

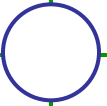
Network of Networks (N2)



# Initiative to Streamline Clinical Trials (ISCT)

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Chair Board N2

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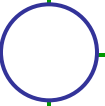
## CCRA Four Recommendations

Create a Pan-Canadian Infrastructure Program that Supports Cancer Clinical Trials

Streamline Clinical Regulatory Environment.

Consolidate or Develop Reciprocity in Research Ethics Boards

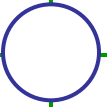
Reduce non-Value Added Steps in Trial Development and Conduct



## Recommendation #2

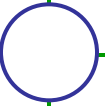
### **Streamline Clinical Regulatory Environment.**

Engage with Health Canada and other key stakeholders to propose non-legislative changes to the Food & Drug Regulations, that will improve efficiency of clinical trials, ensuring safety while reducing work and costs.



## Rationale?

- Impact of compliance with federal regulations (as currently interpreted) and ethical due diligence has **substantially increased the workload** associated with clinical trials
- Research oversight is intended to **ensure the safety and interests** of research subjects/patients.
- The 2001 Clinical Trials Framework of the Food and Drug Regs have increased the workload - but **no clear evidence trial conduct or safety improved.**
- **Massive rise in SAE** reports may obscure true safety signals.
- On site monitoring and responding to Health Canada inspections create **large workload increases - and are not tailored to risk of trial**



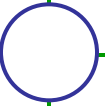
## ISCT Terms of Reference

- Develop guidelines for trials requiring a Clinical Trial Application
- Focus on academic group, institution or investigator.
- Define scenarios where guidance might reduce cost and complexity:
  - Is CTA needed
  - Level of Monitoring needed
  - Levels of data collected
  - Inspections findings
- Obtain data to support the recommendations based on retrospective review, and consider the development of prospective measures and metrics
- Gain consensus across Canada and all therapeutic areas
- Write a position paper/draft guidance document for review
- Disseminate to all stakeholders to review and approve the guidance, and plan implementation.

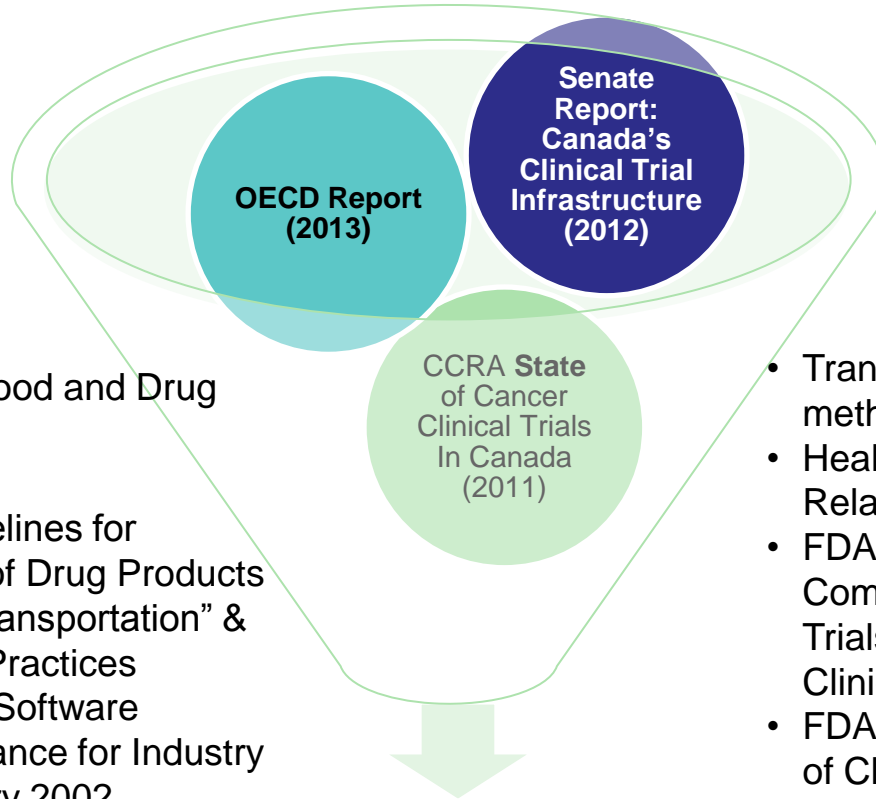


## Nine Key Areas Were Addressed

<b>CTAs</b>	Kathy Brodeur-Robb, Lesley Seymour
<b>Drug Accountability</b>	Kathy Brodeur-Robb
<b>Monitoring</b>	Alison Urton
<b>Equipment and Facilities</b>	Michelle Filice
<b>Delegation of Duties</b>	Jackie Bosch
<b>Validation of Electronic Systems</b>	Jim Pankovich/Karen Arts
<b>Source data Documents</b>	Jackie Bosch
<b>Trial Costs</b>	Jim Pankovich
<b>Inspections/HC Website</b>	Rachel Syme/Karen Arts

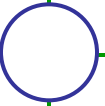


## Resources and Information



- The Health Canada Food and Drug Regulations
- ICH GCP
- Health Canada “Guidelines for Temperature Control of Drug Products during Storage and Transportation” & Good Manufacturing Practices
- General Principles of Software Validation; Final Guidance for Industry and FDA Staff, January 2002
- E11: Clinical Investigation of Medicinal Products in the Pediatric Population and Health Canada Addendum to the ICH 1 Guidance E11:
- Annex 11 to the PIC/s Good Manufacturing Practices (GMP) Guide: Computerized Systems

- TransCelerate risk based monitoring methodology (2013)
- Health Canada Guidance for Records Related to Clinical Trials (GUIDE-0068)
- FDA's Guidance for Industry for Computerized systems used in Clinical Trials - Computerized Systems Used in Clinical Trials, September 2004
- FDA's Guidance for Industry Oversight of Clinical Investigations, A Risk-Based Approach to Monitoring, draft guidance, August 2011
- Office of Human Research Protections
- Code of Federal Regulations (Title 45 CFR Part 46),
- NCI US Clinical Trials Monitoring Branch Guidelines for Auditing of Clinical Trials



## Progress has been substantial

### Summary:

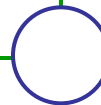
- Nine thematic areas where variation in practice is seen, problems are identified, or opportunities exist to clarify and harmonize
- For each theme, issues or ideas are identified, regulations cited, data sought, guidance proposed

May 24 2013 – Meeting of working group and Health Canada representatives to review and refine proposed guidelines.

Additional consultation and meetings with Health Canada

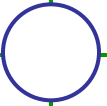
Report is now complete and has been published  
**([www.n2canada.ca/isct](http://www.n2canada.ca/isct))**





## 2. Monitoring

- 15.8.3 “*Sponsor can determine extent and nature of monitoring*”
- & further
  - > the determination of the “*extent and nature of monitoring should be based on considerations such as the objective, purpose, design, complexity, blinding, size, and endpoints of the trial.*”
  - > “*In general, there is a need for on-site monitoring before, during, and after the trial, however in **exceptional** circumstances the sponsor may determine that central monitoring in conjunction with procedures such as investigators training and meetings, and extensive written guidance could ensure appropriate conduct...*”



## 2. Monitoring

### FDA Guidance (2011)

- Guidance intended to “make clear that sponsors can use a variety of approaches related to monitoring”
- “Encourages greater use of centralized monitoring methods where appropriate”
- Combinations of centralized versus on site monitoring are emphasized

### OECD Recommendation (2013)

- members adapt their national regulations and procedures to incorporate a risk-based methodology for the oversight and management of clinical trials.

### Senate Report (2012)

- Strengthen risk-based approaches for monitoring and Adverse Event (AE) reporting, notification of non-compliance and public access to clinical trials information as well as increase inspections and require electronic reporting of Adverse Drug Reactions (ADR)



## 2. ISCT Monitoring Recommendations

ISCT is in agreement with recommendations of the FDA and the OECD with respect to implementation of a risk-based approach to monitoring

Central monitoring of selected critical study parameters and data elements should be the primary strategy for academic trials

Limited on-site monitoring may be appropriate for higher-risk Category B trials and for some Category C trials. The monitoring plan should allow for risk based adaptation of monitoring depending on deviations or data trends identified throughout the course of the trial

Risk based and justified monitoring plans should be summarized in the protocol or an appendix allowing review and approval by Health Canada during the CTA review process

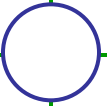


## In Addition

- Inspectors should review the conduct of studies during inspections based on the agreed monitoring plan for the trial to ensure consistency of interpretation.
- ISCT feels strongly that the CTA review period is the appropriate time to identify any concerns Health Canada may have with the proposed monitoring plan, as this is a time when change can be effected most easily.

### ***ISCT action: develop and provide sample documentation***

- ISCT intends to develop sample risk-based monitoring plans and examples to facilitate these recommendations.



## ISCT: What's next?

- Follow-up with Health Canada (done)
- Continue distribution of report with guidance across Canada (underway)
- Create ISCT website and post recommendations (done)
  - Access to sample documents and forms that may be useful to Stakeholders (in progress)
  - A mechanism for notification of planned/new academic clinical trials and which area/s of the Recommendations have been implemented so that the impact can be assessed periodically (to be done)
- Collect feedback
- Follow up with Health Canada



## What can you do?

- Know the regulations
- Know when interpretations “get in the way”
- Familiarize yourself with the report
- Assess where you can adopt the recommendations
- Sign-up for ISCT follow-up
  - [www.n2canada.ca/isct](http://www.n2canada.ca/isct)
- Provide us feedback
- Spread the word!!

# ISCT

## THE INITIATIVE TO STREAMLINE CLINICAL TRIALS

[N2 HOME](#)   [SUMMARY OF RECOMMENDATIONS](#)

[DOWNLOADS](#)

[MAIN DOCUMENT](#)

[GUIDANCE FOR INVESTIGATORS/SPONSORS](#)

[SUMMARY OF RECOMMENDATIONS](#)

[CONTRIBUTORS](#)

[LIST OF CONTRIBUTORS](#)

### CAN WE CONTACT YOU?

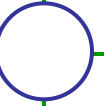
Please fill out your Name and Email Address so that we may contact you in the future regarding your input on the document.

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The 2011 Canadian Cancer Research Alliance (CCRA) report on the State of Cancer Clinical Trials In Canada identified the magnitude of the threat to the conduct of oncology clinical trials. The Report noted that with falling performance metrics, increasing complexity and workload, and an increasingly onerous regulatory environment, clinical trials were at risk, and observed that "Without clinical trials, the outcomes of cancer patients will not continue to improve". The report recommended engaging with Health Canada and other key stakeholders to foster agreement in appropriate interpretations of the Health Canada Food and Drug Regulations and ICH Good Clinical Practice (GCP) guidelines.

The Initiative to Streamline Clinical Trials (ISCT) Working Group, formed in 2012 to address the CCRA recommendations, includes members who are experts in clinical trial conduct across many therapeutic areas. The primary objective of the ISCT was to develop specific, pragmatic and practical interpretations of current regulations, laws and guidelines, in order to facilitate, rather than limit, Canadian clinical trials, by expanding on recommendations such as those of the CCRA and OECD. During the discussions, it became apparent that changes to certain regulations or laws interpretations were also desirable.

The focus of ISCT encompassed *academic clinical trials of drugs and/or biologics* which are required to be, or interpreted as required to be



**QUESTIONS?**

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