Research Chair programs. CIHR was created to transform health research in Canada by: funding more research on targeted priority areas; building research capacity in under-developed areas such as population health and health

services research; training the next generation of health researchers; and focusing on knowledge translation, so that the results of research are transformed into policies, practices, procedures, products and services. CIHR's mandate is to "excel, according to internationally accepted standards of scientific excellence, in the creation of new knowledge and its translation into improved health for Canadians, more effective health services and products and a strengthened Canadian health-care system." CIHR consists of 13 "virtual" institutes, a structure that is unique in the world. These innovative institutes bring together all partners in the research process - the people who fund research, those who carry it out and those who use its results - to share ideas and focus on what Canadians need: good health and the means to prevent disease and fight it when it happens. Each institute supports a broad spectrum of research in its topic areas and, in consultation with its stakeholders, sets priorities for research in those areas. You can read more about CIHR at: www.cihrc.ca

Meet the Sponsors



ACAHO is the national voice of Canada's Research Hospitals, academic Regional Health Authorities and their Research Institutes. The collective *Vision* of these organizations is to advance patient care and the health & well-being of Canadians through research discovery and innovation. Our *Mission* is to create an environment in which research discovery, innovation and learning benefit patients, populations, health systems and the economy. The Association represents more than 40 organizations, with members ranging from single hospitals to multi-site regional facilities.

Members of ACAHO are the leaders of innovative and transformational organizations who have overall responsibility for: (1) provision of timely access to a range of specialized and some primary health care services; (2) training the next generation of health providers; and (3) are leaders in research discovery and the early adoption of innovation in the health system. There are no other organizations in the health system which provide the unique integration of patient care, teaching, and research & innovation that our members do. Our members are vital "hubs" in the health system - in addition to being a national resource. The mandate of ACAHO is provide national *leadership*, *advocacy* and *policy representation* when it comes to the role of the federal government improving the performance of the health system; and advancing the impacts of health research and innovation in the delivery of health care to all Canadians. You can read more about ACAHO at www.acaho.org



The Cameron Institute is an alternative, not-for-profit, public policy think tank specializing in the independent study of current health, social, and economic issues. The Institute researches policy concerns in the health world related to the need for balance between patient safety and access to new, innovative, affordable therapies. It is an objective of The Cameron Institute to provide decision makers with analyses that will help inform choices. The Institute is also dedicated to educating and better preparing patients, providers, and payers to make appropriate administrative and clinical choices.

Our values are freedom, choice and responsibility. Dr. D. Wayne Taylor, the Executive Director of The Cameron Institute, has worked as an executive in the private sector, as a senior civil servant, as a political assistant, and was the Founding Director of both the MBA Programme in Health Services Management and the Health Leadership Institute at McMaster University. He remains a tenured faculty member in the DeGroote School of Business at the Ron V. Joyce Centre for Advanced Management Studies while serving as president of his own private international consultancy. You can read more about the Cameron Institute at: <http://cameroninstitute.com>

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Table of Contents

A Summary & Message from The Presidents.....2

Meet the Sponsors.....3

Starting the conversation - the value of clinical trials to Canada.....6

The International Landscape - What are other countries doing?7

Clinical trial trends in Canada10

What could be behind some of these trends?.....11

What are some of Canada’s strengths in clinical trials?.....12

Leading by example - A cross-country commitment to clinical trials.....14

A Look to the future - A strategic action plan for clinical trials in Canada?.....16

Starting the Conversation...

This document is designed to introduce a conversation. Considering that the focus of the summit will be on action plan development, the organizers felt it may be helpful and efficient to summarize commonly known issues and assumptions that will likely underpin the conversation. In this document, we discuss the value of clinical trials to Canada; what other countries are doing to attract them; what the situation looks like in our country; possible issues and explanations for recent trends; an overview of our strengths, and a look at current initiatives at both the national and provincial levels. While the document will not propose any solutions, it will highlight some considerations that may be relevant in action planning. At the end of the paper, we will provide some questions that may be relevant to the more specific discussion items on site.

The Value of Clinical Trials to Canada ¹

Clinical trials respond to human, social, and financial goals as they relate to the development of new drugs, devices, and vaccines. They are the nexus between science and practice and reveal crucial information about the products they test. In the long term, they will result in the ability to cure or cope with disease; improve quality of life, and prevent decline or disability. In the immediate term, they are important to our understanding of disease, generate knowledge that is used in many different ways in both industry and patient care settings, and offer patients and clinicians rare opportunities for novel and advanced treatment options.

Once completed, data from successful clinical trials help to market and monitor safe use of the drug, device or vaccine. Clinical trials attract world leading clinicians and create employment opportunities for thousands of highly qualified personnel. Finally, they generate important revenues for organizations and for the economy, a consideration which is intimately tied to the well being of our society. In fact, close to 80% of the pharmaceutical industry's investment in Canada is towards the conduct of clinical trials in Canadian healthcare institutions.

Why do patients partake in clinical trials? For people who do not respond or who suffer side-effects from standard or available therapies, participating in a clinical trial can allow them to access innovative products. Since trials are often led by leading clinicians, trial participation may also allow the patient to obtain access to expertise that may not otherwise be available. Finally, some have noted the empowering effects of clinical trials to a patient who feels he or she is helping the future of his or her own condition and others' as well. ²

Why do clinicians partake in clinical trials? In addition to serving the goals of their patients, clinical trials allow clinicians to access and learn about cutting edge drugs or technologies at a very early stage. The opportunity to make this kind of a difference while building their knowledge base, can result in rewarding experiences.

Why do healthcare organizations partake in clinical trials? In addition to supporting the goals of patients and clinicians, participating in clinical trials attracts leading clinicians and has also

been associated with better clinical outcomes for the organization.³ Clinical trial opinion leaders share their experiences with new therapies impacting the “uptake” and proper utilization of new therapies once they become available and provide opportunities to explore unexpected questions and refine treatments. This work enhances patient care overall and is not generally performed in non-trial sites. It can reinforce the development of centres of excellence - through a cyclical combination of trials, outcomes, critical mass, patient choice, leading clinicians, grants, prestigious reputations, donations for technology and equipment, further research, and ultimately, treatment capacity.⁴ Finally, clinical trials are part of the academic mission and the bench to bedside paradigm.⁵ For example, between 1996 and 2006, Canada’s academic healthcare organizations generated at least 75 spin-off companies and hundreds of world-first medical discoveries.⁶ Many of these would be related to various phases of the drug, vaccine, or device production cycle.

What is the value for the economy in Canada? Clinical trials can generate revenues for organizations and for the economy. For example, Canada’s academic healthcare organizations (research hospitals, academic regional health authorities, and their research institutes) attracted close to 300 million dollars of potential clinical trial revenue through new clinical trial contracts in 2007-2008.⁷ While this may not translate into profits for the clinical sites, considering overhead costs usually exceed the trial revenues, it does contribute to the growth and advancement of research institutes which has further benefits. For example, the academic healthcare organizations within which Phase II and Phase III trials take place are overseen by some 1,500 clinician scientists whose research endeavours and budgets enable research opportunities for thousands more staff and students.⁸ Many of these types of jobs can be high-value, high-paying, knowledge-based jobs of the future.⁹

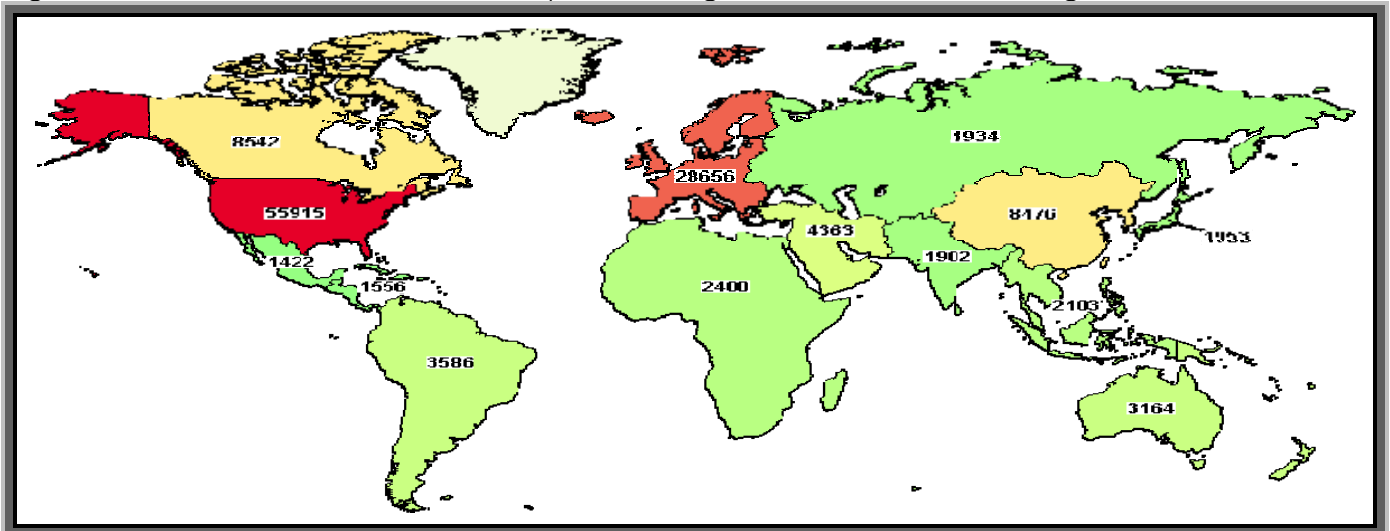
The International Landscape...What are other countries doing?

While clinical trials are of value to Canada, they are also important to other countries for many of the same reasons (Figure 2). In this section, we discuss international examples of clinical trial infrastructure choices designed to address strategic, cost, quality or time issues. We will begin with a summary of key strategies from across the cases and then discuss each case in more detail. Since some of the strategies in the summary may be context-specific or yet to be evaluated, we will not comment on their relative effectiveness. Instead, they are listed as a range of possible options and considerations.¹⁰

- **Central access point for industry:** Establishment of centralized bodies or networks as single point(s) of access for industry. These are also used to facilitate operational issues, training, clinical site coordination, and patient recruitment.
- **Geographic collaboration:** Collaboration across regions, countries and continents to offer larger populations for recruitment and greater harmonization.
- **Standardization or centralization to address operational barriers:** To address operational barriers like ethics review or contract negotiations, the cases show a variety standardization or centralization methods to streamline the processes.
- **Clinical trial site designations:** Application processes or licenses for clinical sites to conduct clinical trials, creating an incentive for standardization.

- **Funding and accountability systems:** The designation, funding and accountability of various institutions for ensuring an effective infrastructure required for clinical trials research.
- **Selecting areas of excellence:** Establishment of clinical areas or foci that create niche markets and enable the consolidation of efforts and resources.
- **Branding for excellence:** Actively identifying and promoting population characteristics, relevant infrastructure, and capacity for clinical trials through targeted marketing and branding that is designed to encourage investment.
- **Electronic submissions:** Mandatory electronic submissions of trial applications resulting in real time data for strategic and monitoring purposes.
- **Product uptake and post market surveillance:** Considering the rate of uptake of resulting drugs and technologies in the market where trial is conducted.

Figure 1: A 2011 map from ClinicalTrials.Gov (US trial registry) showing the number of clinical trials registered in their database from different parts of the globe. (source: Clinicaltrials.gov, 2011)



Central and Eastern Europe: In this region, Poland, Hungary and the Czech Republic conduct the largest number of trials. In 2004, the *EU enlargement* and the implementation of the *European Clinical Trial* directive created a pan-European clinical research market and unified the legal environment. These are believed to have improved the clinical trial supply process, removed custom barriers, and reduced costs and lead time. However, implementation of the directives has been subject to interpretation, resources, timelines and processes in each country, which is currently slowing approval rates and there are also problems in the interpretation of regulations regarding labeling of clinical supplies and in standardizing ethics reviews. By contrast, in Russia and the Ukraine which are not applying the standards, approval times remain faster. Strengths of this market include the centralized healthcare system with strong referral networks, high quality investigational sites, large total population, rapid recruitment, and high quality clinical data.¹¹

Spain: In describing its clinical trial environment from a population perspective, Spain highlights its relatively healthy and wealthy population of 46 million inhabitants. The population

has a fairly high life expectancy and a health system that ranks 7th in the world.¹² The paradoxical increase in clinical trials with a simultaneous decrease in Spanish pharmaceutical companies was attributed to the merger and acquisition of small successful Spanish Parma companies. The researchers from the newly merged companies, brought trials back to Spain from larger international companies. Finally, the public health system includes specialized centres of excellence for trials. In spite of a nursing shortage, staff involved in clinical trials are usually pharmacists and have a reputation for a high level of qualification and experience.¹³

China: In 2005, the Medical Devices and Pharmaceuticals Subgroup of the US-China Joint Commission on Commerce and Trade, offered the Pharmaceutical Research and Manufacturers of America and the Biotechnology Association of America, the opportunity to express concerns directly to the Chinese State Food and Drug Administration. The meeting addressed perceptions and issues related to quality, bureaucracy, intellectual property, and international standard alignment and has since resulted in an increased investment in clinical trials in China. Clinical sites in China wishing to run clinical trials must apply for a designation. This imposes common standards. The costs of a clinical trial in China are also estimated somewhere between 10% to 30% of the costs of conducting the clinical trial in western countries.¹⁴ High levels of urbanization with 50 mega cities, and the concentration of prestigious hospitals in urban centres attracts patients and results in important pools for recruitment.¹⁵

United Kingdom: The United Kingdom markets itself on internationally renowned researchers, regulations associated with high quality, the accessibility of the English language, and important research support infrastructure. The National Clinical Research Network (NCRN) was developed in response to a decrease in the UK's world share of clinical trial patients recruited from 6% to 2%. NCRN's role is to provide practical support across the NHS, increase clinical research, and involve more patients. It consists of eight national networks with 103 local branches. Four hundred organizations are members of these networks which results in thousands of clinical research sites (including primary care). Each year it funds 7,800 NHS staff and trains more than 14,000 people. Over 1200 patients and clinicians are involved in research design, governance and delivery and 2,500 open studies recruit patients each year. In the area of study planning, it provides advice on available support staff and facilities, ideas to clinicians, and intelligence on patient populations. In the area of study set up, it reduces red tape on multi-site studies, manages the approval process and speeds up start up times. In the area of study delivery it funds facilities and people to carry out the research, recruits patients and provides training. The research costs are paid by the funder, the support costs are paid by NCRN and the excess treatment costs are paid by the National Health System. As a consequence, 96% of all NHS sites have active patient recruitment into clinical trials.¹⁶

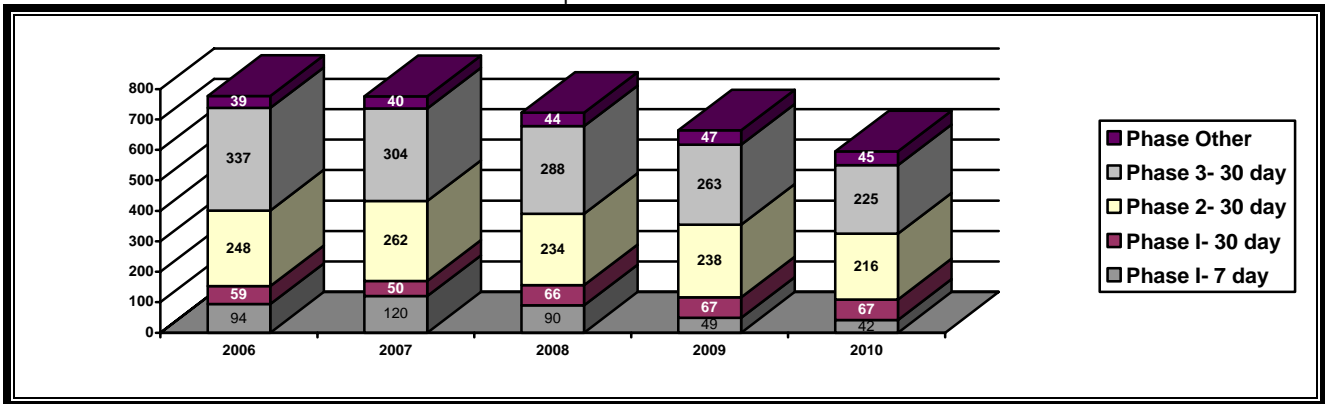
United States: In 2010, the United States held a clinical research infrastructure forum much like our own. At this forum, a vision was expressed 'for a clinical research system that would function like an energy grid – a large Public Works project to ensure universal access to new clinical evidence and its adoption by clinicians'. The vision included a permanent network of resources, including sites, patients, researchers, and support staff, that would be available for clinical trials. The network would be organized by nodes which would have either geographic

or disease-specific foci. Supporting and uniting these networks would be paid staff, academics and experts experienced in clinical trials, who would support, run and organize the infrastructure. Funding would be federally provided. While this vision has supporters and opponents, many other clinical research infrastructure efforts have already been established in the US. For example, since 2006, 46 academic institutions have made up the Clinical and Translational Science Awards program. The goals are to build national clinical and translational research capacity; provide training and career development for clinical and translational scientists; enhance consortium-wide collaborations; improve the health of communities and the nation; and advance T1 translational research to move basic laboratory discoveries and knowledge into clinical testing.¹⁷ In addition, the US is known internationally for its Comprehensive Cancer Systems in which 40 institutions are designated across the country. These forty institutions hold responsibility for cancer drug research and are each provided with \$20 million dollars per year in funding to pay for their own infrastructure, for which they also become accountable.

Clinical Trial Trends in Canada

What might be the effect of all these countries stepping up their efforts in the area of clinical trials? While the data is inconclusive, there are trends that are concerning for Canada. Between 2006 and 2010, clinical trial applications for non-generic drugs decreased from 777 to 596.¹⁸ The decrease is seen for both aggregates and for each of Phase I, II, and most especially, for Phase III trials.¹⁹ (Figure 2).

Figure 2: Declining numbers of phase I, II, and III clinical trial applications (excluding bioequivalence) Data from Health Canada Performance Report 2010



A similar trend was also observed in a study of 5 companies that are believed to hold 50% of the Clinical Trial market share. Comparing data on number of subjects, sites, and trials between 2008 and 2010, a decrease was shown in all three indicators for both Canada and the global market. However Canada's decrease appears to be deeper and more rapid than the global figures (Table 1)²⁰.

Table 1: Declining numbers of subjects, sites, and trials in Canada and Globally as seen from a study of 5 companies Canadian vs. Global data. (Rx&D, 2011).

Indicator	Years	Canada	Global	%Canada of Global	% 2010 of 2008 Can.	%2010 of 2008 Glob.
Subjects	2008	7845	227,389	3.45%	---	---
	2010	4485	168,876	2.66%	-43%	-26%
Sites	2008	975	26,241	3.69%	---	---
	2010	748	22,358	3.35%	-23%	-15%
Trials	2008	135	990	13.64%	---	---
	2010	95	760	12.5%	-30%	-23%

In addition, Rx&D has noted a negative percentage growth in clinical trial sites in Latin America, Western Europe, & North America and an increasing number in Asia, Eastern Europe & in Australia and New Zealand. In another dataset, it has been shown that the cost of clinical trials per patient is much higher in Canada than in most other countries.²¹

What could be behind some of these trends?

While data can leave scope for interpretation, many factors can explain the reduction in clinical trials including the intellectual property regime and reimbursement environment. Notwithstanding these, cost, quality, and speed are three themes that come up as frequent explanations for recent clinical trial trends. These may be further explained in terms of some of the following:

- Operational barriers:** Although many operational issues are starting to be addressed, administrative issues, cost structures, contract negotiations, and diverse ethics reviews within and across provinces still exist and are inconsistent with the “time is money paradigm”. Operational barriers are not only problematic for industry and clinical sites; they may also discourage outstanding clinicians from partaking in clinical trials because of time consuming and comparatively unrewarding business-related risks and issues. In some countries centralized offices have been established to reach out to industry, shepherd them through the process, and help them overcome operational barriers in a consolidated fashion.
- The costs and consequences of unevaluated interventions:** While there is often good intention in addressing operational barriers in principle, sometimes, these efforts can inadvertently introduce interventions that create problems in practice. For example, the introduction of clinical research organizations (CROs) was initially intended to facilitate clinical trial operations, but their proliferation, diversity, and international obligations have had the effect of introducing multiple, uncoordinated and often under-resourced 3rd parties into the process. In the United States, standards for research ethics boards, once thought to bring additional standardization, rigour and safety to the process, are now under review because their burden of compliance has drained time and resources, while showing no demonstrated benefit to patients, safety, clinicians, sites or sponsors.

- **Population size and difficulties in patient recruitment and retention:** Especially for Phase III clinical trials where thousands of eligible individuals may need to be recruited for a clinical trial, a relatively small population may be perceived as a drawback to participation in any single province within the Canadian market. This can be exacerbated by the perceptions that this small population is further divided by jurisdictional issues and distance. In addition, unlike other countries, Canada has yet to develop targeted resources and strategies to market, explain, and attract patients and the public to clinical trials. This can further result in recruitment, retention, and compliance problems.
- **Absence of a centralized problem solving resource:** In spite of a collaborative culture, intention and the efforts of various leaders and associations, Canada does not have a permanent or resourced problem solving forum for addressing either policy related or operational barriers as they relate to clinical trials.
- **Healthcare costs, data, training and capacity issues:** International jurisdictions with very low healthcare costs (such as for diagnostic imaging), tend to attract more clinical trials because these effect the total cost of the trial. For example, the cost of clinical trials per patient in China is about 1/3 of the cost of a clinical trial in Canada, in part due to healthcare costs.²² In addition, nursing shortages in Canada may make it difficult to train staff on protocols. There are challenges in ensuring sufficient resources to build and share databases and to address indirect cost issues. Future availability of clinician scientists may be undermined if we don't give better consideration to salary support and protected time for research - especially in the context of higher and more complex case loads.²³ Finally, to benefit from the role of primary care clinics in clinical research and subsequent uptake, Canada should consider the recommendation of the National Task Force the Future of Academic Health Sciences Centres (AHSCs) to facilitate the expansion of AHSCs towards Academic Health Sciences Networks that could better encompass primary care and other types of care settings. This would require dedicated resources and leadership in each part of the country.²⁴

However, in spite of the challenges, the potential for capacity-building in our country is there. In the next sections we discuss some of our strengths, examples of nation wide initiatives that may help to advance our progress and then discuss the incredibly rich array of initiatives that are occurring regionally and provincially.

What are some of Canada's Strengths in Clinical Trials?

In brief, our strengths include outstanding clinicians, researchers and organizations, a track record of concrete successes which include world first medical discoveries and spin-off companies; quality and integrity in research and clinical practice; the structure of our health system; the interest of the public in clinical trials; the establishment of disease and population specific networks of international repute; existing resources and progress on operational barriers, both nationally and provincially; and a substantiated interest and commitment on the

part of clinicians, researchers, organizations, governments, and industry to excel in clinical trials. In this section, we discuss each of these strengths in turn.

- **High reputation of researchers, organizations, and outputs:** Talented and motivated Canadian researchers have very high rates of academic impact and outstanding reputations. The data that is generated from our trials is considered of excellent quality. We have a strong tradition of basic research that feeds the discovery process. World renowned academic healthcare organizations and universities with a valuation on clinical research and research administration offices can support clinical trials. In addition, recent work on Research Integrity has shown that Canada has a relatively low rate of research misconduct which is important in this area.^{25 26}
- **Diverse population:** In spite of our relatively small population, we benefit from the diverse races and ethnicities that make up the Canadian population. This is often a key scientific and methodological requirement in selecting study populations.
- **Disease and population specific networks and health charities:** Recognizing that clinical trials differ according to population, size, and disease, we have in Canada well established networks and health charities that either dedicated to clinical trials or broader aspects of the population group and disease. Some of these networks are recognized internationally (cancer, cardiovascular, rheumatology etc). All can be further harnessed to facilitate clinical trials.²⁷
- **National progress on operational barriers:** In addition to the valuation on harmonization, there has been progress at the national level in the areas of: national standards for REBs reviewing clinical trials ^{28 29}. A variety of formal and informal networks are also looking at disease or population specific issues (for example related to paediatrics, rheumatology, cardiovascular, cancer, respiratory, ALS etc), while others are more operationally focused (for example related to ethics, standard operating procedures, the creation and distribution of training and quality assurance tools that support investigators and research.³⁰
- **An interested public:** While a potential yet to be harnessed, it is clear that the Canadian public has an interest in clinical trials. Recent examples have been seen in the areas of ALS and multiple sclerosis. While in some cases the discussions are complex, what we can take from these is a clear signal that where appropriate, there is potential to engage the public in supporting these research endeavours.³¹
- **Publicly-funded healthcare and provincial funding for health:** Our publicly-funded healthcare system is known for its quality and reputation. The role of the provinces offers important potential for consolidated procurement of novel technologies. This may be an attractive consideration for companies in considering whether or not to bring trials to Canada.³² National accreditation standards can help global companies both be reassured of quality and potentially achieve accreditation between organizations.

- **National, federal and provincial leadership:** Finally, across the country, there are tremendous examples of leadership and harmonization that can be used to springboard the future of clinical trials in Canada. Canada's granting council for health research, CIHR, has made an important public commitment in its strategic plan to help the field address operational barriers. It has developed, consulted on and provided for the public, its Strategy for Patient Oriented Research which is intended to help facilitate clinical research and multi-site clinical trials.³³ Staff at Health and Industry Canada and in other departments is also committed to assisting the field in this area. Finally, we have a wealth of regional and provincial initiatives that can catapult our progress. We discuss these in the next section.

Leading by Example - A Cross Country Commitment to Clinical Trials

In addition to the currently unfolding national initiatives and considering the value of clinical trials to all Canadians, each province is also organizing to maximize its ability to attract clinical trials to Canada.

Please note that these descriptions are intended only to give examples of what is happening across the country. They are not intended to be exhaustive or used for inventory, analytical or business planning purposes. Our thanks to colleagues who contributed perspectives to this section.

British Columbia: The British Columbia Clinical Research Infrastructure Network (BCCRIN) is a collaborative partnership of provincial health authorities, universities, industry associations and funding agencies. It is a first of its kind, focused on enhancing BC's ability to compete in this area. To achieve this goal, the network is focused on developing best-in-class research processes and infrastructure to support clinical and translational research personnel and activities. Task Forces have been formed to address the harmonization of research contracts, development of a pan provincial strategy on professional development, robust quality systems at our research centres and a research methodology hub of expertise. Key accomplishments to date include the signing of a Memorandum of Understanding among six research-intensive institutions on the harmonization of the negotiation and acceptance of industry-sponsored clinical research contracts. The next major milestone will be the completion of a robust 5 year business plan, whose development will be overseen by community leaders.^{34 35}

Alberta: The main institutions involved in the regulation and conduct of clinical research – Alberta Health Services, the University of Calgary, the University of Alberta, the College of Physicians and Surgeons of Alberta, and Alberta Innovates Health Solutions are united through a common vision. They have struck officially sanctioned working groups to improve the climate for clinical research in Alberta. Their initial progress includes harmonized ethics approval with inter-institutional reciprocity, single provincial pricelists for services provided by Alberta Health Services to investigators, harmonized legal and contractual processes, and rapid work towards harmonized software platforms, among other initiatives. Considering that Alberta Health Services is a single provincial system for both acute and community care, they have experienced relative ease in bringing databases together and in facilitating transformation and collaboration. The presence of two strong universities with their Faculties of

Medicine; a single provincial health region with a strong interest in research and a committed, a proactive vision; and the ability of Alberta Innovations Health Systems to support the process will help to fund programs aimed at outcomes. In addition, the Northern Alberta Clinical Trials and Research Centre (NACTRC), has one of its core strengths a focus on Phase I trials, for which it has a designated 9,000 square foot trial facility, one of very few in the country.³⁶

Saskatchewan: The Saskatoon Centre for Patient Oriented Research is a new collaborative of the Saskatoon Regional Health Authority, the Saskatchewan Cancer Agency, and the University of Saskatchewan. Significant headway has been made in harmonizing provincial Research Ethics Boards standards. Conversations have begun with British Columbia, Alberta, and Manitoba to look at further harmonization across the four three provinces where the population access would reach 10 million. Saskatchewan holds some of the oldest patient databases in North America, has a strong capacity for preclinical and translational work, vaccine development, molecular and other imaging at the Canadian Synchrotron and recently a new research cyclotron, PET-CT, and Canadian Centre for Nuclear Innovation (CCNI-\$30M).³⁷

Ontario: Ontario has been active in streamlining and expediting administrative processes associated with clinical trial start-up. This includes the creation of the Ontario Cancer Research Ethics Board (OCREB), a statement of principles for negotiating clinical study agreements with industry, and regional collaboration across the province to streamline ethics review and contracting processes. In April 2010, the Ontario Government launched its \$161 million Life Sciences Commercialization Strategy, earmarking \$17 million for three clinical trials related initiatives, one of which is: *“A new province-wide coordinating infrastructure to streamline administrative processes and ethics reviews across multiple clinical trial sites in order to increase the speed of patient recruitment.”* Stemming from this strategy, a multi-stakeholder initiative is underway with research hospitals, universities and industry to streamline the ethics review process for industry-sponsored multi-centre clinical trials in Ontario, while maintaining the best of class standards of protection of the rights, safety and well-being of human subjects involved.³⁸ In the area of cancer drug testing, Ontario houses a consortium of 16 Canadian hospitals to form one of six North American sites, and the only non-American centre for the testing of National Institute of Health Funded Phase I and II cancer drugs.^{39 40}

Quebec: In 2009, Quebec’s Minister of Economic Development, Innovation and Exports (MDEIE) released a Biopharmaceutical Strategy for the Province of Quebec. This strategy is designed to be complimentary to Quebec’s Research and Innovation Strategy and Quebec’ Drug policy.⁴¹ As part of this strategy, one of the objectives is to promote Quebec’s image as international pharmaceutical hub and to create a very attractive environment for clinical research. To this end, a “Permanent Forum for Information Exchange” (Forum permanent d’échanges) was established that includes representation from the MDEIE, Ministry of Health (MSSS), Rx&D, Fonds de recherche du Québec- Santé (FRQS), Genome Quebec, and Biotech Quebec. FRQS, which represents Quebec’s 19 research centers and which has provided funding to the research centers to improve partnership strategies with industry and enable the resolution of various operational issues related to clinical trials, has created a “Provincial Coordination Committee” (comité de pilotage) which will implement five working groups

focusing on resolving the most common cross cutting areas involved in clinical trials in partnership with Industry. These are: (1) streamlining and improving multicenter ethics review; (2) harmonization of contracts and contract negotiations; (3) training in ethics for clinical trialists and staff; (4) streamlining and harmonizing administrative processes in research centers and setting up a mentoring environment (5) defining Provincial Clinical Research Performance metrics. The first report from each working group is expected in January 2012.^{42 43 44}

Nova Scotia: Dalhousie University, Capital District Health Authority and the IWK have provided leadership in streamlining procedures for conducting clinical trials in Nova Scotia. A region wide REB and improved collaboration around contracts is being implemented. A larger initiative to bring collaboration across the three Maritime provinces and increased expertise to all Maritime provinces is underway in conjunction with the Canadian Institutes of Health Research Strategy on Patient Oriented Research. As competition for clinical trials increases internationally, we are striving to position the Maritimes as an added value venue, where sophisticated trials using resources such as our 10 bed inpatient Challenge Unit and sophisticated imaging capabilities including research dedicated MRI and MEG can be an advantage.⁴⁵

New Brunswick: Clinical research in New Brunswick is supported through a variety of partnerships with key stakeholders, including the New Brunswick Health Research Foundation, specialized research centres like the Atlantic Cancer Research Institute, the medical programs at Dalhousie Medicine New Brunswick in Saint John and Sherbrooke's Centre de Formation Medicale NB, and the two regional health authorities, Vitalité and Horizon Health Network. Recognizing the importance of creating a favourable research environment, an ambitious strategy to attract and foster research investment, including clinical trial activities, has been undertaken. To date, this has resulted in the creation of a network of research offices throughout the region, the harmonization of policies and procedures in support of research activities, including contract review and pricing, and the development of educational programs to support new and experienced research teams.⁴⁶

Newfoundland and Labrador: Two new initiatives are in place that will streamline and facilitate clinical research trials in Newfoundland and Labrador. In December 2010, construction was completed on the Newfoundland and Labrador Clinical Research Centre. The Centre is a joint initiative of Eastern Health and the Faculty of Medicine at Memorial University, with infrastructure support coming from the Provincial Government and other funding foundations. Many clinical trials across the clinical spectrum will be coordinated through this Centre. On 1 July 2011, new legislation was proclaimed creating the Health Research Ethics Authority (HREA). Under this Authority, all Clinical Trials research in the Province must be approved by a newly created Health Research Ethics Board. The new central review process for clinical trials is anticipated to simplify, coordinate and expedite clinical trial ethical review in the Province of Newfoundland and Labrador.⁴⁷

A Look to the Future - A Strategic Action Plan for Clinical Trials in Canada?

What is the opportunity before us? If we can better leverage our strengths, consolidate dispersed but important efforts; deal with issues related to population size, recruitment, start up times and operational barriers; engage the public; build, expand or reinforce effective infrastructure, and rebrand Canada for continued excellence in clinical trials – we can continue to achieve human, social and financial benefit from clinical trials.

The overarching question for this summit, however is “how”. What action plan can we agree upon to move in this direction? At the summit, we will have focused discussions on the issues of ethics reviews, administrative processes, recruitment, cost structure, and what we need to do to improve the future. As you prepare for this discussion, you may also wish to consider the following questions that may underpin break out discussion room topics:

1. How do we support, foster and accelerate the commitment to addressing operational barriers to clinical research across the country? Where can we achieve short-term wins? What are the most pressing issues? What are the priorities?
2. Are there areas of clinical research where Canada should be focusing its efforts and strengthening its niche or should Canada aim to attract as many areas as possible? If we should focus, what are the areas and what is it about them that brings a competitive advantage?
3. Are there mechanisms that can be used to provide a Canadian interface that would attract industry and help address operational barriers (for example, the UK model)? What kind of infrastructure would efficiently bolster our competitiveness in clinical research?
4. How can we bolster the support of patients, families, and the public for clinical research in Canada? How can we improve recruitment, retention of patients in clinical trials?
5. How can we leverage the full potential of each province in creating a single attractive market to the rest of the world, while ensuring that each province benefits from its own significant investments?
6. How do we frame and market Canada’s clinical trial advantages the rest of the world? What are our strongest cards, competitive advantages, and differentiating factors?

We believe that these questions are answerable and that they will evolve through our conversations together. We look forward to hearing from you - and to a day that will bring us one step closer to the vision that we all share.

Endnotes

- ¹ Much of the material in this section is based on both an outline by the Cameron Institute and an informal submission prepared by ACAHO for staff at Industry Canada. Our appreciation to Dr. Arthur Slutsky, ACAHO Research Co-Chair and Vice President of Research, St. Michael's Hospital, who contributed significantly to the latter.
- ² As an example, a case study on this issue is discussed in the video of an *ACAHO-CIHR Cafe Scientifique* featuring Ms. Jennifer Molson, a former patient of the Ottawa Hospital who discusses her life-saving participation in a clinical trial. Molson, J. 2010. *In Sickness & in Health. Patient Participation in Health Research. A Patient Perspective*. Available: <http://www.acao.org/?document&id=194>
- ³ Majumdar, S.R. Roe, M.T. Peterson, E.D, Chen, A.Y, Gibler, W.B., Armstrong, P.W 2008. *Better Outcomes for Patients Treated at Hospitals That Participate in Clinical Trials*. Arch Intern Med. 168(6):657-662
- ⁴ The relationship between critical mass and quality outcomes is described in the results of a literature review commissioned by CIHR in Tracy, J.& Zelmer, J. (2005). *CIHI Survey: volumes and outcomes for surgical services in Canada*. Healthcare Quarterly, 8(4), 28-30.
- ⁵ ACAHO, 2006. *Moving at the Speed of Discovery, From Bench to Bedside to Business*. Available: www.acao.org
- ⁶ ACAHO, 2007. *From Microscope to Marketplace: Spinoff companies from ACAHO member institutions*. Available: www.acao.org
- ⁷ ACAHO, Forthcoming. Data from Funding Flow Survey.
- ⁸ Ibid.
- ⁹ Archstone Consulting, 2011. Biopharmaceutical's Impact on the Us Economy. Available: <http://www.phrma.org/issues/state-level-economic-impact>
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- ¹² Bohan, P & Hadjebi, O. 2010. *A review of clinical trials in Spain*. Translation Bio-Medicine. 1:2 Available: <http://imedpub.com/ojs/index.php/transbiomed/article/view/225>
- ¹³ Ibid
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- ¹⁵ Ibid
- ¹⁶ Matthews, J. 2011. *Engagement and support for Clinical Research*, NHS, National Institute for Health Research. Presentation slides.
- ¹⁷ English, R. Lebovitz, Y. and Griffin R. *Transforming Clinical Research in the United States: Challenges and Opportunities: Workshop Summary*. Available: http://www.nap.edu/catalog.php?record_id=12900
- ¹⁸ Laberge, N. 2011. *Globalization of Clinical Research: Trends and Implications*. Presentation Slides for Conference given in Argentina. Rx&D.
- ¹⁹ Laberge, N. 2011. *Clinical Trial Applications (CTA) Received – Excluding Bioequivalence (Generic)* Slide from Presentation.
- ²⁰ Laberge, N. 2011. *Globalization of Clinical Research*
- ²¹ Ibid.
- ²² Kermani & Langer, 2007.

²³ CIHR, 2002. *The Clinician Scientist: Yesterday, Today and Tomorrow A Story Told and Recommendations from Canadian Researcher*. Available: <http://www.cihr-irsc.gc.ca/e/22030.html>

²⁴ National Task Force on the Future of Academic Health Sciences Centres, 2011. *Three Missions...One Future - Optimizing the Performance of Canada's Academic Health Sciences Centres*. Available: <http://www.acao.org/?document&id=249>

²⁵ Council of Canadian Academies, 2010. *Honesty, Accountability and Trust: Fostering Research Integrity in Canada*. <http://www.scienceadvice.ca/en.aspx>

²⁶ The Tri Council policy statement on the *Responsible Conduct of Research* will also be undergoing a review and consultation process.

²⁷ For example in Rheumatology (and likely other disease areas) the clinical trials-supported infrastructure enables some of the clinical research that the sites take on; disease surveillance registries, bio-repositories for genetic work takes place within that infrastructure – these trial sites are quite good at dove-tailing research processes into their clinical practices. Also – the discussions regarding trials can lead to other initiatives that enhance patient care overall and may not be generally performed in non-trial sites.

²⁸ The Canadian General Standards Board (CGSB) has spent many years developing a draft national standard for research ethics boards reviewing clinical trials.

²⁹ Funding from CIHR enabled members of Rx&D and ACAHO to work with an expert in the development of a proposed national clinical trial contract template agreement.

³⁰ The Network of Networks (N2) initiative has been instrumental in many of these areas <http://www.cihr-irsc.gc.ca/e/34791.html>

³¹ ACAHO and CIHR, 2010. *Cafe Scientifique: In Sickness and In Health. What does public engagement in health research really mean?*. In May 2010, ACAHO and CIHR collaborated on a community based event which invited members of the public to discuss this topic. Clinical trials were discussed from the perspective of a research ethics board chair, a patient, and a clinician scientist. The room had to be changed twice to accommodate high interest from the public. A video is available: www.acao.org

³² Council of Canadian Academies. 2011. *Innovation and Business Strategy: Why Canada Falls Short. The expert panel on business innovation*. Available: <http://www.scienceadvice.ca/en.aspx>

³³ CIHR, 2010. A discussion paper for a 10-year plan to change health care using the levers of research. Available: <http://www.cihr-irsc.gc.ca/e/41232.html>

³⁴ Our thanks to Ms. Heather Harris-Harper, Director of Operations for BCCRI for providing this paragraph.

³⁵ BC Clinical Research Infrastructure Network. <http://www.bccrin.ca/>

³⁶ Our thanks to Dr. Robert Sheldon, Vice President of Research, Alberta Health Services, who contributed to the development of this paragraph.

³⁷ Our thanks to Dr. Beth Horsburgh, Vice President Research, Saskatoon Health Region, Vice President Research, University of Saskatchewan for providing the information for this description.

³⁸ Our thanks to Ms. Sanober Motiwala & Ms. Alisha Tharani, who prepared this paragraph on behalf of the Council of Academic Hospitals of Ontario (CAHO).

³⁹Information take from: <http://www.brasfamily.com>

⁴⁰ Our thanks to Dr. Christopher Paige, Vice President Research, University Health Network, for helping the authors understand parts of the cancer drug landscape in Ontario and in the northern United States.

⁴¹ Government of Quebec. 2010. *Quebec's Biopharmaceutical Strategy. Maintaining Excellence by Crating Wealth in Quebec*. Available:

http://tweetetesneurones.com/medias/doc/MDEIEstrategie_biopharma_en.pdf

⁴² A list of Quebec's 19 Fond de Recherche Sante Quebec Funded Research centers can be found at:

http://www.frsg.gouv.qc.ca/fr/centregroupereseau/centres/centres_liste.shtml

⁴³ Information on Fond de Recherche Sante Quebec Research Centre Program can be found at:

http://www.frsg.gouv.qc.ca/fr/financement/Programmes_2012_2013/in02_fiche_subventions_regulieres.shtml

⁴⁴ Our thanks to Ms. Joanne Goldberg, Fond de Recherche Sante Quebec for assisting with the development of this paragraph.

⁴⁵ Our thanks to Dr. Patrick McGrath, Vice President Research, IWK for providing this paragraph as a perspective from Nova Scotia.

⁴⁶ Our thanks to Ms. Nancy Roberts, Vice President Quality, Planning and Research and Mr. Barry Strack, Manager Research Services, Horizon Health Network for providing this perspective.

⁴⁷ Our thanks to Dr. Don McKay, Acting Dean Medicine, Memorial University for providing this perspective.