

# Clinical Research Education Symposium



**Clinical Trials BC**

British Columbia Academic Health Science Network

**Island Health Research | Five Days in May 2019 |**  **@VIHealthRes | #5DIM**

# Clinical Trials BC

## Supports and Resources

May 2019

**We're a unit of the BC Academic Health Science Network:**



**Clinical Trials BC**

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British Columbia Academic Health Science Network



**BC AHSN**

British Columbia Academic  
Health Science Network

More information at [bcahsn.ca](http://bcahsn.ca)

**Our Mission: To better connect and catalyze BC's collective expertise and resources to attain substantive measurable improvement in health and health care.**

### Learning Health Systems

#### Enable Health Research

Build upon the BC culture of enquiry, research and learning in health care, and a health system that supports research as a core activity

#### Research to Practice

Accelerate the implementation of evidence-guided practice across BC's health care systems

#### Information for Health System Learning

Promote use of information, data, methodologies and analytics to support health research & system-wide improvement

#### Education & Capacity Building

Foster alignment of health education, training and practice to reflect current and emerging realities, demands and needs

**Transformative Partnerships:** Facilitate partnerships to drive develop, implement and scale up evidence-guided solutions to priority challenges

**Organization Excellence and Sustainability:** Create and sustain a high performance organization that meets client needs through the services it provides and nurtures a culture of enquiry to identify current and emerging foci

### Measurable Outcomes

**Our Vision: A high-performing BC health system for all where collective learnings drive continuous improvement.**

## Guiding Principles

- Good care requires good science
- "People with lived experience" are essential partners
- Address complex problems that cannot be solved through any single entity or jurisdiction alone
- Provincial in scope – scalable
- Alignment with BC health sector priorities to ensure relevance and integration, now and in the future.

**Core goals:**

**Enabling goals:**



**BC AHSN**

British Columbia  
Academic Health Science Network



**BC SUPPORT Unit**

Advancing Patient-Oriented Research



**Clinical Trials BC**



**Research Ethics BC**

# Clinical Trials BC

## **Vision:**

Establish and promote British Columbia as a world-class destination for Clinical Trials

## **Mission:**

To maximize the health, educational, and economic benefits of clinical trials to the citizens of British Columbia



# Clinical Trials BC Strategic Framework

**VISION:** Establish and promote BC as a world-class destination for Clinical Trials

| Business Development  | Capacity Development  | Enabling Environment  | Patient/Participant Engage - Experience  |
|---|---|---|--|
| <ul style="list-style-type: none"><li>• Establish and build on industry relationships</li><li>• Attract and increase investment</li><li>• Facilitate connections</li><li>• Promote technology platforms</li><li>• Measure economic impact</li></ul> | <ul style="list-style-type: none"><li>• Access to online tools &amp; templates</li><li>• Targeted workshops</li><li>• Certification support</li><li>• POR pathways</li><li>• Quick startup guide</li><li>• Mentoring Program</li><li>• Job boards</li></ul> | <ul style="list-style-type: none"><li>• Regulatory Support</li><li>• Quality Framework (QMS)</li><li>• Streamlining processes</li><li>• Access to data</li><li>• New technology/methods</li><li>• CTMS</li><li>• “Voice” for BC clinical research community</li><li>• Barrier busting</li></ul> | <ul style="list-style-type: none"><li>• Build a positive culture for clinical trials in BC</li><li>• Patient/physician surveys, KT</li><li>• Patient engagement/ Patient experience</li><li>• Feedback loops</li><li>• Barrier Busting</li></ul> |

**Stakeholder Engagement** *(industry; patients; BC/national/global clinical research community)*

**Knowledge Translation**

**MISSION:** To maximize the health, educational, and economic benefits of clinical trials to the citizens of BC





## Certified Research Professionals Support

- Invest in people through facilitating certification
- SoCRA or ACRP Clinical Research Professional certification program
- 71 Clinical Research Professionals certified to date
- 17 in 2018 and 8 in 2019
- Support of certification fees \$350 CDN
- Exam preparation sessions
- Recognition

# Network of Networks (N2)



- With funding support from the BC SUPPORT Unit, we provide province-wide access to best-in-class tools and resources from the Network of Networks
- N2 is focused on enhancing clinical research capability and capacity.
- N2 benefits are available for clinical researchers working in health authorities and academic organizations in BC, as well as for some independent investigators.
- Tools and resources that are available through N2 membership include Educational courses (available via CITI-Canada), Standard Operating Procedures, Quality Tools, Tools to Engage Participants and more.

[n2canada.ca](http://n2canada.ca)





# Learning Management System (LMS)

- Access to ACRP e-learning library of 30 educational courses.
- Essential part of achieving the highest level of patient safety, data quality and regulatory compliance
- Up to 100 researchers/research staff in BC
- Over 300 users to date
- Hosted by VCHRI and Clinical Trials BC



New User?

- Email: [education.award@vch.ca](mailto:education.award@vch.ca)



# Enabling Quality



# Our Regulatory Programs for BC

Audit and Inspection Preparedness Program (AIPP)

Compliance Education

Investigators Only Training

Regulatory Guidance and Consultation

Quality Management Systems (QMS) – includes Risk Management

Inter-Provincial Regulatory Review

Resource Bank

# QMS / Risk Management Update

- ✓ Training Program in QMS (for all institutions and programs) - book
- ✓ QMS and subsystems (lunch and learn series/workshops for sites)
- ✓ QMS Manual and SOPs (full set) forms and templates
- ✓ Institutional/Health Authority Assessments and Development Planning (Ongoing)

# Updated and New Resources 2019-20



## General Regulatory Consulting Service

Study set up, study issues assistance, regulatory resource, document reviews



## Province-wide Access to N2 Resources

Free for university, health authority and community research teams

- Clinical Trial Education and Awareness toolkit
- SOPs
- CITI Training Courses e.g. GCP, HC Div 5 Regs, Privacy, Ethics, TDG/IATA



## Workshop/Lecture Series Spring Summer 2019



## Audit and Inspection Preparation Program V4



2019 Clinical Trials BC Syllabus  
Spring and Summer Lecture and Workshop Series

## 2019 Feature Lectures

1. Risk Management
2. HC Guidance 0100
3. Learning From the Canadian Clinical Research Participant Experience
4. Presentation: Canadian Regulatory Environment: Influences, Changes and Trends 2019
5. ICH- E6 (R2) GCP - Implementation Impact and Resources

## ASQ US Series

The **ASQ TOPIC** series was popular under the former BCCRIN dating back to 2011. The Sessions are designed to fit into a short time session. Bring your lunch! These are short mini presentations on hot topics combined with equal time to ask questions. The 'Just ASQ Us' FORUM Dates and ASQ HOT TOPICS will be announced in our newsletter.

## Investigators Only Series (Modules 3-7 available Fall Winter Syllabus of 2019/2020)

Module 1

**Investigator Responsibilities**

Module 2

**Investigator Oversight**

## CORE Workshops

1. Good Documentation Practices (GDP) Records
2. Privacy and Security in Clinical Research
3. Introduction to ICH Guidance Documents - The Basics for Clinical Trials
4. Quality and the Calibration & Maintenance of Equipment in Clinical Trials

## Specialized Series

### Clinical Trials BC Audit & Inspection Preparedness Program (AIPP) 2018 Version

Workshop #1 – Advance Preparation: Be Prepared: From Notice to Knock  
Workshop #2 – Interview Techniques: Inspection Interview Responses  
Workshop #3 – Hosting Skills and Audit Conduct: The Do's and Don'ts  
Workshop #4 – Document Handling: Control of Documents During an Inspection  
Workshop #5 – Exit Meeting  
Workshop #6 – Follow-Up Activities: The Post Audit 5 C's: Common Findings, Classifications, Clarifications, Corrections & CAPA

The Program comes with access to an audit kit, tools and access to the Clinical Trials BC AIPP Manual V3 and workshop handouts at sessions. Training Certificates are issued at the end of the series.

## Clinical Trials BC Quality Management System Training Program

This Training Program was established with BCCRIN in 2012. It has been modified and is now in version 4. A full compliment QMS with nine systems is available for programs, centres and institutions within British Columbia

## Specialized Workshops and Lectures from the CTBC Resource Bank

Clinical Trials BC maintains an archive of lectures. Staff are available to speak on topics of interest or provide an update on any previous topic that has been presented that relates to Clinical Trials. We are also happy to take suggestions for new topics.





# Clinical Research Navigation



Business development  
opportunities



Global marketing of BC's clinical  
trials excellence



Facilitating connections and  
partnerships



[www.bc.cctam.ca](http://www.bc.cctam.ca)



[www.cctam.ca](http://www.cctam.ca)

# Enhancing Clinical Research Participation

## Objectives

Engage with the research community, industry and the public around results of our survey with research participants/decliners

- identify key areas for improvement, barriers to bust
- make recommendations for action



May 7<sup>th</sup> – Co-hosted with Island Health Research

## Recent Activities

2018

- March - workshop with researchers at Island Health
- May - Dialogue with CT participants and the public at Island Health
- Nov – workshop with research teams and CT nurses at Interior Health

2019

- Feb – N2 – overview at AGM
- April – national N2 webinar – recording available

# NOTABLE, NEW, STAY TUNED...

Resource Bank  
Tools 2011 – 2018  
Lectures & workshops 2019

Advanced Training Courses 2019  
Posted

Communities of Practice (eCOPs)  
- Results WG  
- Quality Forum  
- Directors Forum – coming soon

Clinical Trial Management System  
(CTMS)

ACRP Workforce Innovation  
Steering Committee  
(WISC)

Advisory Council  
June 2019

Provincial Clinical Research  
Job Board

Needs Assessment

Updated Strategic Plan  
2020



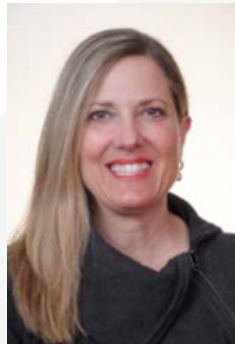
**Clinical Trials BC**

# Thank You and Questions

Twitter: @clintrialsBC

Web: [clinicaltrialsbc.ca](http://clinicaltrialsbc.ca)

Email: [info@clinicaltrialsbc.ca](mailto:info@clinicaltrialsbc.ca)



# Canadian Regulatory Environment Influences Updates Trends

Jean Smart, MGH, MDS, RAC  
Regulatory Affairs and Quality Officer

May 2, 2019 - Victoria BC

# Agenda

International Regulatory Influences

Canadian Regulatory Update

Acts, Regulations, Policies

Guidelines – New and In the Cue

Health Canada and the Directorates Status

Trends

New Compliance Findings

Hot Topics

Resources



# International Regulatory Influences

# ICH

- The new name of ICH is the “International **Council** on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use”
- ICH has been fully restructured
- It is now a **legal international entity**

# ICH

ICH is a joint initiative involving **both** research based industry representatives and regulators of the founding EU, Japan, Canada, USA (and new members Iran 2018) in scientific and technical discussions of the testing procedures required to assess and ensure the

- Safety
- Quality
- Efficacy

of medicines **and....produce international guidance on identified topics**

- **Now 16 Full Members, 28 Observers**
- **Now 25 Working Groups**

# 5 Steps for ICH policies

- New pre process – building a business case
- Step 1 Consensus building to expert sign off
- Step 2 Start of regulatory action to draft guideline
- Step 3 Wide range regulatory consultation to expert sign off (Consensus is reached)
- Step 4 Steering Committee review to Assembly adoption (Adoption official and then a press release)
- Step 5 Implementation  
(56 regulatory authorities and regions plus Non-regulated regions covered by WHO via Suissemedic)

# ICH Central documents for Clinical Trials

- Recent changes and the topics were based on the global findings compiled reports and other submitted reports supporting change
- Impact of the Drafts alone are felt internationally
- **New Emphasis** that Clinical Trial documents should be read and training should be in conjunction with other ICH guidelines relevant to clinical trial conduct (for example, **ICH E6R2, E2A, E3, E7, E8, E9, E11, E17, S1, Q9...**)
- November 10, 2016 ICH Assembly **agreed to the proposed review** of the wider quality package of guidelines relating to GCP and clinical trial design
  - The reflection paper (review ended March 11, 2017)
  - Long term work plan in effect and WG's are active

# New ICH Documents

E9 RI Statistical Practices in Clinical Trials Oct 10 2018

E18 Genomic Sampling and Management of Genomic Data April 26, 2018.

Revision of Q&As for the Electronic Submission of Individual Case Study Reports (E2B(R3)); [May 2018](#)

ECTD v3.2.2 Q&A and Specification Change Request Document v1.31 (M8) [May 2018](#)

eCTD v4.0 Implementation Package v1.2 (M8) [May 2018](#)

eCTD v4 Q&A and Specification Change Request Document v1.2 (M8) [May 2018](#)

Specification for Submission Formats for CTD v1.2 (M8)

Q&As on Nonclinical Evaluation for Anticancer Pharmaceuticals (S9) were adopted through written procedure in [April 2018](#).

[Revised recommendations on Electronic Transfer of Regulatory Information \(ESTRI\) \(M2\) May 2018.](#)

- E2D Guidance Reporting Adverse Reactions of Marketed Health Products
- E11 R1 Clinical Investigation of Medicinal Products in Pediatric Population April 5 2018



# ICH 'In the Queue'

November 2018

- New E11R1A Pediatric Drug Development (extrapolation)
- E20 Adaptive Clinical Trials
- M12 Drug Interaction Studies

GCP Renovation Package

- E8 WG is established and progressing rapidly
- E9 Statistical Practices in Clinical Trials WG is established and progressing rapidly
- Discussion Group - ICH Quality formed

Strategic Planning for Approach to harmonization of Tech requirements for pharmacoepidemiological studies submitted to regulatory agencies to advance utilization of real world data \*

# I PRP

- The **International Pharmaceutical Regulators Forum Programme** is a new agency January 1, 2018.
- Merged The International Pharmaceutical Regulators Forum (IPRF) and the International Generic Drug Programme (IGDRP)
- Met in Kobe Japan in June 2018 and in Charlotte North Carolina November 2018
- Next in Amsterdam in June 2019 and Singapore in November 2019
- **Represent non regulatory stakeholders** and present business cases for guidance

# IPRP

The purpose of the **International Pharmaceutical Regulators Programme** is to create an environment for exchange of information on issues of mutual concern and regulatory cooperation.

- identify the need for harmonization or regulatory convergence,
- **regulatory cooperation, including work-sharing, in specific quality areas.**
- maximize potential efficiencies in addressing the increasingly complex global context of medicines regulation,
- **facilitates the implementation of ICH and other internationally harmonized technical guidelines**
- contributes to the coordination of international efforts related to regulation of medicinal products for human use.

# GHTF to IMDRF

- The Global Harmonization Task Force established in 1992 disbanded in 2012.
- It transitioned to the **International Medical Device Regulators Forum(IMDRF)** in 2013
- 2019 - Carrying a lot of weight and is the leading influence on Medical Device reform internationally.
- Aims:
  - to achieve greater uniformity between national medical device regulatory systems
  - enhancing patient safety and **quality**
  - increasing access to safe, effective and clinically beneficial medical technologies around the world.

# PICs

- PICs is the abbreviation and logo to describe the joint Pharmaceutical Inspection Convention and Pharmaceutical Inspection Cooperation Scheme groups working together
- 37 participating agencies
- Health Canada(HPFBI) is an active and lead member
- Quality and validation are key areas
- facilitate the networking between participating authorities
- mutual training of GMP inspectors
- GMP and quality initiatives are applicable throughout the product lifecycle including products in clinical trials

# PICs

For information on electronic records and systems, refer to:

PIC/S Annex 11 *Guide to Good Manufacturing Practice for Medicinal Products: Computerised Systems* (It is the HC equivalent of US CFR 21 Part 11 Electronic Records and Computerized Systems) and the EU Annexe 11.

*and*

PIC/S Guidance: *Good Practices for Computerised Systems in Regulated “GXP” Environments*

- There is cross-reference to these in our Regulations Amendment 1024 . Three references to these in HC Guidance 0100
- Note: Sites could be asked for a computerized system compliance statement during audit or inspection



# RCC

## New: Regulatory Cooperation Council

- MOU between Canada treasury Board and the US advance Regulatory Cooperation Council August 2018
  - serve as a forum to discuss, coordinate, and provide broad guidance on regulatory cooperation initiatives between Canada and the U.S.;
  - conduct senior-level discussions to proactively identify and discuss challenges, opportunities, and lessons learned regarding Canada-U.S. regulatory cooperation;
  - identify opportunities to bring significant economic benefits to both countries design new regulatory activities with the goal of achieving regulatory alignment, to the extent feasible and appropriate.
- Plan to meet annually as a minimum
- There are challenges
- Not to be confused with Canadian Regulatory Council

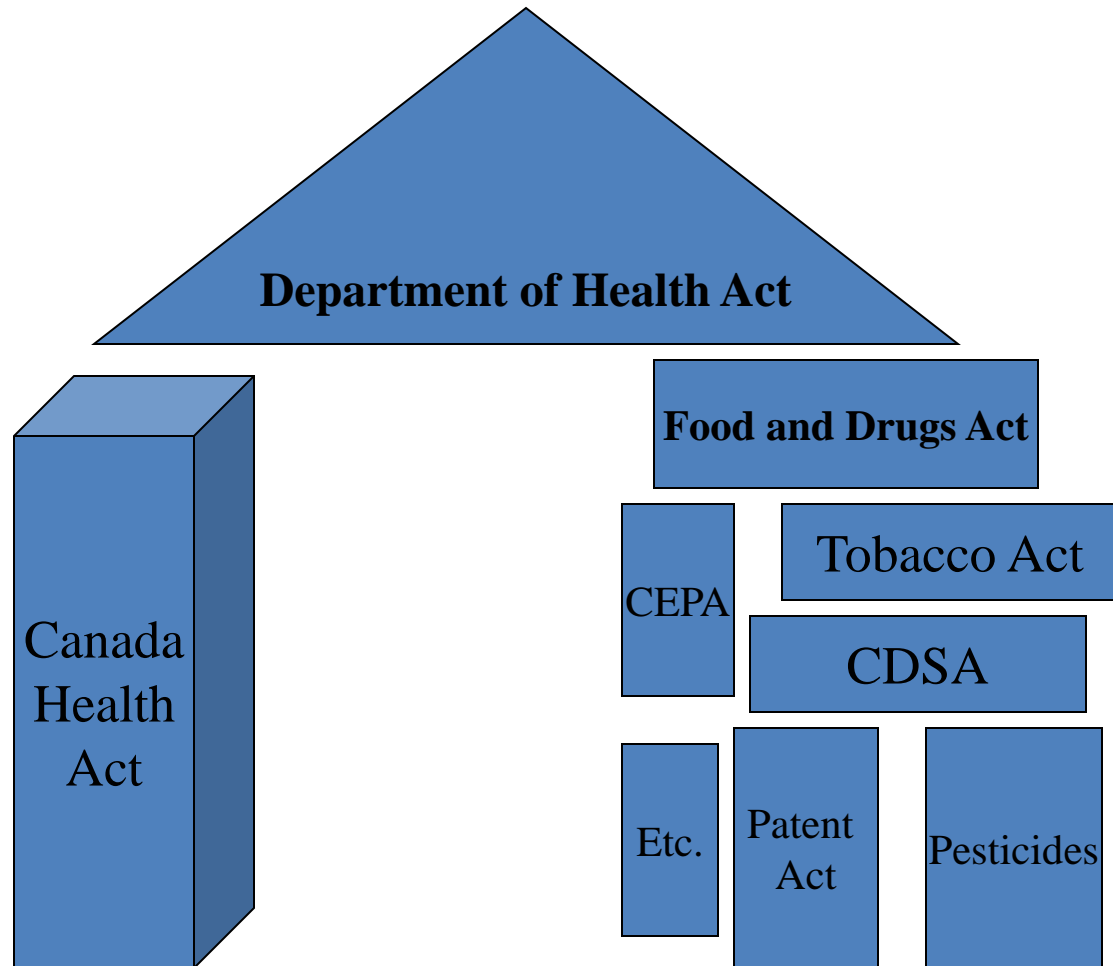
# CCTCC

## Canadian Clinical Trial Coordinating Centre

- Sponsored by Innovative Medicines Canada and CIHR
- 2 year hiatus
- Undergone a full review and consultation
- Strategic planning is in progress with restructuring
- Expect it to resurface in **2019**
- National Clinical Trial Asset Map (CTAM) is now being maintained
- There are 2 Active Working Groups

# Canadian Regulatory Environment 'Responsive'

# Canadian Regulatory Framework



# Canadian Regulatory Framework

The *Department of Health Act* sets out the mandate of the Minister of Health in very broad terms - the promotion, preservation and **protection of the health of Canadians** in all areas not otherwise assigned by law to another department or agency, within the limits of federal jurisdiction.

This is what they are calling for a reform of.

# Canadian Regulatory Framework

## **Food and Drugs Act (1953)**

Hazardous Products Act (1969)

Pest Control Products Act (1969)

Radiation Emitting Devices Act (1970)

Quarantine Act (1872)

## **Controlled Drugs and Substances Act (1996)**

Tobacco Act (1997)

Canadian Environmental Protection Act (1999)

## **Patent Act (relevant provisions passed in 1993)**

Canadian Food Inspection Agency Act (1997)

## **The Cannabis Act (2018)**

...

# Food and Drugs Act

- This Act applies or crosses over to all food, drugs, radiopharmaceuticals, biologics cosmetics, natural and non prescriptive health products and medical devices sold in Canada, whether manufactured in Canada or imported (humans and veterinary).
- The Act and Regulations ensures the safety of and prevent deception in relation to foods, drugs, cosmetics, NNHP's and medical devices by governing their sale and advertisement and in addition sets out the labeling requirements.

# Food and Drugs Regulations

Regulations are law. They can be enforced.

Part A: Administration / General

Part B: Foods

Part C: Drugs

Part D: Vitamins Minerals and Amino Acids - now  
under NNHP Regulations. (mostly repealed)

Part E: Artificial Sweeteners, Saccharin & Cyclamate

Part G: Controlled Drugs - adapted under CDS Act

Part F, H & I : Repealed

Part J: Restricted Drugs- adapted under CDS Act

...



# Other Pertinent Acts and Regulations

## **The Controlled Drug and Substances Act**

The Financial Administration Act

Patent Act (sections 79 - 103)

Access to Information Act

Patented Medicines (Notice of Compliance) Regulations

The Patented Medicines Regulations

Cosmetic Regulations

## **Medical Devices Regulations**

**Natural and Non-prescription Health Products Regulations**

**National level privacy and provincial level privacy regulations**

**Cannabis Regulations**

...

# Guidance Documents

Guidance documents have been prepared to assist in the interpretation of policies and governing statutes and regulations. They are usually written in layman terms with a definition index

- Two Levels
  - Those adopted by Health Canada whole and imbedded into our regulations
    - start with ICH E/M/S/Q + version if not the first one + XXX + Title
  - Those created by Health Canada
    - start with HC Guide XXXX + title + date
    - standards to be followed are referenced in the Guidance

# ICH Guidance E6R2 - GCP

## Health Canada

Adopted E6R2 on November 11, 2016 in Osaka (announced May 29, 2017)

Became effective on May 25, 2017 before the ICH Spring Assembly in Montreal, Canada

Full implementation came into effect **April 1, 2019**

## In Effect in:

EU and Europe

Swissmedic (for WHO)

FDA

## PMDA, Korea and Brazil

Have not 'formally' responded as of May 1, 2019

# Top 10 of 26 Changes to E6

## All Quality Items

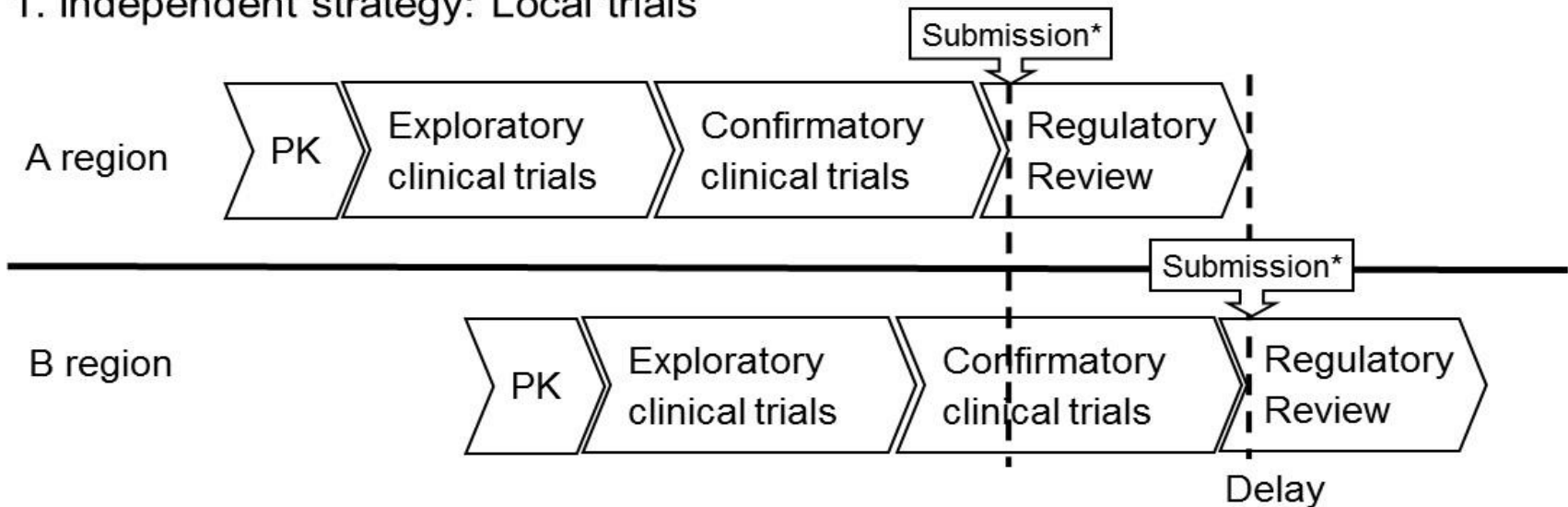
- 1) Quality Management Systems
- 2) Investigator Oversight
- 3) ISF/TMF
- 4) Good Documentation Practices
- 5) Risk Management
- 6) Monitoring
- 7) Non-compliance
- 8) Vendor Oversight
- 9) Control of Data and Essential Documents
- 10) Electronic Systems and Validation

# ICH E17 Multi-Regional Clinical Trials (MRCT)

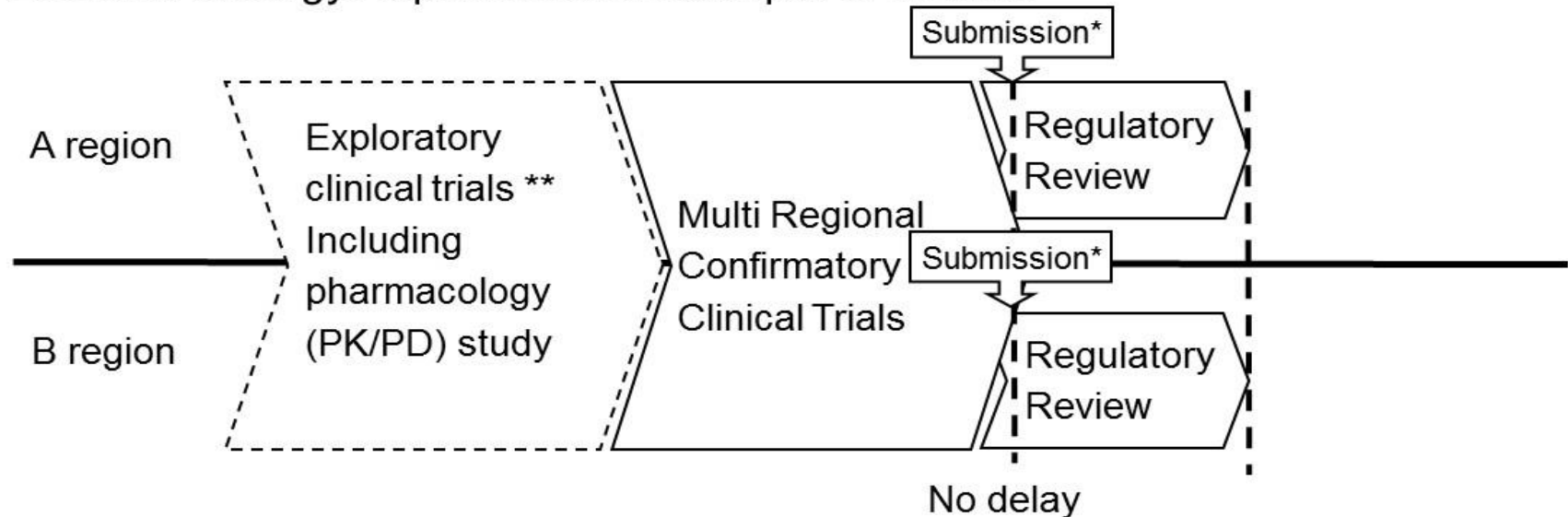
- **Biggest Impact - coming**
- **Came into Effect in Canada April 11, 2019**
- Intended to be used with ICH E5 Ethnic Factors in the Acceptability of Foreign Clinical Data 1996
- Development
  - Early and extensive involvement of the regulatory Authority pre CTA
  - Early Content Expert and Participant Involvement in Protocol Development and **'The Smartt Plans'**: (Statistical Plan, Monitoring Plan, Administration and Operational Plan, **Recruitment Plan**, Risk and Quality Management Plan, Trial Data Management Plan,) + **Participant Plan**
- Ensure trained clinicians and site personnel involved in trials
- Site Selection – Fully Qualified Sites - Resource, Training and Expertise Assessment
- Perform regular monitoring of site performance
  - **Recruitment and GCP compliance**
- Central review of all or part of the trial data
- Regulatory
  - Critical dependency on E6R2 compliance
  - Long range: Global reviews (10 year)

# MRCT Model from ICH E17

## 1. Independent strategy: Local trials



## 2. Global strategy: representative example of MRCTs



# The Other ICH Documents

- E18 Genomic Sampling and Management of Genomic Data now adopted
- E11R1 Paediatric Drug Development Now adopted

# HC Guidance Documents

Guidance documents have been prepared to assist in the interpretation of policies and governing statutes and regulations. They are usually written in layman terms with a definition index.

Examples:

- Bioavailability and Bioequivalence
- Clinical Trials Manual
- Guidance for records related to Clinical Trials (GUIDE - 0068)



# HC Guidance 0100

- Where is it?
  - Expected out in April 2018
  - Announced it would be out April 1, 2019
- December 2017 Draft Version 12 circulated for feedback suggested it would include the revised CTA process, E6R2 content and the records requirements included in Guidance 0068 Records for Clinical Trials is scheduled to be repealed.
- MRCT content not included in the Draft
- HC will be attending the Regional N2 Meeting in Vancouver on May 13, 2019. An in depth look at Guidance 0100 is on the agenda.
- **Big focus item for Canada in 2019**

# HC Medical Device ITA Consultation

- Health Canada Guidance - Applications for Medical Device Investigational Testing Authorizations Draft Oct 6 2017 [closed for comment](#)
- [Current Status of Guidance – unknown \(is slated for 2019\)](#)
- A Review and revision of Medical Device Investigational Testing Authorizations (ITAs) was prioritized in Health Canada's Action Plan - published in December 2018. The Review is to include longstanding issues identified by all stakeholders (including the IMDRF)
- Consultation is now [OPEN](#)
  - [Question format](#)
  - Comments to Health Canada Policy office by June 21, 2019
  - Comments should be from an organization and not an individual
  - Note that written feedback is public information

# Policies

Policy documents are interpretations of the purpose and intent of the Food and Drug Act and Regulations

- They are issued when there is a point that needs clarification or if something has been adopted but perhaps not put through legislation
- Examples:
  - [Drug/Medical Device Combination Products Policy](#) [2005-11-30]
  - [Priority Review of Drug Submissions Policy](#) [2007-12-20]
  - [Notice of Compliance with Conditions Policy](#) [2007-05-16]
- No new Policies in 2018 or slated for 2019

# Canada Gazette

The *Canada Gazette* is one of the vehicles that Canadians can use to access the laws and regulations that govern their daily lives. It has been the "official newspaper" of the Government of Canada since 1841.

Divided in 3 *Parts*

# Canada Gazette Sample

Part II

Registration Enregistrement SOR/2001-203

7 June, 2001 DORS/2001-203 7 juin 2001

FOOD AND DRUGS ACT

Regulations Amending the Food and Drug Regulations (1024— Clinical Trials)

P.C. 2001-1042 7 June, 2001 C.P. 2001-1042 7 juin 2001

Her Excellency the Governor General in Council, on the recommendation of the Minister of Health, pursuant to subsection 30(1)a of the Food and Drugs Act, hereby makes the annexed Regulations Amending the Food and Drug Regulations (1024 — Clinical Trials).

# Health Canada Organization Chart



# Health Products and Food Branch

- Used to be Health Protection and Food Branch
- HPFB's Mandate is to take an integrated approach to the management of the risks and benefits to health related to health products and food by:
- Minimizing health risk factors to Canadians while maximizing the safety provided by the regulatory system for health products and food; and,
- Promoting conditions that enable Canadians to make healthy choices and providing information so that they can make informed decisions about their health.

# Health Products and Food Branch

- **Therapeutic Products Directorate (TPD)** (regulates pharmaceutical drugs and medical devices\*)
- **The Biologics and Genetic Therapies Directorate (BGTD)** (quality of all biologics and radiopharmaceuticals)-blood and blood products, viral and bacterial vaccines, genetic therapeutic products, tissues, organs and xenografts
- **Natural and Non-prescription Health Products Directorate (NNHPD)** natural and non-prescriptive health products (NNHPs) Must have a DIN and go through clinical trials
- **The Marketed Health Products Directorate (MHPD)** coordination of consistency of post-approval surveillance and assessment of signals and safety trends \*



# Health Products and Food Branch Inspectorate

The Inspectorate or **HPFBI** is responsible for the management of inspection, investigation, monitoring activities and enforcement strategies

HPFBI covers: pharmaceuticals, radiopharmaceuticals, natural health products, biologics, medical device and combination products.

- The HPFBI is undergoing revisions and reorganization
- Foreign inspection program in effect
- Just completed the pilot program for sponsor inspections – not to be published

Not doing annual summary reports anymore –results are in the observation DB

Meet the new BC GCP Inspector on May 13, 2019 N2 Regional Meeting

# Top 3 Health Canada Observations for Clinical Trial Inspections 2016

Percent of Observations by category from the total in 1 yr. period April 1 2015 to March 31 2016

1. **Records 40%** (2015 - 30%, 2014 - 27%, previous 7 years average 25.4%)
2. **Quality systems and procedures 30%** (2015 - 26.5% 2014 -31%, previous 7 years average 26.9%)
3. **Qualifications, quality education and training of personnel 10%** (2015 – 12.3%, 2014- 11.4, previous 7 years 8.9%)

There has been a notable increase in the severity of the grading from Risk 3 (Minor) to **Risk 2 (Major)** findings in 2016 (11% increase from 2014).

**Blue highlights** - January 25, 2016 Inspectorate Program Annual Summary Report 2014-2015 (ending March 31 2015.)

**Aqua Highlights:** February 2, 2017 Presented and released by HC but are not yet published in a Summary Report (year ending March 31, 2016)

\*Definition – Observation: a negative finding or nonconformance to the HC Food and Drug Regulations – C.05.010 and C.05.012

Note: all top three observations are quality related

# Health Canada Office of Clinical Trials

## Not New but More Visible

- provide clinical and quality (chemistry and manufacturing) reviews of Clinical Trials Applications for prescription drugs and some natural health products
- monitor safety while investigational product is being used in clinical trials.
- review Special Access Programme requests for access to non-marketed drugs to treat medical emergencies when conventional therapies have failed, aren't suitable, or are not available.

Office of Clinical Trials (OCT)

Carole Legare

Therapeutic Products Directorate

E-mail: [oct\\_bec\\_enquiries\\_enquetes@hc-sc.gc.ca](mailto:oct_bec_enquiries_enquetes@hc-sc.gc.ca)

Fax: 613-946-7996

# PRE

## Panel on Research Ethics

- NCEHR was active in **educating** and auditing REBs and sites in Canada (was a voluntary program 1998 to 2010). It overlapped with our inspectorate. PRE evolved
- PRE's mandate is now to **advise** (new word addition) on evaluation interpretation, implementation and **education needs** and **promote ethical conduct** and advance protection of human research

# PRE

Main initiative was to support the development and evolution of their joint research ethics policy the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (TCPS).

- V2R1 Edition 2014 is in effect with training module
- V3 in Draft 2016 – no change, no Status update available
- Human Cell lines consultation occurred in 2017- no change no status update available
  - Re-think its approach to research involving human cells/cell lines;
  - Consider its response to recent changes in international standards;
  - Strengthen collaboration with those doing work in this area.

TCPS training remains **mandatory** in some institutions and authorities in British Columbia

# CIHR

- 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 heads the SPOR program
- No regulatory authority in Clinical Trials

# CIHR

- 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 (surveillance) and services.
- Interesting... as the definition of 'Clinical Research' changes and RWCT integrate with Phase III and Phase IV Clinical Trials in the ICH E8 and quality associated polices.
- CIHR heads SPOR and the SUPPORT Units (meeting Nov 14 and 15 2018, Ottawa). The 'T' in support is for 'Trials'

# Health Canada Research Ethics Board

- Health Canada is not usually involved in conducting clinical trial research
- The sponsor (individual, corporate body, institution or organization) undertaking the research, obtains ethics approval of an appropriate Research Ethics Board before the clinical trial begins, (Division 5 of the Food and Drugs Act and Regulations.)
- However, if Health Canada is involved in conducting clinical trials - application to Health Canada's Research Ethics Board (REB) for an ethical review of the proposed research by the REB will be required in order to proceed
- HC follows the TCPS



# Rx&D Innovative Medicines

- Canada's Research-Based Pharmaceutical Companies
- Member of the International Federation of Pharmaceutical Manufacturers Associations (IFPMA) and key member of the **IPRP**
- Code of Ethical Practices
  - advertising, samples, **education (now included)**, symposia & training sessions, donations, financial support, gifts, hospitality, post-registration **clinical trials service items, privacy** etc.
  - **Much more active in education initiatives as required by E6R2 and MRCT**

# Regulatory Trends

# Compliance Trends 2018

- 1) Inadequate or missing quality systems QMS (ICH Q9) requirements and procedures (SOPs)
- 2) Inadequate records or record keeping
- 3) Poorly documented or inadequate qualifications, education and training of personnel
- 4) Non-compliance related to the process for informing and/or obtaining informed consent from subjects
- 5) No access to source documents ★

# Compliance Trends 2018

- 6) Inadequate storage and maintenance/archive of records ★
- 7) Improperly maintained essential documents (IMF/SMF) – GDP/ALCOAC ★ during the study
- 8) Oversight issues and inappropriate delegation of authority ★
- 9) Deviations from clinical trial protocols
- 10) Inadequate investigational product accountability at the site
- 11) Missing equipment maintenance records ★
- 12) Unblinding of the clinical trial
- 13) Missing validation documentation ★
- 14) Non-compliant Dosage issues
- 15) Risk Management Plan missing or not maintained ★

# Trending Topics of Concern, Debate or Interest

- E8 General Considerations
- MRCT
- QMS and Risk Management
- Unblinding
- Monitoring
- Tech Advances Electronic
- Electronic Signature & Informed Consent
- Under-Reporting of Clinical Trials
- Electronic TMF and ISF
- Substance use Clinical Trials
- Use of Real World Data in Clinical Trials
- Patient Centricity
- Adaptive and flexible trials
- Wearables and Passive Data collection
- Auto Supplies
- Recruitment Strategies and Plans
- Artificial Intelligence in Clinical Trials

# Summary

- Keep up with regulatory changes and influences
- Participate in ongoing training offerings
- Professional Development is highly recommended
- Strive for compliance and excellence - Awareness of trends and to avoid complacency
- Access available [Resources](#) (Clinical Trials BC, Health Authority and External)

# Thank You

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**BC AHSN**

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Advancing Patient-Oriented Research

**Clinical Trials BC**

**Research Ethics BC**