Proceedings & Implications from the 2011 Clinical Trials Summit

Towards an Action Plan...

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

(with Appendix reflecting Feedback from Request to Reader)

Beginning with the end in Sight...A Request to the Reader

On September 15, 2011, Canada's Research-based pharmaceutical companies (Rx&D), The Association of Canadian Academic Healthcare Organizations (ACAHO), and the Canadian Institutes of Health Research (CIHR), co-sponsored a day-long, in-person conversation on clinical trials. Close to one hundred and thirty individuals from government, industry, academic healthcare organizations, universities and other related organizations attended the event. This document, entitled *"Towards an Action Plan"* is both a record of the proceedings and an analysis and synthesis of their implications.

Our goal through these proceedings is not only to capture the rich and powerful discussions that took place at the Summit, but to help translate them into a strategic action plan. The action plan will be intended as a roadmap that helps all sectors determine how we might re-establish Canada's leadership in clinical trial competitiveness by addressing issues related to cost, quality, speed and relationships as they pertain to clinical trials in Canada. Such an action plan must be specific enough to leverage immediate activity and clear enough to enable advocacy for the overall directions that need to be pursued.

As a consequence, this document is *not* intended to be a passive read. You will note that after the record of discussion on each topic, the steering committee has taken an interpretative license in pushing the recommendations into the realm of potential actionables. To ensure that we are moving in the right direction, we would invite all of the delegates to provide their reflections on these actionables using the accompanying survey form by December 15, 2011. *The results of the "request to reader" are now appended to this document as Appendix A.*

Most importantly, we would like to invite those organizations who have the expertise to help achieve some of these deliverables - either within existing resources or with some seed resources - to self-identify, as some have already done on site during the summit. The feedback we receive will be used in drafting the action plan, which will form the third and final document in what we consider a trilogy of papers from the clinical trials summit.

Once again, we thank you for your participation so far, for your ongoing efforts, and for your commitment to clinical trials in Canada. We look forward to building on the momentum that you have created - and ultimately, to an action plan for the future human, social and economic benefits of clinical trials in Canada.

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Meet the Delegates

On behalf of ACAHO, CIHR, and Rx&D we would like to thank the following individuals who registered for the clinical trial summit, participated on site, or provided leadership on the steering committee. Any errors or omissions are unintended. In recognizing these individuals, please note that the content and analysis of these proceedings should in no way be interpreted as a reflection of their individual opinions or those of their organizations. Steering committee members are noted by an (*).

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Meet the Sponsors

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. You can read more about Rx&D at https://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. You can read more about CIHR at: 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 collective 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. You can read more about ACAHO at www.acaho.org

About the document: The initial version of this document was circulated on November 25, 2011 for delegate feedback. Delegate feedback received through the referenced "request to reader form" and/or in person or phone consultations were used to assess the list of actionables proposed from the proceedings and other considerations. This feedback is summarized by theme and provided in Appendix A. Special thanks to all who assisted with the note-taking at the Summit and to those who responded to the request from the reader and/or questions from the authors. These proceedings were prepared by ACAHO on behalf of the sponsors.

Table of Contents

Executive Summary

This document is a proceedings and implications document from the Clinical Trial Summit of September 15, 2011. It serves as a springboard to a draft action plan for clinical trials in Canada that can help industry, academic healthcare organizations, universities, governments and other related organizations, work together on regaining the human, social and economic benefits of Canada's leadership in clinical trials. The document contains both the proceedings and an analysis of the related implications. It also contains the rationale for the proposed actionables that upon confirmation - and resource discussion - will make up a proposed action plan. The background document to the clinical trials summit, *Starting the Conversation* and the keynote presentations, are available on the ACAHO and Rx&D websites.

Approach

The discussion among the attendees of the clinical trial summit began with general agreement on the following "givens" as a baseline for the conversation:

- Clinical trials are of value to Canada for human, social, and economic reasons. They are of value to other countries for the same reasons. However, other countries may be better leveraging their strengths in order to achieve them. As a consequence, Canada is losing clinical trials (and clinical trial sites) at an alarming rate - possibly because of the cost, quality, speed and relational issues that may discourage clinical trial investment in Canada, as well as increasing infrastructure and expertise in other countries.

- Canada has the potential to address these issues on both a strategic and operational level by leveraging and coordinating our strengths from coast-to-coast. Specifically, cost, quality, speed, and relationships may be improved by addressing issues related to (1) ethics reviews, (2) patient recruitment (3) administrative structures, (4) cost structures, and (5) strategic infrastructure. These became the foci of the discussion groups at the summit.

The rich and multi-faceted discussion points from each of these break out groups are recorded as the proceedings of this document. The proceedings were then analyzed for potential 'actionables' and remaining questions that would be needed to populate the action plan.

The next step is to ask your feedback on these potential actionables, their priority/importance, and where appropriate, help to identify options for "how" they can be advanced. To do this, we will ask individuals to discuss the extent they agree with each actionable and where appropriate, organizations to indicate (1) where potential resources already exist and (2) what elements require broader infrastructure, resource considerations, and advocacy. To this end, *"A Request to the Reader"* form is appended.

Proposed actionables

The actionables proposed through the analysis and synthesis of the discussion on ethics, patient recruitment, administrative structure, cost, and strategic infrastructure are presented below. The reader will note that they generally relate to one of six different types of activities: information sharing as it pertains to common data, tools and templates; the short term adoption of existing potential standards; the development and adoption of a site certification program; the identification of centres of excellence; business planning and policy development work; and establishing coordination mechanisms and potential. Later in the document, we present the actionables grouped according to activity type. However, below we provide a summary by break out group discussion theme.

Summary of proposed actionables by discussion group theme
1. Ethics Reviews
1.1 Leverage a clearinghouse to share ethics forms and templates: Clearinghouses are being developed for sharing ethics review templates and materials across the country and can be leveraged (through marketing and use) to share common forms, templates, and tools (for example a tools website is currently being completed by CAREB) . **1.2 Identify, develop, or review and agree upon a set of research ethics board (REB) metrics:** Metrics for REBs would help inform future discussions on the performance and structure of ethics review boards and would permit future research and decision making on how to optimize the relationship between REB structure and performance across the country. **1.3 Explore implications of national accreditation and education strategies**: While the idea of national accreditation and REB education may have complexities, organizations like CAREB are exploring these issues in their strategy development processes. These strategies should be reviewed and considered in the context of clinical trial infrastructure in Canada. **1.4 Adopt a national consent form template:** Facilitate the review, circulation and adoption of a national consent form template that all sites in Canada could use. **1.5 Develop a national coordinating mechanism for ethics review decision making:** The coordinating body for ethics review issues would ensure that REB plans for clinical trials across the country are (1) integrated with other clinical trial operational considerations; (2) integrated with considerations regarding other non clinical trial REB operations as appropriate; (3) coordinated across the country; (4) that legislative differences are explored/ addressed/considered over time; and (5) would explore issues related to harmonized reviews and boards of record in each province.
2. Patient Recruitment
2.1 Identify centres of excellence/networks for various population groups: Developing a clearer identification of patient recruitment entities/sites for each population would facilitate recruitment for clinical trials. **2.2 Create a database of all patient registries:** common and consolidated 'database of databases' could help to expand and consolidate the available or potential patient pool. **2.3 Establish a coordinating mechanism for patient recruitment issues:** This coordinating mechanism would: (1) focus on the development of a national strategy for patient recruitment; (2) help to elucidate where population specific issues in recruitment will differ from national issues in recruitment; (3) explore and facilitate the use of existing "turnkey solutions" such as the ones presented on site; (4) potentially provide a public interface for clinical trials
3. Administrative Structures

3.1 Identify, collect and harmonize clinical trial performance metrics: This would include but not be limited to performance metrics for ethics review boards to enable monitoring, future decision making, and strategic planning.
3.2 Standardize Training*: Facilitate the spread of existing training and materials as they pertain to standard operating procedures (SOPs) and good clinical practices (GCPs). N2 has programs that can be leveraged.
3.3 Develop a clinical trial site certification program: Explore a proposal for a site certification program that would include the adoption of relevant and common standards, accountability agreements, and appropriate resources.
3.4 Follow up on Model Clinical Trial Agreement: The Model Clinical Trial Agreement is currently in pilot phase and the results should be pursued to ensure that the initiative continues to evolve and achieve the required outcomes.
3.5 Adopt a common Adverse Event (AE)/Serious Adverse Event (SAE) reporting template: Achieve consistency and coordination in AE/SAE reporting by leveraging existing materials and hosting an international summit
3.6 Strengthen national leadership where appropriate: Consider the national leadership, support and direction setting structure that will coordinate, fund, and bring existing expertise, initiatives and organizations together towards the common goals that have been discussed.
3.7 Develop an appropriate Industry interface: Create an appropriate industry interface that would help to eliminate repetitive document requests by standardizing key information elements, creating a site database that would provide information on clinical trial sites and potentially serve as a problem solving and business planning resource.

4. Cost Issues

4.1 Explore further patent protection and SR&ED tax credit improvements: Explore the cost implications of additional years of patent protection (data protection and/or Patent Term Restoration) and potential improvements in SR&ED tax credit administration.
4.2 Identify centres of excellence for patient recruitment: Create clusters of sites willing to recruit patients in particular patient groups for trials.
4.3 Advance model Clinical Trial Agreement (mCTA): Follow up on the pilot of the mCTA to ensure that the initiative continues to advance towards its goals.
4.4 Engage in more CT related efficiency initiatives: Reduce costs by leveraging the process used to develop the mCTA in order to also: enhance efficiency in other areas, including (but not limited to): REB streamlining; Good Clinical Practices (GCP) training; trial management inefficient either due to clinical research organizations (CRO) approaches or lack of harmonization.
4.5 Develop a costing template: Develop a costing template to help achieve transparency in the costs of clinical trials.

5. Strategic Infrastructure

5.1 Scope strategic infrastructure needs & develop business models: Study the scoping requirements for strategic infrastructure and develop the accompanying business models.
5.2 Develop the appropriate value propositions to engage policy leaders: Provincial and federal governments and their representatives may both be interested in clinical trials, but they are not necessarily interested in the same dimensions or rationale. The community needs to be able to articulate both the economic and health benefits, as appropriate, otherwise staff can not mobilize solutions through the appropriate channels.
5.3 Build and maintain the broadest coalition of clinical trial stakeholders: Ensure that patients, populations, existing networks, existing volunteer groups, policy makers, clinical trial sites, and all relevant stakeholders have a forum through which to develop a shared voice, identify and discuss issues and solutions.
5.4 Ensure multiple funder coordination: Considering the magnitude of funding needed, continue

to leverage and coordinate the funding from multiple sources and funders (example Strategy for Patient Oriented Research (SPOR) plus others.
5.5 Favour a balance of population-specific and common elements nationally: Recognizing that not all trials are one-size-fits-all, ensure that due consideration is given to population-specific needs.
5.6 Identify or establish areas of excellence: Study the clinical trial landscape in further detail to identify areas of excellence and strategic foci.
5.7 Develop a site certification program: Consider a site certification program proposal that would bring standardization, accountability and resources to organizations undertaking clinical trial activity. Recognize that many standards are already developed.
5.8 Espouse a bold vision for the integration of research and patient care: In this discussion group, a recommendation was made to reinvest 2% of health spending into research to help close the gap between these inextricably related areas.
5.9 Improve standardization and sharing of best practices*: Support and encourage collaborative workspaces, standardization, and best practices.

In addition to the actions proposed, we have also identified the following questions that may also need to be addressed if we are to develop a coherent action plan:

(1) How to coordinate and resource activities that require multiple players?
(2) How do we prioritize, coordinate, and leverage activities across the country?
(3) What about activities that require difficult decisions or further study?
(4) Is an overarching clinical trial body needed in Canada to coordinate activities?

Conclusions and Next Steps

As a result of the Clinical Trial Summit, we have a set of actionables that upon confirmation, would make up the "specifically what" section of an action plan. In order to move to the final phase, we now have three questions for the reader: (1) Do you agree with each of the actions? (2) What is the best way to achieve each? (3) What is your view on the four higher level issues identified?

On-site, a number of organizations were identified as having the potential tools, resources, will and expertise to leverage some of the deliverables that participants felt are needed to improve the clinical trial landscape. Examples of such organizations includes ACCT Canada (an organization that looks academia-industry interface for the commercialization of technologies), the Network of Networks (known as N2 which looks at operational issues related to clinical research), the Canadian Association of Research Ethics Boards (known as CAREB which looks at strategic and operational issues related to research ethics boards), the co-sponsors (ACAHO, CIHR, and Rx&D) and importantly, all of the provincial clinical trial or disease specific coordinating bodies by virtue of their mandates (for example as discussed in *"Starting the Conversation").* These organizations and others will be invited to further clarify their potential through the *Request to Reader Form*.

There are also likely other organizations who can lead or contribute to these actions and we hope to identify all of these through this process. To this end, we invite you to please complete the accompanying request to the reader form. All forms

received by December 15, 2011 will be considered for the draft action plan which will be developed and circulated shortly thereafter. The results of the consultation will be posted as Appendix to this document once the responses are analyzed.

Finally, on behalf of the steering committee members, Rx&D, ACAHO, and CIHR, we thank you once again for your contribution to this process. Through your leadership and insight, we look forward to reaching the final phase of this project – an action plan for a more competitive clinical trial environment in Canada – with human, health, social, and economic benefits for all.

I. Introduction

On September 15, 2011, close to 130 individuals participated in a conversation on clinical trials. The goal was to develop a multi-sector action plan that could lead us to an improved capacity for attracting clinical trials in Canada.

This document is a summary of the proceedings. However, it is also a synthesis and discussion of the potential strategic, operational, and resource-related implications of what we think we heard. Since this requires some interpretation on the part of the Steering Committee, the paper contains a request to the reader to provide comment on any of the proposed actionables. It also contains the request made on-site for relevant organizations to self-identify if they have the capacity to lead or contribute to any of the actionables within existing resources or with seed funding.

We begin the paper with an overview of the day, an outline of the logic that links what we discussed to our end goals, and describe our progress in the development of a clinical trials action plan based on the feedback we received.

In the second part of the paper, we provide a record of what was discussed in each of the five discussion rooms on the topics that formed the basis of the action plan discussion: (1) streamlining ethics reviews; (2) improving patient recruitment in clinical trials; (3) addressing administrative issues; (4) understanding cost structures; and (5) exploring strategic infrastructure options. Within each of these areas, we present highlights from the substantive presentations and a record of the group's discussion, which includes but is not limited to the summaries of convergence, divergence and recommendations that were presented on site. Most importantly, at the end of each section, we translate the discussion into potential actionables.

At the end of the document, the Steering Committee provides a holistic view of the proceedings, the complete list of actionables proposed, and an invitation to delegates to provide further feedback regarding the nature of the action and any existing potential to achieve them within current resources or with seed funding. We hope you will take the time to read the proceedings and provide us with your feedback. Within a few weeks of receiving your feedback, you will receive a draft of the action plan that will be proposed from this process.

An Overview of Clinical Trial Summit

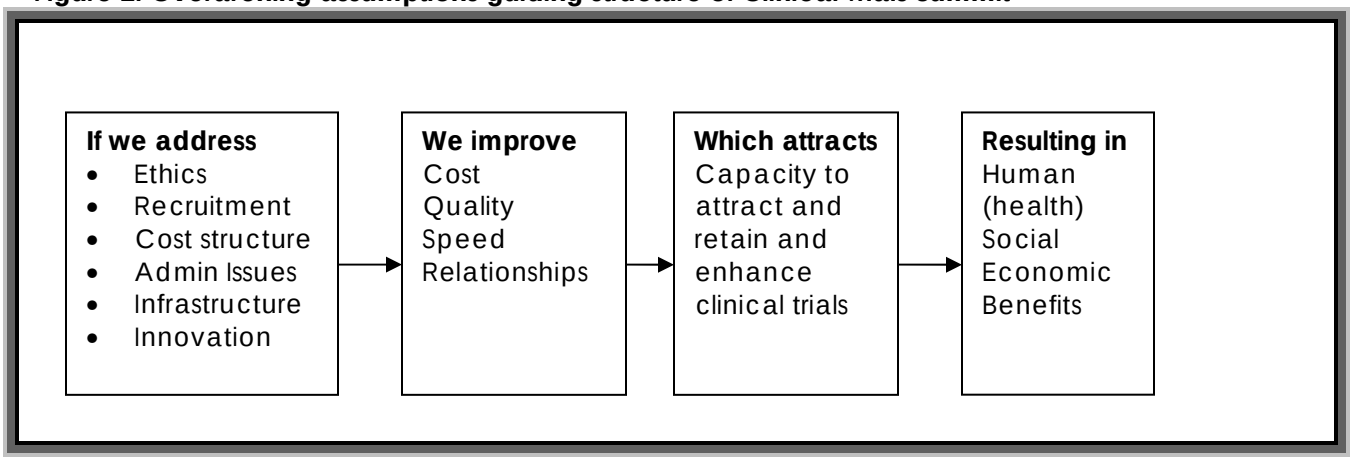
For those unfamiliar with the Clinical Trial Summit 2011, a background document entitled *Starting the Conversation*, summarizes the key problems that the Summit was intended to help address. It contains a review of the common issues, what other countries are doing to address them, what is currently occurring in Canada, and some of the strategic and operational questions that need to be discussed. Keynote presentations that were delivered on-site will also help the reader understand the data, issues, and situational analysis that prompted this Summit. These materials are available on the ACAHO and Rx&D websites.

The summit therefore began with the following "givens" as a baseline for the conversation:

(1) Clinical trials are of value to Canada for human, social, and economic reasons. They are of value to other countries for the same reasons.
(2) Canada is losing clinical trials and clinical trial sites at an alarming rate - and the human, social and economic benefits that go with them;
(3) Other countries are better leveraging their unique strengths to attract trials;
(4) Canada needs to address the cost, quality, speed, and relationship elements if we are to become better performers in clinical trial competition
(5) Canada can address these issues on both a strategic and operational level. By leveraging our strengths from coast-to-coast, we can reclaim our tradition and position of excellence in this area.

At the Clinical Trial Summit, the goal was therefore to spend a day generating potential solutions to the operational barriers and possibilities for an overarching strategic action plan. The overall approach was based on the idea that if we can improve strategic and operational issues related to ethics reviews, patient recruitment, overarching infrastructure, cost structure, and administration, we can improve cost, quality, speed and relationships in clinical trials. These will improve the likelihood of attracting clinical trial opportunities, and ultimately result in more of the human, social and economic benefits that we associate with clinical trials. This logic model is shown in Figure 1.

Figure 1: Overarching assumptions guiding structure of Clinical Trials Summit[1]

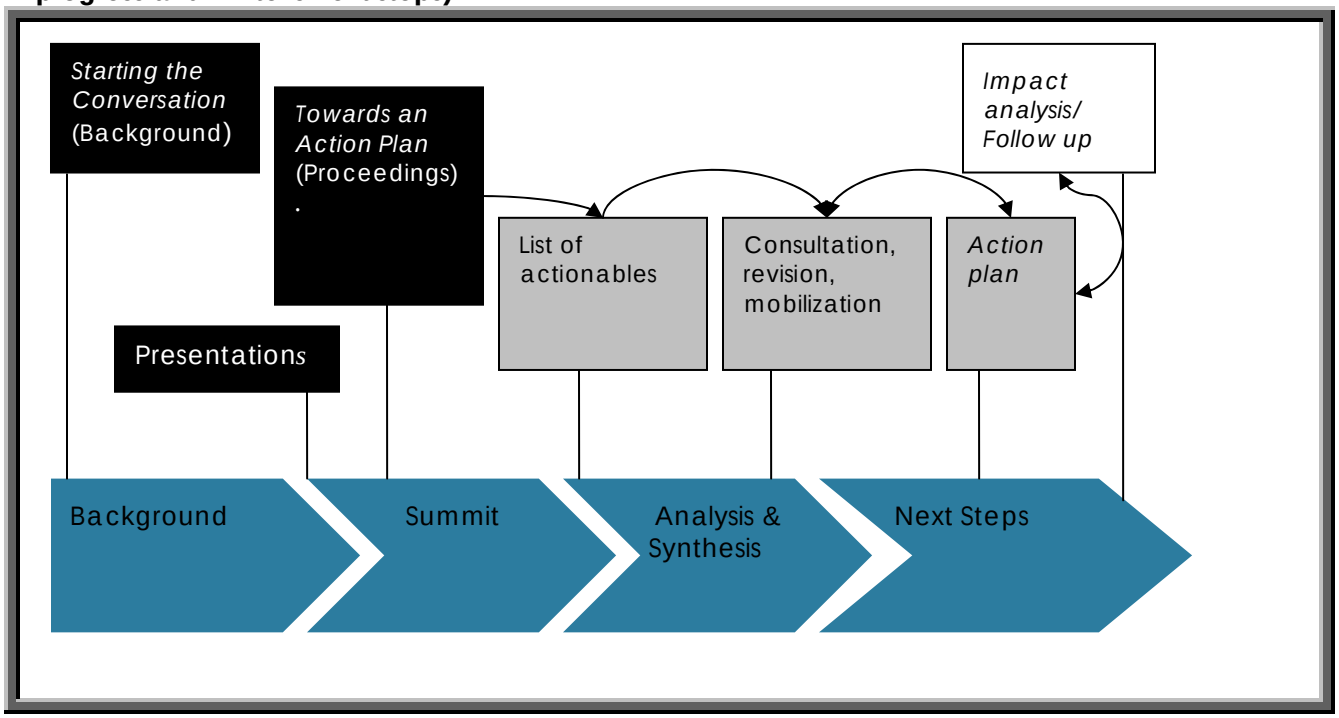


Considering that delegates only had one day together on-site and that an action plan requires knowledge of both "what to do" and "how to do it", the process for going from Clinical Trial Summit to action plan, is an iterative one. Focussed discussion on the five areas was followed by a brief summary of the areas of convergence, divergence and very high level recommendations. In this document, we then present an analysis and synthesis

[1] The structure or idea for this figure was partially adapted from a figure that appears in: Panel on Investment in Health Research, 2009. *Making an Impact: A preferred framework and indicators to measure returns on investment in Health Research*. pp 18. Canadian Academy of Health Sciences, Ottawa, ON, Canada.

of this material into potential actionables. These actionables are now being circulated for validation and input on the mechanisms through which they can be achieved. The process is illustrated in Figure 2.

Figure 2: Overview of the action plan development cycle (black are completed, grey is work in progress and white is next steps).



II. What We Heard...Proceedings & Analysis

This section is a detailed summary of each of the five topics. Each topic consists of highlights from the presentations, a record of discussion, a summary of the areas of convergence, divergence, and recommendations as identified on site, and then a synthesis and analysis of the discussion into potential actionables as proposed by the steering committee.

1. Streamlining Ethics Reviews for Clinical Trials

Can Canada leverage its reputation for ethical standards of practice as it pertains to the safety and protection of clinical trial subjects as a strategic and operational advantage rather than as a barrier to research? This is the question that Linda Barrett-Smith, Director, Research Ethics & Alberta Clinical Research Consortium (ACRC) Initiatives, Alberta Innovates--Health Solutions and Dr. Stanislav Glezer, Vice-President Medical Affairs, Sanofi-Aventis provided in the opening remarks for this discussion. In their presentation, they discussed four issues:

- **National, provincial, regional, and organizational perspectives:** A trade-off occurs between the efficiency of a very broad ethics review and the quantity of multiple smaller ethics reviews. We don't have metrics to ascertain the best

model. Jurisdictional differences across the country make the question more important. Cultural differences, perceptions of competition, and various interpretations of the Tri-Council policy statement at the organizational level also raises the issue of independent review versus an expectation of compliance and reliance on other sites.

- **Resource hurdles:** The resources required to run an ethics review office are underestimated. The voluntary role of research ethics review board member roles accompanied by an incentive structure that doesn't reward research ethics board (REB) service also creates issues. Resources are needed to provide proper training, manage operations, and improve turnaround times.

- **Process efficiency issues:** Issues related to multiple local reviews for multi-centre studies, confusion regarding types of approvals needed, and clearer instructions on how to navigate and sequence through the 'maze' of approvals need to be addressed. They also underscore the need for greater clarity in communications and structure.

- **Multiple potential models:** While we are not aware of data confirming or evaluating these, there appear to be multiple models. Examples include, anticipatory review (informal, agreed mutual sharing of forms and information); dual review (formal agreement for 1st full review and 2nd review for local considerations only); delegated reviews (one review accepted without further review by other REBs); central REB reviews (which would require further consideration on how to represent various organizational perspectives).

1.1 RECORD OF BREAK-OUT GROUP DISCUSSION

What does the perfect system (re REBs) look like from an output perspective?

- Well prepared submissions/proposals
- Predictable turnaround times that are competitive with other countries
- Sufficiently resourced research ethics boards
- Mutual recognition of ethics reviews
- National systems with institution-level responsibility
- Common submission template
- Common consent forms
- Common adverse events reports
- Need for a streamlined system that is predictable
- Common templates with variability minimized
- Recognition of different levels of differences
- A clinical trial system that is appropriately resourced overall
- Compliance with the appropriate standards

What are the barriers?

- Lack of trust and transparency
- Lack of resources especially for education and training

- REBs do more than clinical trials so the entire operation needs to be considered
- Lack of accepted standards and procedures as a baseline
- Too many stakeholders with different cultures
- Metrics for quality improvement and evidence informed decision making
- Jurisdictional and legislative differences (privacy and REBs).

What can be done in the short-term?

- Exchange material across the system (which may encourage standardization)
- Develop national consent template
- Develop common set of criteria for evaluation of REBs and REB models

Summary of convergence, divergence and recommendations

- **Convergence:** Need for a streamlined system with predictable and competitive performance**;** compliance with regulatory / policy requirements**;** respect for national, regional and local differences and concerns**;** appropriate resourcing**.**
- **Divergence:** Lack of clarity on whether centralized vs. local systems are better and whether standards vs. flexibility is more efficient or bureaucratic.
- **Recommendations** (1) Develop dataset for metrics (2) Sharing of materials and common standards (3) Leadership at the national level (4) Resources and incentives (National and Local)

1.2 POTENTIAL ACTIONABLES

How do we improve the cost, quality, speed and relationships necessary to better leverage a safe, effective, and efficient ethics review process, from both the sponsor and the clinical trial site perspective? Both the discussion and the survey of provinces prepared for "Starting the Conversation" shows that each province is making headway in addressing this topic.

In general, variation in approaches, can often signal the opportunity to explore whether there are particular models or parts of models that consistently optimize the outcomes. In this regard, the diversity of models that we currently have creates a natural experiment. However, we currently don't have the metrics to assess these objectively. Having such metrics to assess REB performance would have many strategic and operational benefits.

However, even with this 'black box' on metrics and the relationship between structure and performance, immediate improvements in ethics review cost, quality, speed and relationships could be facilitated through a movement towards common tools, templates, and forms. A national consent template and a national Adverse Events (AE) reporting template were mentioned as immediate opportunities.

Sharing other tools and templates through a common website or portal, would facilitate the development and sharing of best practices. In the short-term, this could create transparency and common ease of access for sponsors. In the longer -

term, viewing the variation could lead towards a discussion and resolution of differences.

While these goals seem within reach, time, focus, analytical, and coordinating capacity is required. It would be essential to leverage the collective expertise of research ethics board staff so that whatever is developed is user-friendly and relevant from both the REB and broader context perspective.

On site, the Canadian Association of Research Ethics Boards (CAREB) indicated that they would be willing to help the co-sponsors and steering committee in leveraging some of these activities. Others are also welcomed to self-identify through the "request to reader" form. The following actionables are proposed in the areas of streamlining ethics reviews.

Table 1: List of actionables proposed for streamlining ethics reviews.

1.1	**Leverage a clearinghouse to share ethics forms and templates:** Clearinghouses are being developed for sharing ethics review templates and materials across the country and can be leveraged (through marketing and use) to share common forms, templates, and tools (for example a tools website is currently being completed by CAREB) .
1.2	**Identify, develop, or review and agree upon a set of research ethics board (REB) metrics:** Metrics for REBs would help inform future discussions on the performance and structure of ethics review boards and would permit future research and decision making on how to optimize the relationship between REB structure and performance across the country.
1.3	**Explore implications of national accreditation and education strategies**: While the idea of national accreditation and REB education may have complexities, organizations like CAREB are exploring these issues in their strategy development processes. These strategies should be reviewed and considered in the context of clinical trial infrastructure in Canada.
1.4	**Adopt a national consent form template:** Facilitate the review, circulation and adoption of a national consent form template that all sites in Canada could use.
1.5	**Develop a national coordinating mechanism for ethics review decision making:** The coordinating body for ethics review issues would ensure that REB plans for clinical trials across the country are (1) integrated with other clinical trial operational considerations; (2) integrated with considerations regarding other non clinical trial REB operations as appropriate; (3) coordinated across the country; (4) that legislative differences are explored/addressed/considered over time; and (5) would explore issues related to harmonized reviews and boards of record in each province.

2. PATIENT RECRUITMENT & RETENTION

Why do patients accept or decline to participate in clinical trials? What are some known solutions for improving the rate of clinical trial patient recruitment? These are the questions that Sandra Gazel, Associate Director Clinical Operations, Abbott

Canada, and Diane Simmons, President & CEO, the *Centre for Information and Study on Clinical Research Participation,* covered in their session. Highlights from their presentation included the following:

What drives poor patient participation in Clinical Trials

(from a study by CanMed in Vancouver Island (Pommerville, Waldner, de Boer, 2011)

Potential reasons at the macro level?

- Perception of good enough access, care;
- Insufficient infrastructure
- Lack of trust and knowledge

Potential reasons from the patient perspective?

- Lack of a guaranteed health benefit
- Likelihood of being in the placebo group
- Participation perceived as inconvenient
- General practitioner or family not supportive

Potential reasons for consent to participation

- Liked or trusted the study coordinator/PI
- Safety and risks were acceptable
- Felt there was a benefit to society
- Enabled better access
- Likely to improve health outcomes
- Free medication

Possible strategies (with potential turn-key solutions) that could be adopted

- Pre-educating study volunteers (reduces screening, better randomization rates and speeds
- Public service campaign (example, medical heroes campaign by sponsors, sites, Food and Drug Administration in the US
- Post-Trial communication (guarantee follow up with volunteers, demonstrate dissemination)
- Grassroots outreach (community, partners, webcasts, workshops, physician speakers)

2.1 RECORD OF BREAK-OUT GROUP DISCUSSION

- **Privacy protection:** The involvement of privacy officers will be helpful in identifying opportunities to discern between practices that truly protect privacy and those that create access to information problems.
- **Awareness building:** The specifics of a trial need to be communicated to patients and physicians in a common, consistent and appropriate way.
- **National registries:** National disease specific registries will help identify patients. We have to find ways to address and go beyond ownership issues.
- **Recognition:** Recognition programs are needed to acknowledge ownership of trials, recognize the contributions of the academic community by involving them up front in protocol development, and enable further collaboration.
- **Collaboration:** Better integration of various players in clinical trial research – academia, healthcare organization, health system, private companies is needed to ultimately reach more patients and providers.

- **Centres of excellence:** Recruitment activities may become more streamlined and efficient if we identify centres excellence in clinical trials for different populations and areas.
- **Personalized medicine:** new fields are difficult to penetrate. There is often a disconnect between the sponsor and physician network and it is unclear who to contact. Quebec, Ontario, and British Columbia have been very successful and provide starting points to build on.
- **Match recruitment efforts with need:** Where is our disease burden highest? Where do we achieve multiple benefits from a focus on clinical trials.

Areas of convergence, divergence and recommendations

- **Convergence:** Need to increase the patient pool; Information management, collaboration, sharing, database access; better understanding of all stakeholder needs as it pertains to enabling the participation of patients in trials.
- **Divergence:** Priority setting on investment in private or public sector: Should pharma be leading awareness and education campaigns
- **Recommendations:** Develop a national strategy for patient recruitment and retention: Creation of a national database linking existing provincial databases: Consider positioning

2.2 POTENTIAL ACTIONABLES

While recruiting patients into a clinical trial can make or break its success for the sponsor, investigator and clinical trial site, ultimately, the decision is one of patient choice. Considering what influences patient choice in other clinical scenarios will likely also be helpful in improving the rates at which Canada recruits and retains patients in clinical trials.

The presentation given by the leads for this discussion showed that information about the existence of a trial, possibility of immediate benefit, likelihood of long term benefit, convenience, level of trust, and even affinity for the clinician and trial site coordinator will influence whether or not a patient chooses to participate in the clinical trial. The questions may become, who is going to find, approach, speak to, and inform these patients and what is the best way to maintain line between what is encouragement as appropriate and voluntary consent. This is where separating the role of the sponsor and principle investigator and a more general approach to engaging and informing the public's interest in and understanding of clinical trials, could be very helpful.

Another potential lever for addressing patient recruitment is a clearer recognition of the linkage between clinical trial participation and modalities of care. When we improve the coordination of research and clinical practice, as well as access to disease information for clinicians and patients, we may also have the opportunity to increase awareness and support for clinical trial participation. In this regard, a population or disease specific approach may also be helpful.

Finally, as in any competitive industry seeking to provide a public benefit and to derive benefit from public engagement, we need to provide an appropriate interface and information for the patient and the public.

Table 2: List of actionables proposed for Patient recruitment & Retention (*denotes actionable is similar to one that appears earlier).

2.1	**Identify centres of excellence/networks for various population groups:** Developing a clearer identification of patient recruitment entities/sites for each population would facilitate recruitment for clinical trials.
2.2	**Create a database of all patient registries:** A common and consolidated 'database of databases' could help to expand and consolidate the available or potential patient pool.
2.3	**Establish a coordinating mechanism for patient recruitment issues:** This coordinating mechanism would: (1) focus on the development of a national strategy for patient recruitment; (2) help to elucidate where population specific issues in recruitment will differ from national issues in recruitment; (3) explore and facilitate the use of existing "turnkey solutions" such as the ones presented on site; (4) potentially provide a public interface for participation in clinical trials

3. ADMINISTRATIVE ASPECTS

What do we need to address when it comes to improving administrative aspects as it pertains to clinical trials? Are the solutions the same from both the sponsor and clinical trial site perspective? These were the questions that Ms. Karen Arts, Director Business Development Clinical Trials, and Dr. Neil Maresky, VP Scientific Affairs, Astra Zeneca Canada used as the basis of the introduction to this discussion. Tables 3 and 4 summarizes parts of their presentation.

Table 3: Administrative aspects that need to be improved

AT THE START UP PHASE
Contract timeliness: implement the mCTA
Ethics review timeliness: implement multi-centre ethics review, provincially
Costs: Standardize across sites and sponsors.
REB submissions: Streamline paperwork and shift to e-submission.
Repetitive document requests: central site information database.
AT THE RECRUITMENT PHASE
Quality and compliance: solid SOPs and quality initiatives.
Performance measures: Standardize performance metrics nationally.
Adverse events (AE) and Serious Adverse Events (SAEs): Adopt CAREB guidance document on SAEs.
Performance measures: Standardize performance metrics nationally
Site training and certification: Standardize GCP training & mentorship.

Table 4: Potential Solutions Proposed by either site, sponsor, or both

POTENTIAL SOLUTIONS	Sites	Sponsors
Develop standard (master) templates	✓	✓
Standardize costs associated with clinical trials	✓	✓
Adopt standard E-training and certification	✓	✓
Develop centres of excellence	✓	✓
Develop national performance metrics with regular reporting		✓
Leverage rapid regulatory authority approval timelines		✓
Focus on recruitment and launch Canadian recruitment initiative	✓	
Streamline & reduce redundancy in feasibility & start up processes	✓	
Create better & more transparent communication opportunities across sponsors & sites	✓	

3.1 RECORD OF BREAK-OUT GROUP DISCUSSION

- **Investigator led clinical trials:** An action plan should consider the proliferation of principle investigator led clinical trials, alongside sponsor led trials.
- **Exploring the role of Health Canada:** Health Canada needs to explore the modernization of the regulatory process (for example, Clinical Trial Information (CTI) forms still need to be faxed); greater clarity on what patient evaluation information is really needed would be helpful; a coordination process could be outlined for when data is accepted from other countries; site auditing and the issue of national standards in other countries should be considered; as well as recruitment numbers when patients are drawn from multiple countries.
- **Generation of a multi-site database for metrics:** It was noted that metrics are difficult to collect because the data resides within individual sites. The Rx&D database initiative demonstrates that national coordination of the data is in fact possible and this could even serve as a leverage point. It does however require ongoing input, coordination, and communication. Data ownership and access would also need to be discussed.
- **Direction, leadership, and authority:** Although the direction is there, we need to consider meaningful execution, coordination, and authority in order to leverage the potential of initiatives that currently exist.
- **Contract Timeliness:** When the model Clinical Trial Agreement (mCTA) pilot is launched, we need to consider the feedback received. Changes requested to the mCTA should be provided with a rationale. Once these changes are identified, assessed and addressed, there may be a need to request a standard of acceptance. Senior leaders in the system from both the sponsor and clinical trial site sides would need to lead this. This item was flagged for national leadership.
- **Ethics/Ethics Review Timeliness:** This was considered an issue that is currently being led in each province for the time-being. The issues of e-submission, consent templates, processes and adverse event reporting are top of mind. It was felt that any tool that could assist in standardizing and streamlining

paperwork should actually be shared with all so that we can work towards commonality. In addition, we need to consider what happens after the ethics review. For example, a common letter of acceptance would be helpful.

- **Coordination across provinces**: In addition to the tools being streamlined provincially, some felt there is the need for an over-arching coordination and potentially reciprocity between the provinces, and accreditation of boards. There should be alignment of provincial, national and international standards.
- **Adverse Events/SAE Reporting:** This was flagged as a global issue that would benefit from bringing together regulatory agenda in the European Union, United States, and Canada. The suggestion here is to have an international summit (led by Canada) to achieve a standard that is coherent for sponsors, sites, and across international boundaries. It was noted the CAREB has done significant work in this area and can serve as a leverage point.
- **Repetitive document requests:** Sites need a system by which they give sponsors documents with all of the questions that may be asked. Sites need to develop these marketing tools to reduce repetitive inquiring. A feasibility assessment tool needs to be developed.
- **Site training and certification**: There is a great deal of material available. The question here is who is able to coordinate agreement. A coordinating mechanism and resources are required.

On site summary of areas of convergence, divergence and recommendations

- **Convergence:** Standards training (Good Clinical Practices (GCPs), Standard Operating Procedures (SOPs) etc.: Create a central site information database**:** Standardize performance metrics, ethics review, scientific review
- **Divergence:** On the approach of Clinical Research Organizations in clinical trial initiatives and some standardized quality training
- **Recommendations:** Leverage Network of Networks (N2) platform to standardize CGP/SOP training; collect & harmonize performance metrics through collaboration**;** standardize consent form, e-submission, information sharing

3.2 POTENTIAL ACTIONABLES

The administrative issues that affect clinical trials include many of the same issues that pertain to improving ethics reviews and patient recruitment. In addition, this group has highlighted the potential use of common training for Good Clinical Practices (GCPs) and Standard Operating Procedures (SOPs). On site, it was noted that the "the Network of Networks (N2)" has prepared training manuals and programs that could be further leveraged.

In addition to having common GCPs and SOPs, the potential of a site certification, as has been achieved in other countries, was noted as a potential mechanism for eliminating variation, recognizing organizations for efforts made in streamlining their processes, and signaling friendly environments for sponsors. Finally, the issue of performance metrics that applies not only to Research Ethics Board performance but also to all clinical trial activity needs to be considered.

Table 5: List of actionables proposed for administrative issues (*denotes actionable is similar to one that appears earlier).

3.1	**Identify, collect and harmonize clinical trial performance metrics:** This would include but not be limited to performance metrics for ethics review boards to enable monitoring, future decision making, and strategic planning.
3.2	**Standardize Training*:** Facilitate the spread of existing training and materials as they pertain to standard operating procedures (SOPs) and good clinical practices (GCPs). N2 has programs that can be leveraged.
3.3	**Develop a clinical trial site certification program:** Explore a proposal for a site certification program that would include the adoption of relevant and common standards, accountability agreements, and appropriate resources.
3.4	**Follow up on Model Clinical Trial Agreement:** The Model Clinical Trial Agreement is currently in pilot phase and the results should be pursued to ensure that the initiative continues to evolve and achieve the required outcomes.
3.5	**Adopt a common Adverse Event reporting template:** Achieve consistency and coordination in AE/SAE reporting by leveraging existing materials and hosting an international summit
3.6	**Strengthen national leadership where appropriate:** Consider the national leadership, support and direction setting structure that will coordinate, fund, and bring existing expertise, initiatives and organizations together towards the common goals that have been discussed.
3.7	**Develop an appropriate Industry interface:** Create an appropriate industry interface that would help to eliminate repetitive document requests by standardizing key information elements, creating a site database that would provide information on clinical trial sites and potentially serve as a problem solving and business planning resource.

4. COST STRUCTURE

What drives up the costs of clinical trials? How much does it cost each of the sponsor and the trial site and what are the impacts? These are the questions that Linda Bennett, Executive Director, Canadian Rheumatology Research Consortium and Dr. Shurjeel Choudhri, Senior Vice President and Head Medical and Scientific Affairs, Bayer Inc., discussed in their introductory remarks. These factors are listed in the tables shown below.

Table 6: An overview of what can affect the costs of clinical trials

Increasing Cost Drivers
Unique procedures per protocol
Total procedures per protocol
Total eligibility criteria
Protocol/trial complexity
Case report form pages per protocol

Number of amendments
Time from protocol ready to last patient visit
CRO involvement
Regulatory compliance burden
Total investigative site work burden (increased by complexity and downloading of work)
Decreasing patient enrollment and retention rates
Enrollment rates for study participants; recruitment targets are not met
Retention rates for study participants
Canadian clinical trial costs/patient higher than G7 average for oncology & cardiology trials
Canadian clinical trial overhead costs highest of G30
Impact on Sites
Decreasing site remuneration rates per protocol (for work required)
Decreasing capacity to offset trial costs with hospital-based or other types of resources
Decreasing number of clinical staff, students, clinicians willing to set up trials infrastructure
Increasing R&D Costs
Sponsors see increasing clinical costs per patient
Decreasing success rates by phase of trial (relative to failure rates)
Increasing mean clinical development times

Figure 3: What Affects the Value for Money Invested in Clinical Trials?

Value of return on clinical trial investment = recruitment targets met + procedural costs + IRB costs + startup costs + efficiency + quality (of data) + speed + complexity + overhead + SR&ED credits + regulatory approval timelines + lost opportunity cost.

Site costs for study start-up = ~$12,000-$15,000 per study (inability to recover the investment due to insufficient budget and capacity to recruit patients decreases site viability)

Sponsor costs to start up one study site = ~$22,000 (if there is poor recruitment, value for investment goes down and site and/or the country won't participate in future development).

4.1 RECORD OF BREAK-OUT DISCUSSION

- **Universal health care system:** The Canadian healthcare system ensures good baseline quality of health care allowing protocols to focus on the specific clinical trial question. In some nations, participation in clinical trials provides healthcare access so this is a very different set of incentive structures for clinical trial activities. Canada's choices must be aligned with its fundamental values and strengths.

- **Nation-wide, coordinated approaches:** Countries such as the UK and Spain have been able to develop national approaches for enhancing the clinical research environment nationally. In Canada, the approach has been fragmented due to disconnected provincial initiatives without any overarching national or federal coordination. Some believe that the focus of competition has been between provinces when it should actually be with the international market.
- **Competitive edge:** How do we compensate for what other countries can simply do more efficiently and how do we build on our own strengths?
- **Global economic issues**: The Canadian dollar is 20-30% stronger than in years past which raises the cost of doing business. There is more competition, but unlike consumer commodity vendors, the pharmaceutical companies cannot simply lower prices.
- **Geographic issues:** Canada's large size, combined with a small population, impacts not only the cost to open a trial site, but the cost of travelling to sites or hire external personnel to do so.
- **Recruitment problems:** Canada is a quality-focused, research-based country, but recruitment reliability is down, which hurts efforts to bring trials here. We must improve not only time to first patient, but also time to the last patient recruited.
- **Volume problem:** Ideally, if Canada were able to deliver a large number of patients at a single site, it would be more cost-effective for all stakeholders. The overall cost to conduct trials in Canada is significantly impacted by the lack of recruitment volume and the lack of consistency in performance.
- **Moving from maintenance to advancement:** Canada has a reputation for having qualified sites that can produce high-quality data, which has helped the country mitigate its trial losses, but not to gain position.
- **Critical mass for streamlined therapeutic Ares:** Therapeutic areas being developed by pharmaceutical companies have been streamlined which also creates unique challenges. For example, it can be difficult to find critical mass for certain cancers.
- **Identifying centres of excellence:** Trials have to be placed where the population is high for the particular trial type; each site's capacity for a given patient population will need to be accurately determined. Canada must at a minimum meet its recruitment targets within the timeline.
- **Market penetration program:** In drug development, time to peak market penetration (vs. time to receipt of marketing approval) matters. Data shows that key opinion leaders and clinical trialists are early adopters of new therapies in the marketplace, presumably due to their trials-related expertise and experience with the product. If there are no trials in a country, the uptake of new therapies and ultimately patient care will be significantly impacted. Formal analyses of the market determine companies' decisions to work in a particular area.
- **Geographic location of disease:** Hepatocellular cancer, for instance, is more prevalent in China and Japan, while there are few patients with it in Canada. Companies are evaluating sites carefully, to ensure they have both the population and the infrastructure to deliver on trial commitments.
- **Alternate revenue sources from clinical trials:** Another way Canada can increase involvement in the development of new therapies might include conducting clinical trials, but also contributing members/expertise to protocol committees etc and to move into evidence development. Canada has

recognized experts in various areas, and can potentially attract research into the country.

- **Costs that can be manipulated:** Looking at the equation presented earlier (see above), it was acknowledged that Canada cannot compete successfully in the area of procedures or Institutional Review Board costs.
- **Study administrative activities:** contract negotiation time, if decreased, would reduce legal expenses and financial costs incurred due to delays in start-up (expect the new model Clinical Trial Agreement (mCTA) to save both time and money as would harmonized IRB approval). The move to outsourcing global clinical trials to contract research organizations (CROs) has added a 3rd party to the clinical research environment. Often this leads to inefficiency, duplication of efforts and substantial delay.
- **Impact of administrative improvements:** Efforts to remedy these challenges will save time and money and enhance the likelihood of trial execution success in at least two ways: 1) the shorter the study start-up process, the longer the site has to recruit patients to a clinical trial and 2) the more efficiently and tightly a trial is managed the more time/resources the site has to focus on identifying patients for trials (less time/resources wasted).
- **Overhead costs:** Overhead could be reduced where possible, although further exploration would need to given to identify where and how.
- **Scientific Research & Experimental Development (SR&ED) sponsor perspectives:** SR&ED credits were thought valuable to clinical trials. However, the revenues come in a year after a trial ends which ends up back in central operational budgets. As such, for the sponsor, they are not applied to the research cost centres. As a consequence, the savings are often missed when "cost of research" is considered. The documentation is also complex.
- **SR&ED perspectives including clinical trial sites:** Incorporated trial sites can also claim SR&ED tax credits and their rate of return is higher than what pharmaceutical companies receive. This is applied as a tax refund which can help some sites maintain financial viability in the context of the above-noted challenges (without the SR&ED, the sites would have closed). It is therefore important to have clinical sites well represented in discussions regarding improvements in SR&ED tax credit program.
- **Patent protection:** A question was raised whether it would be better to work to get one more year of patent protection to compensate for the time needed for drug development, rather than focus on the SR&ED. Procedure costs might also be harmonized across the country, which would make it possible to predict costs.
- **Cost versus competitive advantage:** There was a perspective offered that perhaps "cost" is a 'red herring'. Rather than focus solely on cost reduction, the issue may be - what are Canada's strengths and where does Canada want to compete?'. Is there a niche that Canada could dominate? Would this position the country as one that delivers value for money invested?
- **Impact of incremental gains:** It was noted that individually incremental costs are of little value, but collectively they do matter. There is a need to define "incremental value," and the incremental cost-effectiveness ratio must be studied in a specifically defined area.

On site summary of areas of convergence, divergence and recommendations

- **Convergence:** It remains important to bring clinical trial activity to Canada**:** consider the dollar cost/patient and the overall value of the data produced**:** enhance quality, efficiency and delivery on recruitment commitments
- **Divergence:** value of SR&ED credits to attract clinical trials into Canada **;** overhead costs and how to reduce them
- **Recommendations:** Achieve transparency in how clinical trial costs are justified; create site certification programs for non-study-specific training (GCP training, etc); concentrate on areas of strength while building strength in new areas

4.2 POTENTIAL ACTIONABLES

The main themes in the cost discussion overlap the ethics review, patient recruitment, and administrative issues discussion and also address broader and overarching issues. Improvements in standardization, start up times, recruitment and research ethics board (REB) efficiency will assist with costs. Developing a cost template will help to achieve transparency and better track the overhead costs. Centres of excellence will allow for volume and standardization opportunities. At a policy level, patent protection issues and the SR&ED program administration - especially in light of the recent Federal Review of R&D programming - may be opportunities for further exploration.

Table 7: Potential actionables related to cost issues

4.1	**Explore further patent protection and SR&ED tax credit improvements:** Explore the cost implications of additional years of patent protection (data protection and/or Patent Term Restoration) and potential improvements in SR&ED tax credit administration.
4.2	**Identify centres of excellence for patient recruitment:** Create clusters of sites willing to recruit patients in particular patient groups for trials.
4.3	**Advance model Clinical Trial Agreement (mCTA):** Follow up on the pilot of the mCTA to ensure that the initiative continues to advance towards its goals.
4.4	**Engage in more CT related efficiency initiatives:** Reduce costs by leveraging the process used to develop the mCTA in order to also: enhance efficiency in other areas, including (but not limited to): REB streamlining; GCP training; trial management inefficient either due to clinical research organizations (CRO) approaches or due to lack of harmonization.
4.5	**Develop a costing template:** Develop a costing template to help achieve transparency in the costs of clinical trials.

5. STRATEGIC INFRASTRUCTURE

What do we mean by strategic infrastructure? In the introductory remarks by Dr. Jean Marie Leclerc (Vice President of Research, Novartis) and Dr. Robert McMaster (Executive Director, Research, Vancouver Coastal Health Authority), Drs. Leclerc and McMaster take us on a tour of what is happening around the world in terms of

overarching clinical trial infrastructure. Models that they discussed included those from the United Kingdom, Central and Eastern Europe; the United States; Spain and Argentina. The following are highlights of clinical trial infrastructure components.

- Clinical Trial Site Registration; Certification; Accreditation, i.e., ISO or other certificate of Registration & site Management (e.g. National Institutes of Health GCRC; UKCRC registered clinical trial unit).
- Clinical Trials/Research Networks (e.g. United Kingdom Clinical Research Consortium; European Clinical Research Infrastructure Network; Irish Clinical Research Infrastructure Network; Queensland QCTN; possibly CIHR's Strategy for Patient Oriented Research).
- Quality Systems and Assurance: (e.g. common data & information management)
- Data Centres with quality compliance
- Professional Development: Personnel training & certification (e.g. Good Clinical Practice (GCP) certification)
- Primary Care Research Networks: Local, Provincial & National
- Selecting key areas and branding for excellence
- Electronic submissions and databases
- Funding and accountability mechanisms

5.1 RECORD OF DISCUSSION

1. **Importance of infrastructure:** We need to acknowledge the fact that infrastructure for clinical trials does make a difference in achieving successful outcomes. An example is seen in Ontario where the impact of adding or removing infrastructure was measurable.
2. **Infrastructure components & scoping questions:** We need to be clear on what we mean by infrastructure – for example part of it may include, people - coordinators, support, expertise, and time, especially for clinicians
3. **Importance of not low-balling the cost:** If we low ball the cost and succeed in getting funds which are simply not sufficient, we will disillusion funders and get further behind. It's important that the Strategy for Patient Oriented Research (SPOR) is recognized as part of the solution, but not the entire solution as it has a significant funding limitation. We may need more funding and/or cobbled funding from multiple sources to meet the target of effective infrastructure.
4. **Disease and population specific focus:** While there are common elements to infrastructure across population groups, there are also benefits to maintaining disease specific foci rather than trying a blanket approach for everything.
5. **Certification of institutions**: We need to tie funding for institutional infrastructure to accountability for performance in the area of clinical trials. A successful model already exists from the United States Cancer Centres.
6. **Continuous professional development**: Continuous professional development can build on available resources, as an example, the Network of Networks (N2)

provides some centralized training modules which are endorsed by some companies.

7. **Collaborative workspace:** Since problem solving on the same issues is occurring across the country, a collaborative workspace could allow for information and tool sharing across the country. It could also allow for a needs assessment of what is needed against what is available.
8. **Scoping questions that need to be determined:** We need to answer some scoping questions - what is the infrastructure going to be for? What is the primary purpose? What are we going to measure? Do we focus by phase of clinical trial?
9. **Patient and industry dimensions of infrastructure:** The infrastructure that we choose has to be as patient-oriented as it is pharma company-oriented. (i.e. overall, at individual institutions, by study, for investigator training, GCPs, ethics training etc).
10. **Strategic and operational integration of research and clinical care**: The separation of research and clinical care is a forced separation and needs to be better reconciled. Research is often part of clinical care and vice versa. The question is "how" do we reconcile these? For example, if every province invested 2% of its healthcare budget in CTs the problem would the problem be solved? The way to convince the Provincial government is by cost-benefit. Pragmatic trials and following of costs and savings. "why" outcomes are better where care and research are integrated.
11. **Bold vision:** Balance the tension of what happens if there isn't enough funds – against the benefits that could accrue if we did have them . For example, how do we achieve a bold vision – should a % of health budgets be reinvested in CTs? If we agreed - what would we do with that funding? (ex. UK did this- UK has national health system – Canada has Ministry's of Health)
12. **Health Accord renegotiation:** Health accord renegotiations could become an opportunity to push the concept that better research and patient care occurs when the research and care dimensions are better aligned.
13. **Leveraging both federal & jurisdictional interests:** Recognize that different levels of Government will look for different outputs, outcomes and rationales. While all arguments may be correct, we need both provincial and federal support so the value propositions relevant to each need to be clear and appropriately framed.
14. **Culture and vision shift:** We need the metrics, language, will, and effort to communicate the linkage to jobs, waste, care, outputs, revenues, etc. We need to recognize that this Government believes in autonomy of the provinces – so this may not be the best or only strategy. The question is who is in the best position to help the clinical trial industry and what language and metrics do they need to help justify and shepherd the needs of this group through the policy channels.
15. **Business model intelligence:** Business model intelligence really needs to be considered so we don't make error of investing without potential to see benefit.

16. **The problem of underfunding:** The dollars currently on the table is not enough. (for example in UK 200 million pounds). The question is what level of infrastructure will make a measureable difference – for example in SPOR – at what point of funding can you expect to see measurable results?
17. **Multi-stakeholder approach:** Opportunity to create a big vision of which SPOR could be a part – SPOR may be the Networking portion. Create networks of diseases. Leverage multiple resources towards the same goals.
18. **Interprovincial and national collaboration:** Especially for inter province clinical trial activity, collaborative agreements will be needed to expedite and increase activity (for example, harmonized ethics, contracts, and intellectual property agreements).

Summary of areas of convergence, divergence and recommendations

- **Convergence:** Effective delivery of care requires seamless integration with research: Adequate and sustainable infrastructure to support Networks**:** Tailor different approaches for different therapeutic areas with centralizing function. Common to all (i.e. certification).
- **Divergence:** Where to start – should we be leading test examples? **;**Is patient education a place to start?; Should there be dedicated centres/networks for each area?
- **Recommendations:** Reinvest 2% of healthcare spending into applied health research and infrastructure for patient outcomes and evaluation **;** Build a broad coalition of clinical trial stakeholders**;** Identify strategic foci and priorities for initial infrastructure (study required)

5.2 POTENTIAL ACTIONABLES

In a sense, strategic infrastructure is the mechanism through which we can ensure that operational improvements in research ethics, patient recruitment, administrative structures, and costs, link the strategic goal of attracting more of the human, social and economic benefits of clinical trials to Canada.

It recognizes that we can make incremental improvements in operational structures, but that these hold a much higher potential when they are coordinated and leveraged off of each other. They also need to be considered in the context of the broader policy health and economic landscape – and in relation to what is happening nationally and globally. Our progress on issues also needs to be monitored, measured, marketed and hopefully celebrated.

For this section, it is important to note that the discussion ensued independently of and prior to the report backs from the more operational discussion groups. However, it is clear that general themes remain consistent and overlap. In addition, given the nature of this conversation, the actionables are at a higher level of implementation and at a somewhat larger scale.

Table 8: Potential actionables related to the area of strategic infrastructure

5.1	**Scope strategic infrastructure needs & develop business models:** Study the scoping requirements for strategic infrastructure and develop the accompanying business models.
5.2	**Develop the appropriate value propositions to engage policy leaders:** Provincial and federal governments and their representatives may both be interested in clinical trials, but they are not necessarily interested in the same dimensions or rationale. The community needs to be able to articulate both the economic and health benefits, as appropriate, otherwise staff can not mobilize solutions through the appropriate channels.
5.3	**Build and maintain the broadest coalition of clinical trial stakeholders:** Ensure that patients, populations, existing networks, existing volunteer groups, policy makers, clinical trial sites, and all relevant stakeholders have a forum through which to develop a shared voice, identify and discuss issues and solutions.
5.4	**Ensure multiple funder coordination:** Considering the magnitude of funding needed, continue to leverage and coordinate the funding from multiple sources and funders (example SPOR plus others).
5.5	**Favour a balance of population-specific and common elements nationally:** Recognizing that not all trials are one size fits all, make sure that due consideration is given to population specific needs.
5.6	**Identify or establish areas of excellence:** Study the clinical trial landscape in further detail to identify areas of excellence and strategic foci.
5.7	**Develop a site certification program:** Consider a site certification program proposal that would bring standardization, accountability and resources to organizations undertaking clinical trial activity. Recognize that many standards are already developed.
5.8	**Espouse a bold vision for the integration of research and patient care:** In this group, a recommendation was made to reinvest 2% of health spending into research to help close the gap between these inextricably related areas.
5.9	**Standardization and sharing of best practices*:** Support and encourage a collaborative workspace, standardization, and sharing of best practices.

III. Towards an Action Plan...Actionables & Implications

In an editorial prepared for Canada's Top Innovation Leaders 2011, one steering committee member and a summit participant noted the following as their preliminary reflections on the Clinical Trials Summit:

(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.

Source: 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.

Indeed, these reflections appear to hold when we look at the areas of convergence, divergence and recommendations from each break out room discussion. A collation is shown in Table 6.

What were the recommendations? The recommendations from the break out group discussion were listed throughout the proceedings and summarized. They range from operational issues to paradigm shifts. Considering their breadth and the context in which they were proposed, we have translated the recommendations and other information to into the actionables listed throughout the proceedings summarized in Table 9.

What were the areas of convergence? These are summarized thematically as follows (1) leveraging quick wins as they pertain to sharing and adopting existing tools, templates, standards (2) sharing information through common databases or clearinghouses (3) identifying centres of excellence (4) exploring certification and standardization potential for common elements (5) improving the interface with the public and with industry (6) coordinating longer term issues and linkages between strategically linked issues (7) respecting national, provincial and regional differences.

What were the areas of divergence? The areas of divergence included the following (1) what is the effect and impact of Clinical Research Organizations (CROs)?; (2) Is centralization or standardization the better option when it comes to achieving effectiveness and efficiency?; (3) At what point does standardization for efficiency become bureaucracy at cross-purposes to efficiency?; (3) What is the best starting point for a national strategy?; (4) What strategies will reduce overhead costs?; (5) What is the optimal structure for supporting all clinical trial related activities? In some cases, areas of divergence reflected uncertainty rather than polarized opinions.

Table 9: Collation of on site report back summaries.

	Convergence	Divergence	Recommendations
1. Ethics	**Streamlined**, clear, predictable ethics review system with predictable and competitive performance; **Compliance** with regulatory/ policy requirements; **Respect** differences at the national, provincial, regional and organizational levels; **Appropriately resourced**	Centralized vs. local systems Standards vs. bureaucracy	**National Dataset:** Develop dataset for metrics **Information Sharing:** Sharing of materials and common standards **National Leadership:** Leadership at the national level **Resources and incentives** (National and Local)
2. Patient Recruitment	**Patient pool** Need to increase the patient pool; **Information**: management, collaboration, sharing, database access, **Needs assessment:** Better understanding of all stakeholder needs	**Priority setting** on investments & sources **Responsibility:** who should lead awareness and education campaigns	**National Strategy:** Develop a national strategy for patient recruitment and retention **National Database:** Creation of a national database linking existing provincial databases
3. Administrative issues	**Standards training** (GCP, SOP etc). **Information sharing:** Create a central site information database **Performance Metrics:** Standardize performance metrics, ethics review, scientific review	**Role of CROs:** in clinical trial initiatives and in standardizing quality training	**Standardization:** Leverage N2 platforms to standardize GCP and SOP training consent form, e-submission, information sharing **Performance Metrics**: Collect & harmonize performance metrics through collaboration
4. Costs	**Value of clinical trials:** It remains important to continue to bring clinical trial activity to Canada; **Multiple cost factors:** Consider the dollar cost/patient and the overall value of the data produced; **Enhance quality and efficiency** and delivery on recruitment commitments	**Value of SR&ED credits** to attract clinical trials into Canada. **Overhead costs** and how to reduce them	**Clinical trial costing & efficiencies:** Achieve transparency in how clinical trial costs are justified and achieve efficiency in these areas. **Certification programs:** Create certification programs for non-study-specific training (GCP training, etc) **Concentrate on areas of strength** while building strength in new areas

	Convergence	Divergence	Recommendations
5. Strategic infrastructure	**Paradigm & policy shift:** Effective delivery of health care requires seamless integration with research. Economic benefit requires consideration of health. **Adequate and sustainable infrastructure** to support Networks **Disease specific approaches:** centralizing function for common elements (i.e. certification).	**Where to start**: should we be leading test examples? Is patient education a place to start? **Optimal structure:** Should there be dedicated centres/networks for each area?	**Policy shift:** Reinvest 2% of provincial healthcare budgets into applied health research and infrastructure for patient outcomes and evaluation **National coalition:** Build a broad coalition of clinical trial stakeholders **Needs assessment:** Identify strategic foci and priorities for initial infrastructure (undertake study)

PROPOSED ACTIONABLES FOR AN ACTION PLAN

Throughout the analysis and synthesis of the proceedings, we identified 28 potential actions that could correspond to the key issues surfacing from the discussion on each of the five topics. In the request to the reader, you will have the opportunity to comment on whether or not you agree with these proposed actionables. A summary of the actionables by discussion theme is collated in Table 10.

Table 10: Summary of actionables from each of the five thematic discussion groups

Ethics Reviews
1.1 Leverage a clearinghouse to share ethics forms and templates: Clearinghouses are being developed for sharing ethics review templates and materials across the country and can be leveraged (through marketing and use) to share common forms, templates, and tools (for example a tools website is currently being completed by CAREB) .
1.2 Identify, develop, or review and agree upon a set of research ethics board (REB) metrics: Metrics for REBs would help inform future discussions on the performance and structure of ethics review boards and would permit future research and decision making on how to optimize the relationship between REB structure and performance across the country.
1.3 Explore implications of national accreditation and education strategies: While the idea of national accreditation and REB education may have complexities, organizations like CAREB are exploring these issues in their strategy development processes. These strategies should be reviewed and considered in the context of clinical trial infrastructure in Canada.
1.4 Adopt a national consent form template: Facilitate the review, circulation and adoption of a national consent form template that all sites in Canada could use.
1.5 Develop a national coordinating mechanism for ethics review decision making: The coordinating body for ethics review issues would ensure that REB plans for clinical trials across the country are (1) integrated with other clinical trial operational considerations; (2) integrated with considerations regarding other non clinical trial REB operations as appropriate; (3) coordinated across the country; (4) that legislative differences are explored/ addressed/considered over time; and (5) would explore issues related to harmonized reviews and boards of record in each province.
2. Patient Recruitment
2.1 Identify centres of excellence/networks for various population groups: Developing a clearer identification of patient recruitment entities/sites for each population would facilitate recruitment

for clinical trials.
2.2 Create a database of all patient registries: common and consolidated 'database of databases' could help to expand and consolidate the available or potential patient pool.
2.3 Establish a coordinating mechanism for patient recruitment issues: This coordinating mechanism would: (1) focus on the development of a national strategy for patient recruitment; (2) help to elucidate where population specific issues in recruitment will differ from national issues in recruitment; (3) explore and facilitate the use of existing "turnkey solutions" such as the ones presented on site; (4) potentially provide a public interface for clinical trials
3. Administrative Structures
3.1 Identify, collect and harmonize clinical trial performance metrics: This would include but not be limited to performance metrics for ethics review boards to enable monitoring, future decision making, and strategic planning.
3.2 Standardize Training*: Facilitate the spread of existing training and materials as they pertain to standard operating procedures (SOPs) and good clinical practices (GCPs). N2 has programs that can be leveraged.
3.3 Develop a clinical trial site certification program: Explore a proposal for a site certification program that would include the adoption of relevant and common standards, accountability agreements, and appropriate resources.
3.4 Follow up on Model Clinical Trial Agreement: The Model Clinical Trial Agreement is currently in pilot phase and the results should be pursued to ensure that the initiative continues to evolve and achieve the required outcomes.
3.5 Adopt a common Adverse Event (AE)/Serious Adverse Event (SAE) reporting template: Achieve consistency and coordination in AE/SAE reporting by leveraging existing materials and hosting an international summit
3.6 Strengthen national leadership where appropriate: Consider the national leadership, support and direction setting structure that will coordinate, fund, and bring existing expertise, initiatives and organizations together towards the common goals that have been discussed.
3.7 Develop an appropriate Industry interface: Create an appropriate industry interface that would help to eliminate repetitive document requests by standardizing key information elements, creating a site database that would provide information on clinical trial sites and potentially serve as a problem solving and business planning resource.
4. Cost Issues
4.1 Explore further patent protection and SR&ED tax credit improvements: Explore the cost implications of additional years of patent protection (data protection and/or Patent Term Restoration) and potential improvements in SR&ED tax credit administration.
4.2 Identify centres of excellence for patient recruitment: Create clusters of sites willing to recruit patients in particular patient groups for trials.
4.3 Advance model Clinical Trial Agreement (mCTA): Follow up on the pilot of the mCTA to ensure that the initiative continues to advance towards its goals.
4.4 Engage in more CT related efficiency initiatives: Reduce costs by leveraging the process used to develop the mCTA in order to also: enhance efficiency in other areas, including (but not limited to): REB streamlining; Good Clinical Practices (GCP) training; trial management inefficient either due to clinical research organizations (CRO) approaches or lack of harmonization.
4.5 Develop a costing template: Develop a costing template to help achieve transparency in the costs of clinical trials.
5. Strategic Infrastructure
5.1 Scope strategic infrastructure needs & develop business models: Study the scoping requirements for strategic infrastructure and develop the accompanying business models.
5.2 Develop the appropriate value propositions to engage policy leaders: Provincial and federal governments and their representatives may both be interested in clinical trials, but they are not

necessarily interested in the same dimensions or rationale. The community needs to be able to articulate both the economic and health benefits, as appropriate, otherwise staff can not mobilize solutions through the appropriate channels.
5.3 Build and maintain the broadest coalition of clinical trial stakeholders: Ensure that patients, populations, existing networks, existing volunteer groups, policy makers, clinical trial sites, and all relevant stakeholders have a forum through which to develop a shared voice, identify and discuss issues and solutions.
5.4 Ensure multiple funder coordination: Considering the magnitude of funding needed, continue to leverage and coordinate the funding from multiple sources and funders (example Strategy for Patient Oriented Research (SPOR) plus others.
5.5 Favour a balance of population-specific and common elements nationally: Recognizing that not all trials are one-size-fits-all, ensure that due consideration is given to population-specific needs.
5.6 Identify or establish areas of excellence: Study the clinical trial landscape in further detail to identify areas of excellence and strategic foci.
5.7 Develop a site certification program: Consider a site certification program proposal that would bring standardization, accountability and resources to organizations undertaking clinical trial activity. Recognize that many standards are already developed.
5.8 Espouse a bold vision for the integration of research and patient care: In this discussion group, a recommendation was made to reinvest 2% of health spending into research to help close the gap between these inextricably related areas.
5.9 Improve standardization and sharing of best practices*: Support and encourage collaborative workspaces, standardization, and best practices.

UNDERSTANDING THE PROPOSED ACTIONABLES FOR AN ACTION PLAN

There are many actionables proposed in Table 10. In part, these will require prioritization, however, in many cases the actionable will solve different problems. In addition, the actionables relate to a few common activity types. These include sharing tools and information, developing metrics, adopting standards, coordinating the activities of multiple stakeholders, developing a site certification program, identifying centres of excellence, and engaging strategic, business, and policy planning for clinical trial activities and decisions. Table 11 shows which actionables might pertain to each of these types of activities. This type of assessment may be useful when we come back to the question of "how".

Table 11: Summary of actionables by activity type

Sharing Tools & Information
1.1 Leverage a clearinghouse to share ethics forms and templates
1.4 Adopt a national consent form template
2.2 Create a database of all patient registries
3.2 Standardize Training for SOPs & CGPs
3.5 Adopt a common Adverse Event (AE)/Serious AE (SAE) reporting template
4.5 Develop a costing template
5.9 Improve standardization and sharing of best practices
Developing metrics

1.2 Identify, develop, or review an agree upon a set of REB metrics
3.1 Identify, collect and harmonize clinical trial performance metrics
4.5 Develop a costing template
Adopting standards
1.4 Adopt a national consent form template
3.2 Standardize Training for GCPs and SOPs
3.5 Adopt a common Adverse Event (AE)/Serious AE reporting template
3.3 Develop a clinical trial site certification program
3.4 Follow up on Model Clinical Trial Agreement
4.3 Advance model Clinical Trial Agreement (mCTA)
4.4 Engage in more CT related efficiency initiatives
5.9 Improve standardization and sharing of best practices*
Coordination of multiple stakeholder activities
1.3 Explore implications of national accreditation and education strategies
1.5 Develop a national mechanism for ethics review structure decision making
2.3 Establish a coordinating mechanism for patient recruitment issues
3.4 Follow up on Model Clinical Trial Agreement
3.6 Strengthen national leadership where appropriate
3.7 Develop an appropriate Industry interface
Site certification programs
3.2 Standardize Training
3.3 Develop a clinical trial site certification program
5.7 Develop a site certification program
Centres of Excellence
2.1 Identify centres of excellence/networks for various population groups
3.2 Standardize Training
3.3 Develop a clinical trial site certification program
4.2 Identify centres of excellence for patient recruitment
5.6 Identify or establish areas of excellence
Business & policy planning
4.1 Explore further patent protection and SR&ED tax credit improvements
5.1 Scope strategic infrastructure needs & develop business models
5.2 Develop the appropriate value propositions to engage policy leaders
5.3 Build and maintain the broadest coalition of clinical trial stakeholders
5.4 Ensure multiple funder coordination
5.5 Favour a balance of population-specific and common elements nationally
5.6 Identify or establish areas of excellence
5.8 Espouse a bold vision for the integration of research and patient care
5.9 Improve standardization and sharing of best practices

MOVING FROM "WHAT" TO "HOW"

Now that we have identified and rationalized "what" the actionables might be, we would like to turn the focus of the discussion to the question "how" we might implement them. On-site, a number of organizations were identified as having the potential tools, resources, will and expertise to leverage some of the deliverables. These included ACCT Canada, the Network of Networks (N2), Canadian Association of Research Ethics Boards (CAREB), CIHR, ACAHO, and Rx&D (co-sponsors), and needless to say all of the provincial clinical trial coordinating bodies by virtue of their mandates (see examples in *"Starting the Conversation").*

Many of these organizations and others will likely further discuss their potential through the attached request to reader form. However, there are also some other important and complex questions to be answered, these may relate to:

(1) How to coordinate and resource activities that require multiple players?
(2) How do we prioritize, coordinate, and leverage activities across the country?
(3) What about activities that require difficult decisions or further study?
(4) Is an overarching clinical trial body needed in Canada to coordinate activities?

These are important questions that will be considered in the action plan. In the final section of this document, we will describe next steps.

IV. Next Steps & Concluding Remarks

You have now read a comprehensive document that helps to summarize not only the proceedings, but also the logic that we have followed in developing potential actionables that would form part of the action plan.

To move to the last phase of this three-part process, we would like to know what you think of the actionables and identify potential resources, before we populate the action plan. We would also like to invite open comments on some of the broader issues as identified above. To this end, we invite you to please complete the request to the reader form that accompanies this document. All forms received by December 15, 2011 will be considered in the action plan which will be developed and circulated shortly thereafter. The results from these request to reader forms will be available in Appendix A to this report once they are collated.

Finally, on behalf of the steering committee members, Rx&D, ACAHO, and CIHR, we thank you once again for your contribution to this process. Through your leadership and insight, we look forward to reaching the final phase of this project – an action plan for a more competitive clinical trial environment in Canada – with human, social, and economic benefits for all.

Appendix A
Summary from "Request to the Reader" and additional consultations on proceedings

Given that the Clinical Trial Summit was only a day long and that our goal is an action plan that is implementable, we summarized and interpreted the proceedings into the "actionables" that are summarized throughout this document. These actionables were not necessarily stated explicitly at the summit. Considering the interpretation required, we wanted to know if there were resulting errors or omissions in the actionables. We also wanted to know where opportunities for accomplishing them existed. As such, we asked delegates to provide feedback, either using 'the request to reader form' or through in person, phone or group consultation. Common themes are summarized here.

- **Focus & prioritization:** With the exception of comments expressing concern about the value of enforcement, centres of excellence, and the inclusion of a 2% figure in describing a bold vision for research funding, most of the actionables appeared to be reasonable interpretations of the discussion. It was noted however that the number of actionables proposed would need to be streamlined, focussed and prioritized in order to be effective.

- **Accountability, coordination and implementation:** The need for an accountability and implementation structure and resources for any ensuring action plan was also a common theme. It was noted that we should not purposefully aim at creating new structures, but leverage existing ones to the extent possible. The ACAHO VPRs and Rx&D, as well as some staff in government departments, felt that CIHR's Strategy for Patient Oriented Research might be a logical place to begin such consideration. In addition it was noted that we have many initiatives that need to be leveraged and coordinated and any implementation body, should also be able to assist with this.

- **Leveraging federally funded REB improvement opportunities:** In at least one consultation with a key stakeholder group, the suggestion was made to consider the work of the existing federally funded initiatives related to ethics reviews, especially if work completed could be leveraged as a baseline for future learning.

- **Ethics application and consent forms:** It was noted that a common ethics review application template appears in the proceedings, but is not noted as a proposed actionable. A number of groups identified ongoing or completed work in these areas that could be leveraged. These groups were noted. Special consideration also needs to be given to well established networks and consortia so that infrastructure investments are leveraged in national standardization efforts.

- **National coordination capacity:** Comment was provided about the funding each province was already investing provincially in accreditation type considerations. The

need and opportunity for national coordination was highlighted. It was noted that it would be essential to ensure that the right individuals and organizations are involved.

- **Representation at the summit:** It was noted that the summit had excellent representation from across the ACAHO and Rx&D groups but that it still had under-representation of various other groups, for example, clinical research organizations, the private research sector, and investigator led trials. These sectors are of growing importance. It will be important to consider these groups going forward.

- **Patient recruitment & registries:** Various groups noted that they were doing ongoing work in patient recruitment strategies. Patient registries were noted as extremely important but also potentially very complex. When done properly they provide the opportunity for consent to contact patients and assess patient eligibility. However, they also have privacy, confidentiality, linkage and ownership issues. A number of existing registries were identified. The capacity to leverage other recruitment strategies should also be considered.

- **Metrics:** A few respondents expressed concern that the entire discussion on ethics reviews seemed to suggest that REBs are too slow. However, this is difficult to ascertain without metrics. Clarification was sought as to whether the issue is it the performance of an individual REB or the consequence of multiple REBs performing well, but differently, causing complication and cost. In addition, existing reports (CCRA) on metrics related to cancer trials was highlighted.

- **Site certification and standard operating procedures:** Comments were received regarding the Network of Networks (N2) standard operating procedures and training modules. A number of organizations are also looking at accreditation and certification standards for various population groups.

- **Centres of excellence:** Some comments were received about the benefit of identifying centres of excellence in the context of clinical areas and recruitment. Some population groups are looking at this, however, it was felt that these would be complex to identify and agree upon more broadly. It was felt that they would not necessarily result in increased recruitment.

- **SR&ED:** It was noted that extensive work have been done on SR&ED issues and that these should be leveraged rather than to repeat the analysis and recommendations.

- **Vision and infrastructure:** It was noted that the issue of coordination and support for the integration of health and research is more than issue of cash infusions. It is also an issue of salary, support, and infrastructure. Existing work in cancer was highlighted and that there were many other coordination opportunities that should be considered on a longer term basis.

In conclusion, the consultations on these proceedings provided a general level of comfort with the actionables and identified a large number of opportunities for implementing them. These will be further discussed in the action plan which will form the final document in this trilogy.