An Action Plan to Help Attract More Clinical Trials to Canada

To Your Health & Prosperity...

Canada's Research-Based Pharmaceutical Companies

R&D

Les compagnies de recherche pharmaceutique du Canada

CIHR IRSC

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

ACAHO

Association of Canadian Academic Healthcare Organizations

Association canadienne des institutions de santé universitaires

ACISU

March 30, 2012

Updated with an Appendix
Reflecting Feedback on Final Draft

From Summit to Action...

On behalf of Rx&D, CIHR, and ACAHO we are pleased to provide you with a copy of the action plan that has arisen from the 2011 Clinical Trials Summit. This action plan is the result of the feedback and advice of many individuals. We thank all involved.

This action plan contains three goals and nine recommendations. The first relates to the capacity and resource for its implementation and coordination of other types of clinical trial (CT) improvement activities. Many of the other recommendations build on the foundational proposition of the clinical trials summit – that by improving cost, quality, speed, and relationships in CT start up times and operations - Canada has the opportunity to become a preferred partner in a global competition for clinical trials.

Through this action plan, our aim is to collectively assist clinical trial companies to succeed in our country and in so doing, generate the human, social and economic benefits of clinical trials. The goals are to help (1) halt and reverse the downward trend in clinical trial investments; (2) improve business practices as they pertain to clinical trial operations; and (3) create a stable, forward looking opportunity for CTs into the future.

While we encourage you to read the full action plan, a 'one-pager' of the recommendations is also included. The recommendations fall into three strategies.

- A national headquarters & resources for implementation, coordination, performance metrics & a future vision for CTs, health services & research (recommendations 1-3)
- Achieving trust and profitability through operational efficiencies in those areas that impact clinical trial start up times and costs (recommendations 4-7)
- Signaling globally Canada's interest in Clinical Trial Improvements through communication with global offices & improvements in Intellectual Property protection and SR&ED policy (recommendation 8-9);

Please also note that this action plan relates mostly to clinical trial activities that occur at large publicly funded clinical trial sites, mostly within academic healthcare organizations, and with the Canada-based pharmaceutical, device and vaccine companies. Other national initiatives are looking at the role of other critical stakeholders in Canada's clinical trial landscape. Our intent is to leverage efforts whenever possible.

Finally, while this marks the third and final paper in the clinical trial summit trilogy, it also marks the beginning of an important road ahead. As next steps, Rx&D, CIHR and ACAHO will be working on communications and implementation considerations to help mobilize the action plan as swiftly as possible. We hope that within a year, many of these recommendations will be on their way to success – to health and prosperity!

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A C A H O
A C I S U

Clinical Trial Summit Sponsors

Canada's Research Based Pharmaceutical Companies (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. www.canadapharma.org

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 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. www.cihr.ca

The Association of Canadian Academic Healthcare Organizations (ACAHO) is the national voice of Canada's Research Hospitals, academic Regional Health Authorities and their Research Institutes. Their vision is to advance patient care and the health & well-being of Canadians through research, discovery and innovation. ACAHO's *Mission* is to create an environment in which research discovery, innovation and learning benefit patients, populations, health systems and the economy. ACAHO 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. www.acaho.org

About the document: This document was prepared by ACAHO on behalf of and with significant contributions from representatives of all three sponsoring organizations. This action plan is intended as our best reflections on the issues and opportunities as discussed through the summit and the subsequent feedback we received to the proceedings. Feedback onthe final Draft released March 30, 2012 is included in this final version of the same document as an appendix. The authors express appreciation to all participants and reviewers, Correspondence or questions can be directed to saryeddine@acaho.org.

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Executive Summary

"To Your Health and Prosperity...An Action Plan to Help Attract More Clinical Trials to Canada" contains nine short term recommendations to help regain the human, social and economic benefits that come to our country through clinical trials. It is designed to further leverage a precious opportunity for both health and the economy.

Clinical trials (CT) are required to bring safe, innovative and effective drugs, vaccines and devices to market. They are the first time science is tested with human subjects in a highly controlled setting. On an experimental basis, they have the potential for the relief of pain and suffering and they may reverse or halt the effects of disease or disability. Clinical trial contracts are worth millions of dollars and thousands of jobs. The successful completion of trials provides the confidence to bring new drugs, devices and procedures into practice. These can result in cost savings to our health system, better quality of life, and more revenues, jobs, and spin-off effects for our economy.

However, Canada is not the only country to appreciate the benefits of clinical trials. Comparator nations that are organizing and competing for CTs, without compromising safety or quality, will win contracts from us. Global head offices sponsoring clinical trials will only invest in those countries that provide the best comparative return on investment for their increasingly scarce research dollars.

Goals

Idiosyncrasies in our business landscape, once viewed as innocuous inconveniences, are now costing Canada substantially in lost opportunity. When a company interested in conducting clinical trials comes to Canada, it faces multiple forms, processes, and standards before it can even start a trial. Individual ethics board reviews for the same protocol may have different requirements, results, and inconsistent turnaround times. Eligible patients may be difficult to find, recruit and retain in trials. Contracts may differ.

All of these result in costs and delays. They discourage CT investment in Canada. Through this action plan, our aim is to help clinical trial companies succeed and stay in Canada. The goals are to: (1) halt and reverse the downward trend in clinical trial investments; (2) improve business practices as they pertain to clinical trial operations; and (3) create a stable, forward looking opportunity for CTs into the future.

Approach

Like other stakeholder groups, Canada's Research Based Pharmaceutical Companies (Rx&D), the Canadian Institutes for Health Research (CIHR), and the Association of Canadian Academic Healthcare Organizations (ACAHO), also felt it was important to offer a consolidated action plan, relevant at the national level. It is important to note that this action plan is focused primarily on large publicly funded clinical trial sites and

pharmaceutical, vaccine, or device companies. While our focus is necessary, the intent is to coordinate solutions with other clinical trial stakeholders wherever possible.

With this scope in mind, a multi-sector steering committee led by Rx&D, CIHR and ACAHO organized a Clinical Trial Summit that was held in September 2011. Close to one hundred and thirty individuals from academia, healthcare, industry, government, and other types of organizations participated. The Summit resulted in a series of steps that attendees believe can be taken to help reverse the decline in CT investment that Canada is experiencing and improve the clinical trial landscape. The keynote addresses and background papers providing data and situational analyses and examples of current provincial, national, and international initiatives, are now widely available on both the ACAHO and Rx&D websites. The actionables and logic behind the recommendations in this paper are also available in the proceedings which have now also been posted on the same websites.

Action Plan Recommendations

The Summit began with the premise that by improving cost, quality, speed and relationships as they pertain to clinical trial start-ups times, we can increase the profitability and attractiveness of Canada as a CT business partner. In specific terms, the Summit participants looked at the operational issues affecting clinical trial start up times, which include ethics reviews, patient recruitment, and administration. They also looked at policy, infrastructure, and cost issues that impact the ability to undertake clinical trial activity in Canada. The summit resulted in a series of 28 actionables that form the basis of the nine recommendations in this action plan. It is important to note that the first recommendation is foundational to the remaining eight and is intended to ensure implementation and follow through of the recommendations in this action plan.

1. Establish implementation and coordination headquarters and resources: Preferably by leveraging the capacity of an existing forum (Rx&D and ACAHO are recommending alignment with the CIHR Strategy for Patient Oriented Research if possible), establish an implementation committee and resources that would oversee and enable implementation of this action plan and that could coordinate, link and leverage, different activity types and inter-provincial clinical trial improvement activities.

2. Measure, monitor, manage and market CT performance improvements: Drawing on available datasets, select and collect meaningful and parsimonious metrics on clinical trial performance and return-on-investment that allow Canada to: (a) measure, monitor, and discuss progress; (b) identify issues; and (c) demonstrate return on investment for sponsors, sites, and all levels of government.

3. Integrate health system & research infrastructure to ensure quality & sustainability: Espouse a bold vision for the integration of research and health care. This would ensure sustainable infrastructure, staffing, resources, and career support for the generation

and integration of research. It would also ensure receptor capacity to improve patient care, population health and the economy as per the broader Strategy for Patient Oriented Research and recommendations from the National Task Force on the Future of Academic Health Sciences Centres.

4. Improve efficiencies of ethics reviews & advance strategic issues (like accreditation): Leveraging the appropriate bodies and expertise undertake a feasibility assessment and proposal for a common application form, consent form template, elements of an accreditation system, and information sharing mechanisms for ethics reviews. Also support the work of Health Canada in evaluating standards and accreditation options.

5. Develop a 'database of registries' & consider a national patient recruitment strategy: Improve patient recruitment times by developing a database of registries with appropriate consent and privacy considerations, that will help to identify patients that may be eligible for clinical trial participation. Identify, implement and share tools that have proven effective for this purpose. This will improve recruitment rates and speed.

6. Adopt common Standard Operating Procedures (SOPs), training and certification: Fund and leverage the Network of Networks (N2) to help disseminate common SOPs and Training resources. Work with N2, ACAHO, Rx&D, CIHR and other interested parties to develop a site certification approach to identify organizations that have these standards and training in place.

7. Improve and use the common clinical trials contract: implement the model Clinical Trials Agreement (mCTA) currently being pilot tested by CIHR, Rx&D and ACAHO, ensuring that the proper adjustments are made after the pilot and that appropriate communication and dissemination occurs, including to global head offices if necessary.

8. Optimize intellectual property protection policy & SR&ED Tax Credits: Advocate to bring intellectual protection (IP) policy to bring IP policy to levels commensurate with Europe within the Canada-European Union Comprehensive European Trade Agreement (CETA). Help to improve administration of Scientific Research & Experimental Development (SR&ED) tax credit so that credits are received in time to offset costs of trials. Ensure that global head offices are aware of these improvements once they are made.

9. Signaling our interest globally - open a concierge (storefront) service for investors: Start by providing international companies with information on Canada's clinical trial assets, offerings and improvements, then develop a concierge (storefront) service that would provide a centralized access and information point to global companies.

Risks and Rewards

What are the risks and rewards associated with this action plan? In our view, the main risk is inaction, since among the nine recommendations, there are three strategies.

- **Establish national presence for implementing and coordinating CT improvements:** establish capacity for national implementation, the coordination of provincial activities, performance measurement and management, and support a bold future vision for clinical research (recommendations 1-3)
- **Improve business operations with better cost, quality & speed of CT start up times :** through streamlined ethics reviews (recommendation 4); patient recruitment tools and registries (recommendation 5); common standard operating procedures, training & certification (recommendation 6); a universal contract template (rec. 7);
- **Signaling globally Canada's interest in CT improvements and investments:** through changes in Intellectual Property protection and SR&ED policy (recommendation 8); and opening a national concierge service for clinical trials (recommendation 9).

Considering the nature of these recommendations, the major costs are for staffing and coordination activities. They will improve quality and they will not increase our exposure. We are already loosing clinical trial opportunities. Proposed efforts to improve the cost, quality, speed and relationships as they pertain to starting a clinical trial and ensuring a robust policy framework and investment incentives, will only help us. They will improve our business practices, which if not sufficient to increase our investment *per se*, are necessary to keep them. The impacts are summarized below.

From...Today's Vignette of CT Business	To... Tomorrow's Vision for CT Business
Multiple disjointed initiatives between provinces, regions, & areas of improvement	Clinical trial improvement headquarters and resources to coordinate improvement activity across provinces and domains.
One time efforts, estimates, anecdotes, and perceptions about performance	Regular performance metrics for measuring, monitoring, managing &marketing progress.
Disjointed, unpredictable policy & funding landscape for the generation of research and its timely application in practice	A bold vision and resulting policy and funding landscape for generation and integration of research and clinical practice.
Multiple ethics applications, consent forms, metrics & accreditation questions	Clarity on options for accreditation and a plan for common consent and application forms
Difficulty recruiting patients and unknown or disjointed patient registries	Timely recruitment from registries from which to draw potentially eligible patients
Variability in standard operating procedures and uncertainty in training at clinical sites	Common standard operating procedures, training and site certification for those sites demonstrating the application of standard and training.
Delayed payment of SR&ED tax credits that become un-attributable to the CT	SR&ED tax credits that are received on time and assessed against cost of the trial.
Intellectual property policy that falls short of that of the European Union	Intellectual property policy that encourages Canada's attractiveness for CT investment
Lack of storefront to inform sponsors of Canada's CT assets	A "storefront" and communication products that identifies Canada's CT assets o help clinical trial

Conclusions

As with most issues of business and strategy, writing the action plan is only one part of the journey. The real question is whether we can mobilize, organize, and accomplish what we set out to achieve.

To this end, Rx&D, ACAHO, and CIHR will be seeking feedback on the draft action plan and fleshing out implementation considerations. We will then move to the actual dissemination, communication and implementation – whether that means participating directly, approaching relevant parties, or helping to find the resources.

We hope that in a year's time, some recommendations in this plan will have been completed and that we will be well on our way to attracting more clinical trials to our country – with the human, social and economic benefits that come with them.

To Your Health & Prosperity...

I. Introduction

"Now, here, you see, it takes all the running you can do, to stay in the same place. If you want to get somewhere else, you must run at least twice as fast as that." L. Carroll, author, mathematician, logician

Clinical trials are needed to bring drugs, devices, and vaccines developed through science, safely to market. They bring innovation from the bench to the bedside. If the trial proves to be successful, it can even give the participants a chance to be relieved of pain, illness, disability or discomfort by accessing innovations, even before they are commercially available.

Canada is a great country in which to do clinical trials. We have a track record of quality and safety, many clinical trial successes, outstanding researchers and clinical sites, a great healthcare system, a motivated industry, and supportive government partners.[1] [2] However, to maintain this capacity, we need to address some critical concerns and adapt to international trends.

Globally, clinical trial companies are facing research budget reductions. Canadian clinical trial offices need to demonstrate to global headquarters, that Canada is a worthwhile and profitable country in which to invest their research dollars. However, the cost, quality, speed, and relationships involved in starting a clinical trial in Canada put us at a disadvantage.[3] Comparator countries are actively competing for this shrinking clinical trial investment and we are seeing the consequence in a disproportionate decline in clinical trial investment in our country.[4]

Our goals in this action plan are therefore threefold: (1) We want to help halt and reverse the decline in clinical trial investment in Canada; (2) we want to improve our business practices both as a mechanism for our first goal and as a way forward; and (3) we want to ensure a robust clinical trial environment for the future. This document is an action plan to help achieve these goals. It is based on the following premise:

> Improving the cost, quality, speed, and relationships needed to start a clinical trial - by focusing on how we can facilitate ethics reviews, patient recruitment, administrative issues, cost control, and infrastructure – will increase the return-on -investment, profitability, and success of clinical trial investments in Canada. This will help attract more trials back to our country with more of the human, social and economic benefits that come with them.

It is <u>essential</u> to note that the motivation and need for a focus in these areas <u>are not</u> about the current performance of any one group of people, professions, functions or organizations. The issue is the complexity of the entire system and how that impacts costs and the attractiveness of Canada as a preferred partner and national business environment for investment. Consider the following scenario:

> What would doing clinical trial business in Canada look like for a global company that is working on a few different trials with many different investigators across several different sites, in various disease areas, and across more than one province?

While the question may not have been studied empirically, the answer could be exactly what the scenario proposes - with all the forms, variation, paper, and personalities that come with it. The question then becomes whether this positions Canada competitively vis-à-vis the business environment of other countries. What if the scenario were more like this?

> Irrespective of the number of trials, clinical trial sites, or regions, we know that the applications, forms, strategies to ensure recruitment and retention, standard operating procedures, and training are robust, predictable, cost-effective, and timely. Within better costs and timeframes, the same safe, high quality results and outcomes that Canada is already known for, will be delivered.

We believe this scenario reflects a more streamlined and competitive business environment. It builds on the Clinical Trial (CT) Summit conversations that indicate a clear shift in concern - from how each of industry and academia, different clinical trial sites and different regions operate - to a very conscious orientation on how Canada presents internationally for clinical trials, compared to other countries.[5]

With this in mind, we begin this document with an overview of the approach used to develop it. We discuss key messages from the Clinical Trial Summit and the actionables that were recommended. Recognizing that an action plan needs not only to discuss "what" needs to be done", but "how", we have synthesized the actionables discussed in the summit proceedings with strategic and resource considerations to provide the nine recommendations that constitute this plan. At the end of the document we offer a discussion on expected impact, risk, implementation and evaluation.

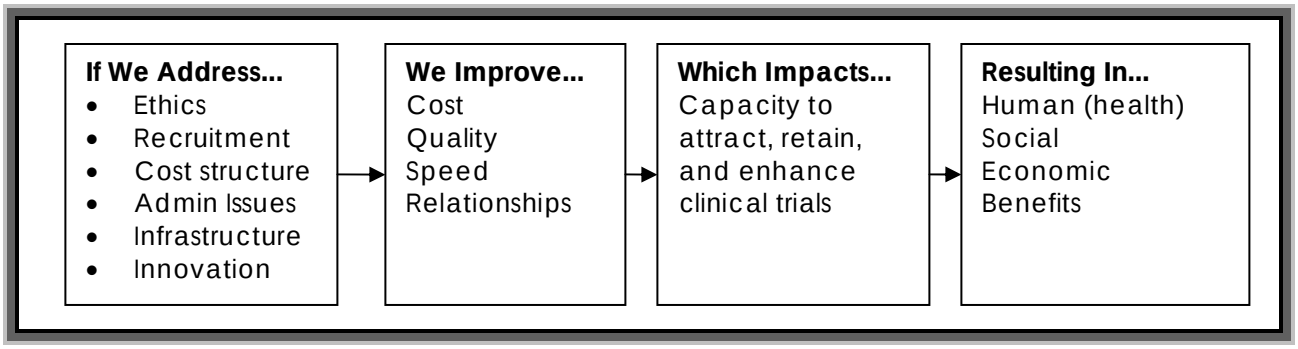
II. Approach

"Never underestimate the power of a few committed people to change the world. Indeed, it is the only thing that ever has". M. Mead, Anthropologist.

This action plan was developed in response to a 'need, capacity, and opportunity'[6] to improve Canada's ability to attract clinical trials. A multi-sectoral steering committee from members of Rx&D, CIHR, and ACAHO provided leadership to the structure and framework for the clinical trial summit.[7] The attendees included individuals from the Canadian offices of clinical trial companies, universities, academic healthcare organizations, and coordinating bodies. A background document and keynote addresses captured a situational analysis of the issues and examples of what is being done to address current challenges across Canada and in other countries. These materials are available from the Rx&D and ACAHO websites.

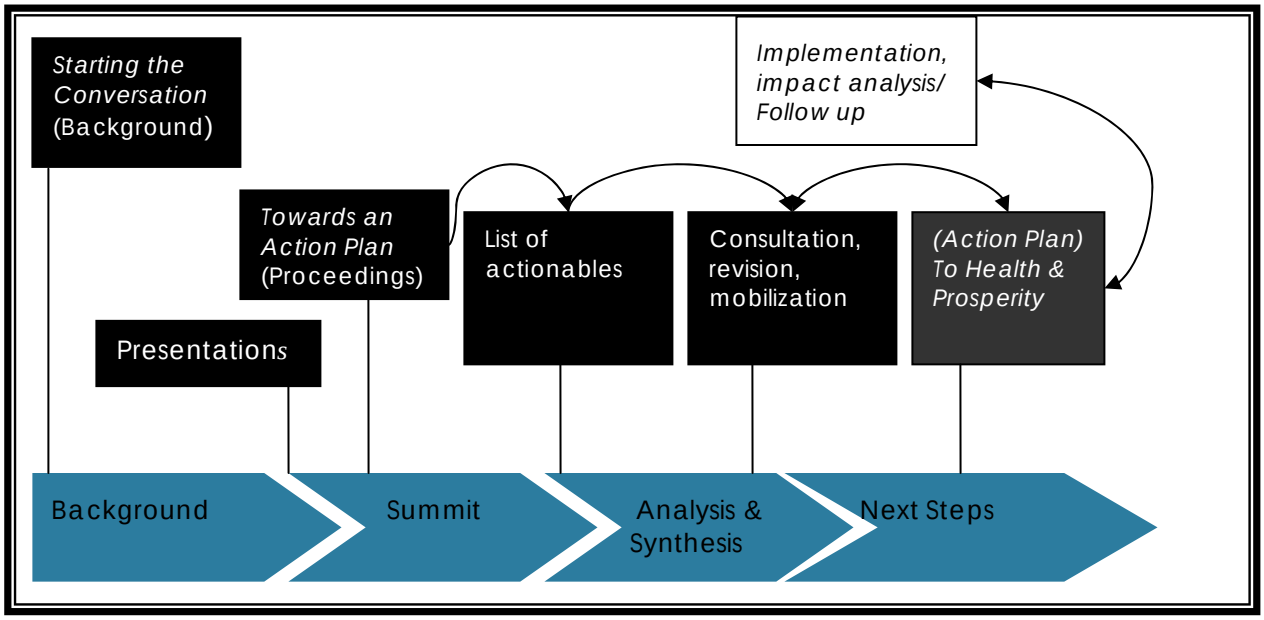
The summit itself was organized around discussions on how to facilitate ethics reviews, patient recruitment, administrative issues, costs, and infrastructure with the rationale that these impact the cost, quality, speed and relationships necessary to get a clinical trial off the ground. Figure 1 shows the guiding assumptions involved.

Figure 1: Overarching Assumptions Guiding Structure of Clinical Trials Summit and Action Plan[8]



The results of the summit were then captured in a proceedings paper which contained proposed actionables based on the discussion. It was circulated to attendees for validation, and participating organizations were asked to comment on resource or leadership capacity or interest in any of the proposals. The results were analyzed along with other strategic opportunity and implementation considerations and it is on this basis that we propose this action plan. The validated proceedings paper is available on the ACAHO and Rx&D websites.[9] Figure 2 describes the process.

Figure 2: Overview of the Action Plan Development Cycle (black boxes are completed, while is white is next steps).



It should be noted that this action plan relates specifically to clinical trial activities that occur at large publicly-funded clinical trial sites, mostly within academic healthcare organizations (i.e. research hospitals, academic regional health authorities and their research institutes) and with the Canada-based members of Rx&D as well as medical device and vaccine companies. Other important national initiatives may be looking at the role of clinical research organizations, colleges, physician offices, regulators, and academically funded trials. While our focus is necessarily specific, it is in no way intended to undermine the importance of other groups in Canada's clinical trial landscape. Rather, the intention is to coordinate and leverage common solutions wherever it is possible and to benefit all by contributing this focus to overall clinical trial improvement activities.

In fact, the origins of this plan are expressed in an editorial in *Canada's Top Innovation Leaders 2011,* where a steering committee member and a summit participant noted the following as their observations from the CT Summit:[10]

"(1) If we are deliberate about choosing and coordinating strategies, there are quick wins available for addressing individual operational barriers to our competitiveness. These range from strategies to reduce the time needed to negotiate contracts, set up a study, ensure ethical standards of practice are met, standardize various operating procedures, control costs, and engage the public in clinical trial opportunities.

(2) The solutions that we need to be able to implement are not only within the walls of any one organization or sector, but across them. The success of our individual or regional activities will be accelerated or undermined by the national leadership and coordination available to tie a diverse range of activities together and present an attractive storefront to global offices.

(3) When it comes to the human, social and economic benefits of clinical trials to Canada, it is hard to tell which voice belongs to academia, healthcare, government or industry. Within the field, it is clear that our competition is neither internal nor sectoral, but global. The questions we are now discussing are no longer whether or for whom, but what and how."

Further, in presenting this action plan, we are focusing on elements that may be helpful to address across the country. It is not the intention of this plan to encumber, supplant, or distract from regional, provincial or disease-specific initiatives. All of these are needed. However, this action plan will help to identify opportunities for facilitating coordination where it makes sense to do so. It will also bring a national perspective on how we might be able to coordinate and leverage many of the provincial initiatives occurring across the country.

III. Action Plan

"If there is a chance in a million that you can do something, anything, to keep what you want from ending, do it. Pry the door open or, if need be, wedge your foot in that door and keep it open.- P. Kael, Film Critic.

The goals of this action plan are to help (1) halt and reverse the downward trend in clinical trial investments; (2) improve our business practices as they pertain to clinical

trial operations; and (3) create a stable, forward looking opportunity for the future. As described earlier, to achieve these goals, the actionables from the clinical trial summit proceedings, which related to each of ethics reviews, patient recruitment, administrative issues, costs, and infrastructure, were used as the basis for the recommendations.

We then considered feedback from the 'request to the reader' regarding where resources and strategic opportunities existed, as well as what the critical success factors might be for the action plan. The result is the following 9 recommendations, of which the first is ensuring implementation capacity. We discuss the background and rationale for each. We also include in shaded boxes, comments provided by those delegates who responded to "the request to the reader" form.

1. A national headquarters and resources for implementation and coordination

Our first recommendation encapsulates implementation and resource consideration for this plan. Without this, the recommendations may not come off the written page. An essential component of this action plan is therefore the establishment (or leveraging) of a clear, respected, and trusted body for the oversight of clinical trial improvement activities in Canada. This would ensure that activities within the plan can be coordinated, prioritized, structured for maximum fit, measured, and monitored. In addition, it could also serve nationally as a coordinating body for linking provincial initiatives where needed; a contact body for issues that need to be noted; and could signal internationally, Canada's intention to improve the clinical trial landscape.

Since the release of its 2009 Strategic Roadmap, CIHR has made and maintained an important commitment to helping the research community overcome barriers to research.[11] More recently, it has initiated a Strategy for Patient-Oriented Research (SPOR), the aim of which is to improve the health of Canadians by strengthening the generation and use of the evidence base.[12] To do this, one goal of SPOR is to strengthen organizational and regulatory support for clinical studies in Canada and enhance patient and clinician engagement in this type of research.

The national steering committee for SPOR consists of senior leaders from universities, healthcare organizations, and industry, including members of the research community, CEOs of hospitals and regional health authorities, and industry representatives. While the current SPOR funding is limited, the intention is to help build a robust multi-funder infrastructure and show a concrete return on investment, when it comes to conducting research that is patient-oriented.

For these reasons, we believe that there is a natural fit between SPOR's goals and the goals of this action plan. As such SPOR is a logical starting point for a discussion on a clinical trial improvement oversight and coordinating body for Canada. Organizations like ACAHO, Rx&D and many others could work with the SPOR leadership to develop

the business case and business plan and would help advocate for the additional resources needed to staff and operate such a coordinating function in the short term.

In striking such an implementation and coordination committee, it would be important to consider how the coordination of provincial bodies advancing clinical trial improvements and opportunities would occur. It would also be necessary to consider the roles of organizations like the Canadian Association of Research Ethics Boards (CAREB), the Network of Networks (N2), and other related organizations, so that diverse domains of clinical trial improvement activity are leveraged and coordinated.

In fact, considering the marginal costs and the efficiency of a coordinating function for national clinical trial improvements, compared to the size of the potential benefits, this type of request could be an attractive proposition for the 2013 Federal Budget Consultations which take place this August 2012.

For these reasons, our first recommendation is to appoint a national headquarters for coordinating clinical trial improvement activities, preferably through SPOR. If accepted, work can then be done to determine the business plan, staffing and resource needs in the short term and to ensure that these resources can be found.

Selected comments from CT Summit delegates...

- *"A strategy for re-establishing Canada as a leader in clinical trials research is timely and necessary. As identified in the [proceedings] document, the success of the strategy will be dependent on the collaboration among those stakeholders involved with the conduct of clinical trials" .*
- *"There are too many groups working on various things and what is needed is coordination of efforts at a national level with a clear mandate and deliverables..."*
- *"Clearing houses and metrics are good ideas, but unless there are 'carrots and sticks' and an overarching coordinating body, it will be difficult to see these adopted".*
- *"A process has begun, led by the Canadian Partnership Against Cancer (CPAC) to provide support to clinical trial teams in cancer centres and hospitals (human "infrastructure" for trials). This is envisaged to include substantial funding for trial teams and a national coordinating centre to track impact and evaluate this method of supporting trials, especially those from the academic sector. It will be based on the highly successful NCRN model in UK/England which began in 2000...A Canadian Steering Committee has just been established ...to begin the process of moving this cancer trials initiative forward in Canada but much work remains. Close interaction with CIHR SPOR, N2 and other relevant groups is planned".*
- *"We strongly disagree with the notion of "enforcement" in the context of this overall initiative... and suggest that coordination of efforts and collaborations where feasible are more productive in our environment".*

Recommendation 1. Establish implementation headquarters and resources: Preferably by leveraging the capacity of an existing forum (Rx&D and ACAHO are recommending alignment with the CIHR Strategy for Patient Oriented Research if possible), establish an implementation committee and resources that would oversee and enable implementation of this action plan and that could coordinate, link and leverage, cross-domain and inter-provincial clinical trial improvement activities.

2. Measuring, Monitoring, Managing, and Marketing World Class Performance...

Our second recommendation encapsulates the evaluation and communication of progress towards the goals of the action plan. We know that what we measure, we manage; where we focus, we succeed. Once a national headquarters is established for clinical trial improvement activities, we need to be able to track our progress and show a return on that effort. This is important not only to those working on improvement initiatives, it is important to those funding them, and ultimately to our clinical trial investors, investigators and to the public.

The metrics we choose must obviously align with the three goals of this action plan: (1) to halt and reverse the downward trend in clinical trial investments; (2) to improve our business practices as they pertain to clinical trial operations; and (3) to create a stable, forward-looking opportunity for clinical trials.

As it pertains to the first and second goals, of halting the downward trends and improving our clinical trial business environment, we need to know if implementing the recommendations in this action plan is having the desired effect - if they are not, we need to know why. If they are, we need to communicate this to all stakeholders, provincial and federal governments, and most importantly to those investors, who on such accounts, might consider coming back to Canada.

At the CT Summit, a number of performance metrics initiatives were highlighted. For example, Canada's Research-Based Pharmaceutical companies (Rx&D) presented a comparative analysis of Canada's performance to international performance.[13] The Canadian Cancer Research Alliance's (CCRA) *Report on the State of Cancer Clinical Trials in Canada* has important cost-benefit analysis indicators. In the summit background document, *Starting the Conversation,* we saw metrics from Health Canada and examples of how metrics are being collected in countries like Spain, where electronic submissions create an automated dataset for strategic analyses.[14] [15]

Selected comments from CT Summit delegates...metrics

- *"Identifying and harmonizing trial metrics should be easy, and an extension of the ACAHO, CIHR, & Rx&D working group. The key will be collecting this information - dead easy if everyone had electronic systems in place".*
- *"Good to look at metrics to ensure that we are competing in a global market".*

- *"I fully support the identification and development of REB metrics as these currently are not in existence. REBs struggle to operationalize efficiency and quality , therefore a well developed set of metrics would greatly facilitate this. Without national benchmarks or metrics to measure efficiency, it is challenging to respond to criticisms such as "REB reviews take too long"*

- *"Please circulate the CCRA report on the state of cancer trials to all attending...it contains very interesting cost/benefit analysis"*

While these initiatives by no means constitute an exhaustive list, the point is that such metrics already exist. The effort must move from debating the data and the cost benefit of collecting it, to ensuring we have baseline information and interpretation, otherwise, it will take too long for action and eventually our losses will far exceed our capacity to regain them. From an investor's point of view, showing that progress is being made could be as important as the aspired endpoint.

With respect to the third goal of this action plan – achieving a forward looking environment for clinical trials - the metrics we choose, must help to describe the human, social and economic returns of clinical trial investment. They must be useable by the public and by different levels of government. They must also be relevant to human, social and economic returns. Collecting data for measuring, monitoring and marketing progress of this action plan and return on investment of clinical trials forms the second recommendation in this plan. As will be discussed next, it is also an important part of the third recommendation.

Recommendation 2. **Measure, monitor, and market CT performance improvements:** Select and collect a parsimonious set of metrics on clinical trial performance and return- on-investment that allow Canada to (1) measure, monitor, and discuss progress, (2) identify issues, and (3) demonstrate return on investment for sponsors, sites, and all levels of government.

3. A Bold, Long Term Vision for Health and Research – with Near Term Returns

While many of the recommendations in this action plan will be about improving clinical trial operations for immediate returns, the third goal of this action plan – creating a path towards a stable future opportunity for clinical trials is also essential. Demonstrating the value proposition of clinical trials – in terms of the human, social and economic returns – is important, but it is only an enabler to a longer-term vision. The capacity to derive human, social and economic benefit from any type of research, including clinical trials, rely on capacity for innovation, inquiry, and willingness to change practice based on best available and new knowledge.

While the integration of research and innovation in health service delivery is an intuitive, logical and some may say ethical proposition, the jurisdictional and policy landscapes influencing how we generate and use research and innovation in health need to be modernized. We have not yet designed a system in which research and innovation link deliberately to receptor capacity. This means we need a health research and service

delivery eco-system with appropriate staffing, incentives, resources and infrastructure. This is the problem that motivates SPOR and the supports that must go with it.

Groups ranging from the National Task Force on the Future of Academic Health Sciences Centres, to the Council of Canadian Academies, have described major idiosyncrasies in the policy landscape that pertains to Canada's highest cost area and the enormous potential for mediating these costs through research, innovation, commercialization, and strategic procurement.[16]

We currently have a policy and funding disconnect in the capacity to integrate patient care and research in practice, even though the two are enmeshed. Canada's academic healthcare organizations are organizations which have deliberately espoused innovation as their business strategy and that describe the missions of their organizations as creating the environments in which research and innovation benefit patients, families, populations and the economy. However, we need a more robust and stable policy environment to support them.

We have the opportunity in Canada to espouse a bold vision for the integration of research, innovation, and patient care that will ensure better funding models, training and infrastructure for research and service delivery, as is partially described in the Strategy for Patient-Oriented Research. If we reach for such a vision, we will also boost our attractiveness for clinical trials in the long –run and help to achieve better models for sustainability and cost control in clinical trials, health care and in research. It is for this reason that we support a bold vision for the integration of research and innovation.

Selected comments from CT Summit delegates...

- *"What is needed more than an infusion of cash is a collaborative integrated culture where research contributes to sustainability of the health care system, and the health care system values research. There is much that could be done "in kind", or with memorandum of understanding, to support research on the health care campus, such as provision of corporate services like IT, HR, finance all of which are duplicated in the current "parallel universe" that is research. Cooperation around clinical data is key -- currently there is a huge research investment to duplicate recording of information captured in the clinical setting".*

- *"As an organization we are currently working to embed research within clinical practice to ensure that patients receive the best outcomes from evidence-based medicine. In addition to research, we have a Best Practice Implementation department that works to integrate knowledge translation into our research studies and then work with our sites via implementation science to facilitate change in clinical practice in a real-world setting".*

Recommendation 3. **Integrating health system and research infrastructure -** Espouse a bold vision for the integration of research and health care that would ensure sustainable infrastructure, staffing, resources, career support for the generation and integration of research to improve patient care, population health and the economy. This would include the goals of the broader Strategy for Patient-Oriented Research and recommendations of the National Task Force on the Future of Academic Health Sciences Centres to bolster receptor capacity.

4. Protecting People, Promoting Research – Ethics Review Boards and Clinical Trials

Canada has a stellar reputation for safety and for the protection of human subjects, in large part because of both the quality of its health system and the ethics review process. Ethics review boards are tasked with protecting human subjects in a manner that is safe, efficient and effective. They must balance the risks of research with the need to conduct it, the potential harms with the potential benefits. They need to manage uncertainly, multiple regulations, and multiple processes. Sometimes, they are tasked with activities that are beyond the purview of a review board, largely because an REB can sometimes look like a very clear and convenient location to make a number of other non-ethics related checks and balances.

To add to this natural complexity, when multiple review boards reviewing clinical trials exist, we create a landscape for an investor that can be very confusing and complex. Multiple forms, policies, protocols, and people may have different specifications, but with the exact same goals. The consequence is time, cost, delay, and potentially frustration and mistrust.

During the Clinical Trials Summit, participants discussed three questions (1) what does the ideal REB system look like; (2) what are the barriers; and (3) what is likely to be possible in the short term. The following were highlighted:

Ideal

- Mutual recognition of ethics reviews
- Well prepared submissions/proposals
- Common submission template
- Common consent forms
- Common adverse events reports
- Common templates with minimal variation
- Predictable, internationally competitive turnaround times
- Sufficiently resourced research ethics boards and clinical trial systems
- Compliance with the appropriate standards and respect for provincial differences

Barriers

- The absence of accepted standards and procedures as a baseline
- A lack of resources especially for education and training
- Poor recognition that REBs need to do more than review clinical trials

- The multiplicity of stakeholders and cultures which impacts on trust/ transparency
- Poor metrics for informed decision making and quality improvement
- Jurisdictional and legislative differences (privacy and REBs).

Possible

- Exchange material across the system
- Develop a national consent form and application template
- Develop a common set of criteria for evaluation of REBs and REB models
- Explore the implications of national accreditation and education strategies
- Consider a national coordinating mechanism for ethics review decision making.

Since the time of the Summit, there has been two developments that relate to these issues: (a) The Canadian General Standards Board (CGSB) released the final version of the common REB standard for ethical oversight of biomedical clinical trials. An evaluation of the standard is now anticipated; and (b) Health Canada has requested letters of intent for a fact finding initiative that would look at the feasibility of an REB accreditation system. The evaluation and feasibility results should be considered for their potential to contribute to the goals of this action plan.

In addition, given the openness to and benefit of common application and consent forms as well as the need for metrics, we recommend that a committee be struck to conduct a feasibility assessment that will enable these two initiatives to move forward.

Selected comments from CT Summit delegates...

- *"Most of the actionables focus on improving efficiency through streamlining the review process and while this is a desirable objective, the quality of the reviews and the safety of research participants cannot be ignored".*

- *"Past attempts to develop an accreditation model and to implement a national governance body for human research protection programs have failed, primarily due to potential for the model to involve significant cost implications. It is clear that the problems related to encouraging clinical trial activity in Canada are national in scope. Many provinces have dedicated substantial resources toward implementing provincial programs to harmonize / streamline ethical reviews of clinical trials (e.g. BC 1 Million through Michael Smith Foundation, Ontario 11 Million through the Ministry of Research and Innovation, Alberta 2 Million through Alberta Innovates—Health Solutions). If a portion of that funding could be dedicated to developing and implementing a national accreditation system for research ethics boards which would be coordinated through a National Advisory Committee on Research Ethics comprised of representatives from stakeholders such as ACAHO, Health Canada, the Panel on Research Ethics, CAREB, CIHR, RX&D, and possibly representatives from the participating provinces, a self-sustaining system is possible".*

- *"MICYRN has developed and tested a Canadian national federated REB review process and enters Phase I to put in place and evaluate in 2012. Commensurate with this is an agreed-upon Common application form, national consent form template, and coordinating mechanism for ethics review decision making. To establish the federated REB, we have conducted reviews of privacy legislation and ethics/REB legislative differences across provinces".*

- *"In terms of ethics needs, the biggest need is for leadership... the demise of NCEHR requires a Health Canada PRE-CAREB-CIHR effort to form a new body with oversight of health research, including*

accreditation of REBS, education of research and REBs as well as patients, examining and setting guidelines for new ethical issues in health research".

- *"The Canadian Association of Research Ethics Board (CAREB) can and should be instrumental in leading the Ethics related initiatives, some of which are already underway..."*
- *"There should also be a focus on accreditation for physician investigators not just REBs".*
- *"Consent form needs...specific wording related to confidentiality, privacy, and injury- it will be difficult to agree. If this could be done this could significantly improve study start ups but assume this will be a difficult task. Suggest consultation with Pharma".*
- *"We have done considerable provincial work on the consent form and will be implementing systems to capture REB and clinical trial metrics at the provincial level, recognizing these actions need to be coordinated inter-provincially. Through both the ethics harmonization and the CT streamlining initiative managed by Alberta Innovates-Health Systems".*

Recommendation 4: Improve efficiencies of ethics reviews and advance strategic issues: Leveraging the appropriate bodies and expertise, undertake a feasibility assessment and proposal for a common application form, consent form template, elements of an accreditation system, and information/form sharing mechanisms for ethics reviews. Also support the work of Health Canada in evaluating standards and accreditation options and explore strategic issues like accreditation and harmonization.

5. Patient Recruitment

While recruiting patients into a clinical trial can make or break its success for the sponsor, investigator and clinical trial site, the capacity to recruit patients comes down to: (1) issues of patient choice and (2) eligibility. The patient has to be able to find the trial and the trial has to be able to find eligible patients.

Considering what influences patient choice in other clinical or social scenarios will be helpful for the patient. Providing general information about the existence of a trial, the possibility of benefit, the likelihood of long-term benefit, convenience, can be helpful. At the Clinical Trials Summit, we heard about a number of grass root strategies that can be used to help encourage patients to partake in clinical trials if there is a benefit to them in doing so.

However, even if a patient wants to partake in a clinical trial, he or she may not be eligible to do so. Clinical trials are becoming more complex and their inclusion and exclusion criteria mean that it is harder to find the right patients to begin with. We need to be able to leverage registries and databases especially because the Canadian population is relatively small and sparse compared to other countries and regions that are trying to consolidate clinical trial assets in order to offer access to the largest possible populations.

Selected comments from CT Summit delegates...on recruitment

- *"CRRC established a multi-stakeholder recruitment initiative (pharma companies, rheumatologists, coordinators, arthritis patients) to explore the barriers to recruitment into arthritis trials in Canada and to build some solutions".*
- *"Q&T Research has developed a concept based on «a network of trust» with the Sherbrooke-based population 1. Presenting clinical research as «caring» to counteract the «scaring» image 2. Provide an added value that shows real care, the Radio Health capsules we have implemented in 2009 are an good examples".*
- *"BC CRIN has identified patient recruitment as a key priority and is working to develop a provincial strategy. This could easily be expanded or part of a national strategy".*
- *"US versions [recruitment tools] have been developed and thoroughly tested; these can be customized for Canada: brochures, DVDs, newsletters and posters for pre-education; "Medical Hero" public service campaign with TV, radio and print adverts; process for communicating summary trial results in lay language to study volunteers; grassroots outreach through a program called AWARE..."*

Selected comments from CT Summit delegates...on registries

- *"Patient Registries are key to recruitment (number of patients, state of disease, drug naïve or not). The cost to system is maintaining the Registries, in terms of need for qualified, professional staff who can abstract and enter high quality data".*
- *"Maternal Infant Child and Youth Research Network (MICYRN) has developed a 'database of databases' and determined that there are at least 100 pediatric clinical research networks in Canada; each one of these maintains patient information in an unsupported, ad hoc, non-standardized fashion (which we are working to improve). de facto, pediatric networks extend beyond local/regional sites because of the need to ascertain sufficient numbers of patients with any condition".*
- *"The database of databases referenced...must be developed in coordination with best practices in relation to research ethics and databases... individuals with that expertise would need to be consulted".*
- *"The Rick Hansen Institute currently has a life-long, patient registry of people with traumatic spinal cord injury and we will be expanding into non-traumatic spinal cord injury. Our registry currently has ~2700 participants with 50-70 participants added each month. We have 31 sites across Canada".*
- ***"** Our particular strength is our registry, I am looking to work with other disease registries to streamline privacy and operational issues. Our registry is currently being migrated to a state-of-the-art web-based platform that we use for the registry plus our clinical trial/research studies. A key feature of our registry - as new people consent to join they also consent to contact for future research studies, therefore ,as we develop new studies we know the exact number of participants that are eligible at each of sites. We review the registry participants against the eligibility criteria for the new study and then directly contact those people who are eligible".*

Rec. 5. Develop a 'database of registries' & consider a national recruitment strategy: Improve patient recruitment times by developing a database of registries with appropriate consent and privacy considerations, that will help to identify patients that may be eligible for clinical trial participation. Identify, implement and share tools that have proven effective for this purpose. This will improve recruitment rates and speed.

6. When Trust Becomes Efficiency - Certifying for Standards and Excellence

Let's reconsider the scenario offered in the introduction to the action plan. A clinical trial company wants to do multiple trials with multiple sites in Canada. Should it be required to review, assess and accommodate multiple standard operating procedures (SOPs) and forms, and accept different levels of training depending on the site? Does this have costs and consequences? Is there a more efficient way?

A commonly repeated proposal at the CT Summit was for the use of common standard operating procedures and common training and mentorship for Good Clinical Practices (GCPs) required in trials. Organizations that adopt these, could then be certified and the costs related to variability, uncertainty, and complexity of working with multiple sites would be decreased significantly.

Where could common SOPs, training, and certification capacity come from? The Network of Networks (N2) has developed a large number of such SOPs and training modules. These modules were developed by individuals in the field, for the field.

Currently, the N2 is a voluntary and grassroots organization funded by membership fees and the in-kind contributions of the individuals involved. It has had incredible success with very little resource. Many of the people who would likely have the expertise to assist in the domain of standard operating procedures, training and certification are likely already members of N2, which presents an opportunity.

To leverage this, we believe what with some additional resource for staff support and operations, N2 could assist the entire clinical trial community through the dissemination and application of existing training and standard operating procedures. If organizations adopting these could be recognized through a certification program this could signal business friendly environments, accountability and reduce uncertainty.

Selected comments from CT Summit delegates...

- *"I have been involved with N2 since it's formation ...and believe they are they best group to undertake standardized training initiatives for Canada. We have been incredibly successful as a grass-roots organization -both in creating training materials and facilitating Canada-wide collaboration".*
- *"Overall standardization is becoming a focal point of convergence with initiatives like ACRES at http://www.acresglobal.net recently initiated by Dr. Gerg Koski".*
- *"Sites are dealing with an increasing amount of non homogenous requests, training, regulatory requirements all of which are draining financial resources up to a point where clinical research is becoming a too expensive option for many physicians".*
- *"N2 was formed because clinical researchers face common challenges in their quest to conduct world class research. Network of Networks (N2) is an established and successful national initiative that brings together multiple existing disease networks and other stakeholders to enhance Canada's research capability and capacity. Its current >42 member organizations represent > 3000 investigators and affiliated staff. Because of this N2 provides the opportunity to speak to clinical research issues with one*

voice and offers a forum to develop and share tools, resources and best practices. It is N2's belief that with adequate additional funding N2 is well positioned to play an important role in the outcome of the Summit and the execution of the action items described in this document".

- *"BC Clinical Research Infrastructure Network (BCCRIN) is exploring clinical trial site certification program (ex UK system):".*
- *"We are currently working with Accreditation Canada to create centres of excellence for spinal cord injury (standardized standard-of-care) across Canada. To ensure that these sites can quickly participate in all types of research studies, we are including a program of "clinical research standards" for our sites as we undertake the Accreditation Process. We are particularly interested in the interest/outcomes for "site certification" that evolves from this summit".*
- *"Who would set standards for centres of excellence? Would these centres be pre-audited? There is no process in place to develop centres of excellence and this would be required as a prerequisite"*
- *"No one can object to standardizing training, but the key here is providing sustained salary support in order to attract and retain qualified professional staff to carry out the work. Any business knows that it is far more economical to invest in retention of qualified staff, than to lose this investment when people leave and have to repeatedly train novices".*
- *"Common Adverse Events/Standard Adverse Events are of interest and worthy of being expanded and applied to many more logistical aspects that are repetitive and unnecessary, an example: Financial disclosure forms. There are as many forms and approaches as we have projects, some are with annual updates, others with bi-annuals".*

Recommendation 6: Adopt common SOPs, training and certification: Establish funding for the Network of Networks (N2) to more broadly disseminate common SOPs and Training resources. Work with N2, ACAHO, Rx&D, CIHR and other interested parties to develop a site certification approach to identify organizations that have these standards in place.

7. Getting to Yes - Advancing the model Clinical Trial Agreement

For the first time in Canada, a model Clinical Trial Template Agreement (mCTA) has been proposed for pilot purposes in negotiating regular Phase II and Phase III single and multisite clinical trial agreements between sponsors, clinical sites, and principal investigators. The template is a direct response to calls from the field for such a resource. It was developed by members of ACAHO and Rx&D through CIHR funding, who have worked together on drafting the mCTA for pilot purposes with Counsel and advice from the Canadian Medical Protective Agency.[17] It is now being pilot tested in the field by CIHR.

To this end, members of ACAHO and Rx&D, as well as other interested parties, are currently participating in a 6 month pilot of the mCTA which is scheduled to end March 31, 2012 pending sufficient data. During this period, pilot participants are asked to use this template as the basis of clinical trial agreement negotiations and to record changes on the feedback form provided. This will allow an objective assessment of what elements of the template need to be changed in order to accommodate the needs and interests of all parties.

Ultimately, the goal of the template is again to simplify and expedite the start-up times for clinical trials in Canada and take one step closer towards increasing the attractiveness of Canadian clinical trial sites as preferred partners internationally. At the end of the pilot period, changes may be required to the mCTA and care must be taken to implement these changes and monitor its use.

From the field...

- *"We fully support the mCTA, effective patient recruitment strategies that optimize Canada's position in attracting CTs but not centres of excellence per se (too narrow), identification of areas of expertise and strategic foci for CT activity in Canada, and a strategic infrastructure to support these activities".*
- *"The Model Clinical Trial agreement has been raised by Rx&D and member pharmaceutical companies may adapt. Potential push back by pharma legal departments".*

Recommendation 7: Improve and use the model clinical trials contract - implement the model Clinical Trials Agreement currently being pilot tested by CIHR, Rx&D and ACAHO, ensuring that the proper adjustments are made after the pilot and that appropriate communication and dissemination occurs, including to global head offices if necessary.

8. Maximizing incentives – Patent Protection and Tax Credits

Clinical trial summit attendees noted the importance of the SR&ED tax credits to clinical trials. These can be an effective instrument for helping to cover costs. However, currently, the SR&ED tax credits come in a year after the trial ends. These revenues end up in central operating budgets and are therefore not applied against the research cost centre for the trial. The savings are then missed when "cost of research" is considered by global head offices. In addition there is a significant paper work burden.

As the Government of Canada considers the implications of the Federal Review of support to R&D, the SR&ED tax credit may enter into stages of review and adjustment. This may present an opportunity for making other adjustments that could benefit the clinical trial community. We need to be vigilant for this opportunity and ask actively for improvement as its costs will likely be much lower than the benefits.

In addition, as the Canada-European Union Comprehensive Economic and Trade agreement (CETA) is being negotiated, it is important to support improvements in Canada's intellectual property protection policy. Currently, compared to the European Union, Canada offers no restoration of patent protection time for regulatory delays and clinical development time; no effective appeals mechanism for innovators in patent invalidity proceedings; and two years less of data protection. European countries, who on average spend less of their GDP on healthcare, offer these policy incentives. It is certain that the goal of improving the clinical trial landscape will be supported by increased intellectual property protection.

Recommendation 8. Optimize intellectual property protection policy & SR&ED Tax Credits - Advocate to bring intellectual protection (IP)policy to bring IP policy to levels commensurate with Europe within the Canada-European Union Comprehensive Economic and Trade Agreement. Help to improve administration of SR&ED tax credit so that credits are received in time to offset costs of trials. Ensure that global head offices are aware of these improvements once they are made.

9. Communicating Canada's CT assets and improvements to Global Head Offices

We often think of clinical trials as scientific endeavours or as a modality of clinical care. However, clinical trials are also business ventures and businesses must meet the needs of the customers who will make their operations sustainable. While this includes clinical trial sites, investigators, patients and clinicians, it also includes global pharmaceutical, vaccine and device companies, without whose dollars, we will not be able to pursue non-investigator led trials. As has been done in other countries, we need to find better ways of communicating, courting, marketing, and working with global head offices.

This can begin modestly through the national headquarters proposed in Recommendation 1. It could begin with communication materials that simply alert global head offices to the initiation of an action plan and serious interest in regaining business. It could then grow in terms of making available asset maps, and it can grow in terms of more active marketing approaches such as those used in the United Kingdom. At a minimum, the provincial initiatives aimed at forming clinical trial stakeholder outreach in each province should be recognized and highlighted.

Recommendation 9. Open a concierge (storefront) service for investors – Start by providing international companies with information on Canada's clinical trial assets, offerings and improvements, then develop a concierge service that would provide a centralize access and information point to global companies.

V. Risks & Rewards of this Action Plan

This action plan is designed to take us from the vignette of how companies do clinical trials in Canada today, to a vision of a better business landscape, more clinical trial investment, and a fertile ground for clinical trials into the future.

From...Today's Vignette of CT Business	To... Tomorrow's Vision for CT Business
Multiple disjointed initiatives between provinces, regions, and domains	Clinical trial improvement activity headquarters to coordinate improvements.
One time efforts, estimates, anecdotes, and perceptions about performance	Regular performance metrics for measuring, monitoring, managing &marketing progress.
Disjointed, unpredictable policy & funding landscape for the generation of research and its timely application in practice	A bold vision and resulting policy and funding landscape for generation and integration of research and clinical practice.
Multiple ethics applications, consent forms,	Clarity on options for accreditation and a plan for

metrics & accreditation questions	common consent and application forms
Difficulty recruiting patients and unknown or disjointed patient registries	Timely recruitment from registries from which to draw potentially eligible patients
Variability in standard operating procedures and uncertainty in training at clinical sites	Common standard operating procedures, training and site certification for those sites demonstrating the application of standard and training.
Delayed payment of SR&ED tax credits that become unattributable to the CT	SR&ED tax credits that are received on time and assessed against costs.
Intellectual property policy that falls short of that of the European Union	Intellectual property policy that encourages Canada's attractiveness for CT investment
Lack of storefront to inform sponsors of Canada's CT assets	A "storefront" and communication products that identifies Canada's CT assets o help clinical trial

In our view, the major risk to implementing this action plan is inaction. Inaction will inevitably lead to further loss in Canada's ability to attract clinical trial investments.

We have had the advantage and disadvantage of having watched this type of clinical trial improvement activity unfold in other countries and have seen their success. Improving cost, quality, speed, and relationships as they pertain to starting a clinical trial and ensuring that we have a robust policy framework and investment incentives, will not have a negative impact. They will not compromise values or safety and the marginal cost of this type of activity is very modest. The goal of the action plan is not to ask for resource, but to build the capacity compete for it.

VI. Next Steps & Concluding Remarks

"The world cares very little about what a man or woman knows; it is what a man or woman is able to do that counts". - Booker T. Washington, Educator

As with most issues of business and strategy, having an action plan is only the first part of the journey. The real question is whether we can mobilize, organize, and accomplish what we set out to achieve.

To this end, Rx&D, ACAHO, and CIHR will circulate this action plan for comment. They will develop and determine the communications, resources and implementation details that would need to go with this action plan. They will then begin approaching the parties named to consider their interest in leading and facilitating implementation.

It is our hope that the SPOR leadership in particular, will find this document useful and appropriate to their own goals and mandates. We also hope that in a year's time, many of the recommendations in this plan will have been completed and that we will be well on our way to attracting more clinical trials to our country – with the human, social & economic benefits that come with them – to the health and prosperity of all.

APPENDIX
An Action Plan to Help Attract More Clinical Trials to Canada
Summary of Feedback on Final Draft

On March 30, 2012, ACAHO, Rx&D and CIHR released the Final Draft of the Action Plan from the September 15, 2011 Clinical Trials Summit to all delegates; members of ACAHO, members of Rx&D as well as to other stakeholders. This was the third and final consultation on this initiative. The feedback has been very positive. Most of the feedback is related to its implementation. As such, while no substantive changes are being proposed to the final draft, the content of this Appendix becomes an essential part of the action plan for those leading implementation. We begin with a summary and then discuss each recommendation.

Summary of Feedback on Final Draft

Support for this action plan and its recommendations: The feedback to this action plan has been very positive from across the country. Eight formal letters/emails were received. Only one indicated major concerns. The language in most of these letters as well as in the feedback to the proceedings will be helpful in implementation and in advocacy.

Implementation considerations: Many comments were received about how the implementation needs to occur. Specific considerations received for each recommendation are included in this appendix. Composition of the implementation committee will be essential as well as the manner in which the committee links to the field.

Importance of baseline and performance measurement: Recommendations 4, 7, and 9 have already begun for various reasons. If the intent is to go forward with recommendation 1 (implementation oversight), recommendation 2 (evaluation/metrics) needs to be prioritized or the recommendations could proceed without any capacity to assess or communicate impact.

Options for addressing the stated limitations and next steps: Circumscribing the scope of this plan around industry led trials and expediting start up times, was done purposefully to provide a reasonable chance of implementation success and a starting point. Deliberate consideration for the limitations is required in order not to "orphan" issues, neglect next steps, or miss opportunities to coordinate with other groups.

Reconceptualizing "standardization" and consultation for each recommendation: This initiative was developed through a stepwise consultation process. Top down approaches to implementing the operational recommendations are not recommended. This could very easily fail to capture the leverage points that would balance standardization with flexibility. For example, in recommendations 4, 5 and 6, matrix models of standardization may work far better as a starting point than applying a one size fits all approach. Further discussion below.

Communications: Since the CT Summit, nearly all of the communications about this initiative have occurred via written document and accompanying emails. This has been unusually successful, but a more full-some communication plan is needed.

Cost considerations and leveraging a starting point: Proper costing of this action plan is essential. Success is what will determine the capacity to spin off into next steps and more strategic issues. Recommendations 4 and 7 already involve contributions from 3 CIHR FTEs. Recommendation 6 may entail over $1.5 million dollars for 3 years. Recommendation 3 requires long term funding considerations.

Specific Considerations related to Implementation

Recommendation 1 (Implementation):

- How do we ensure that the action plan does not orphan important clinical trial groups that are not covered in this action plan?
- Should the action plan be applied to academically led trials by ensuring coordination through the implementation committee?
- How will the implementation committee be structured?
- What are the opportunities for ensuring that specific considerations as they pertain to children's clinical trials, dementia clinical trials, cancer trials, rheumatology?
- What is the preferred relationship with the private sector research organizations? What about other parts of the clinical trial ecosystem, SMEs?
- How will other mid-late stage trial management issues be considered i.e. beyond start up?

Recommendation 2 (Evaluation):

This recommendation needs to be approached from a managerial and marketing standpoint and not from a metric development perspective. It is about: (1) being able to tie the metrics to the plan's goals (2) use the metrics to monitor changes or lack thereof (3) adjust the plan as needed; and (4) market the results. Some of the indicators may need to capture the satisfaction of investors. It is noted that N2 is currently evaluating the metrics from the Metrics Champion Consortium in the US for application in Canada.

Recommendation 3 (Strategic issues):

This recommendation could have its own action plan. It is where the potential for a culture shift necessary to improve clinical research can materialize. It is recognized that many of the issues in this recommendation are related to the broader SPOR initiative. They require significant funding and policy innovation.

To bring this recommendation to a more concrete level, in addition to the SPOR support units, a "credentialed hospital" program, such as that used in the US cancer system could tie accountability for infrastructure could to funding. This recommendation will require new funding and policy innovation in the longer term. Career support for scientists and incentive for innovation is essential.

Recommendation 4 (Streamlining ethics):

The size and complexity of this recommendation is noted. There is an emphasis on the need for appropriate consultation models in this initiative. This needs to include individual REBs as well as academic healthcare organizations, ethicists, provincial or national accountability structures, and Health Canada. It was noted that common forms and templates need to recognize different situations, for example, while some level of standardization is possible, the templates may be different depending on whether the study is high risk, low risk, involves children, substitute decision makers etc. Standardization should occur only where it makes sense to do so. The consultation model is essential.

Recommendation 5 (Patient Recruitment):

Some individuals feel that the focus should be on a national recruitment strategy. Others support recruitment databases but complexities need to be negotiated:

- What are the privacy issues and how can these be addressed?
- What are the ethical issues and how can these be addressed?
- How do people withdraw from the database?
- Who will manage and govern the database?
- Will individuals in the database be overburdened?
- Will individuals not in the database have access of opportunity?

Recommendation 6 (Standard Operating Procedures & Certification):

The Network of Networks (N2) Board of Directors has provided a letter of support in principle for this action plan and recommendation 6 in particular. They welcome an initial discussion on the scope, costs, funding, and staffing required.
Some reviewers have suggested that in addition to N2's SOPs, there may be SOPs in specialized areas that are already in place. For provinces or research networks that have already adopted population specific practices, an equivalency or matrix model should be considered.

Considering the costs to the organization of adopting the SOPs, certification for SOPS may need to have "levels" that allows organizations to be recognized according for the level they choose to adopt or wish to invest in.

The intention in this recommendation is not regulation or bureaucracy. The intent is to reduce variation where it makes sense to do so and to communicate to global head offices a very clear message about what is in place.

Recommendation 7 (mCTA): Model Clinical Trials Agreement: Significant feedback on this recommendation would have gone directly to CIHR through the pilot. Follow up is essential.

Recommendation 8 (Intellectual Property and SR&ED): The only additional comment was to also look at IP and tax incentives in countries like Korea in addition to the EU.
Recommendation 9 (Clinical asset map and concierge service): No additional comments were received on this recommendation.

Note: In their feedback letters, Alberta Innovates, BC Clinical Research Network, Maternal Infant Youth Clinical Research Network, Bloorview Kids Rehab, Saskatoon Health/University of Saskatoon, MNRCC, CAREB, N2, Canadian Cancer Research Alliance, Rick Hansen Institute, Ottawa Heart Institute have all offered expertise in assisting with the leadership, set up or reference to existing tools or products to the plan.

Endnotes

[1] ACAHO, Rx&D, CIHR, *Starting the Conversation*. 2011
[2] Canadian Cancer Research Alliance, 2011. *Report of the State of Cancer Clinical trials in Canada.*
[3] Slutsky, A. 2011. *A SWOT, So What, Now What. Slide* presentation from Clinical Trials Summit, ACAHO
[4] Laberge, N. 2011. *Globalization of clinical research and metrics survey.* Slide presentation from Clinical Trials Summit, Rx&D.
[5] McMaster, R. & Harris Harper, H. 2011. *Does Canada Have a Place on the Clinical Trial Podium.* Innovation Leaders Insert, Globe & Mail, Hill Times.
[6] Phraseology is attributed to Dr. Geoff Fernie, Vice President Research, Toronto Rehabilitation Institute
[7] Members of the Clinical Trial Summit Steering Committee and their organizations at the time of the Summit included: Ms. Karen Arts – Director, Business Development, Clinical Trials, Ontario Institute for Cancer Research; Dr. Shurjeel Choudhri – Senior VP and Head, Medical and Scientific Affairs, Bayer; Ms. Joanne Goldberg – FRSQ; Dr. Rav Kumar, PhD – VP R&D Operations, GSK; Dr. Rob McMaster – Chair, Executive Management Team, BCCRIN; Dr. Jean Rouleau - Doyen de la faculté de Medicine, Université de Montréal; Mr. Jean-Jacques Rousseau – Manager, Life Sciences Program, Ontario Ministry of Research and Innovation, Dr. Tina Saryeddine, PhD, MHA, CHE, Assistant Vice-President Research and Policy Analysis, Association of Canadian Academic Healthcare Organizations; Dr. Arthur Slutsky – VP Research, St. Michael's Hospital; Dr. D. Wayne Taylor, F.CIM – Executive Director, Cameron Institute
[8] The Structure of this diagram is adapted from *Making an Impact*, report of the Canadian Academies of Health Sciences.
[9] ACAHO, Rx&D, CIHR, 2011. Towards an Action Plan – Proceedings and Implications from the 2011 Clinical Trials Summit.
[10] McMaster, R. & Harris-Harper, H., 2011. Does Canada Have a Place on the Clinical Trial Podium? Editorial published in Canada's Top Innovation Leaders, 2011
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[12] CIHR, 2011. Canada's Strategy for Patient Oriented Research
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[17] Vogel, L. 2011. *Boilerplate being tested for clinical trial agreements. CMAJ November 8, 2011 vol. 183 no. 16 First published October 3, 2011, doi: 10.1503/cmaj.109-4016*