Clinical Research Education Symposium

island health

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

British Columbia Academic Health Science Network

BC AHSN

British Columbia Academic Health Science Network

More information at 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

Core goals:

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

Enabling goals:

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.

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

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
• Establish and build on industry relationships • Attract and increase investment • Facilitate connections • Promote technology platforms • Measure economic impact	• Access to online tools & templates • Targeted workshops • Certification support • POR pathways • Quick startup guide • Mentoring Program • Job boards	• Regulatory Support • Quality Framework (QMS) • Streamlining processes Access to data • New technology/methods • CTMS • "Voice" for BC clinical research community • Barrier busting	• Build a positive culture for clinical trials in BC • Patient/physician surveys, KT • Patient engagement/ Patient experience • Feedback loops • Barrier Busting

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

Clinical Trials BC

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

ACRP
ASSOCIATION OF CLINICAL RESEARCH PROFESSIONALS

Vancouver CoastalHealth Research Institute
Healthier lives through discovery

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)

Clinical Trials BC

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
- 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 7th – 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

Email: info@clinicaltrialsbc.ca

Clinical Trials BC

Canadian Regulatory Environment Influences Updates Trends

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

May 2, 2019 - Victoria BC

Clinical Trials BC
British Columbia Academic Health Science Network

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 *

IPRP

- 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

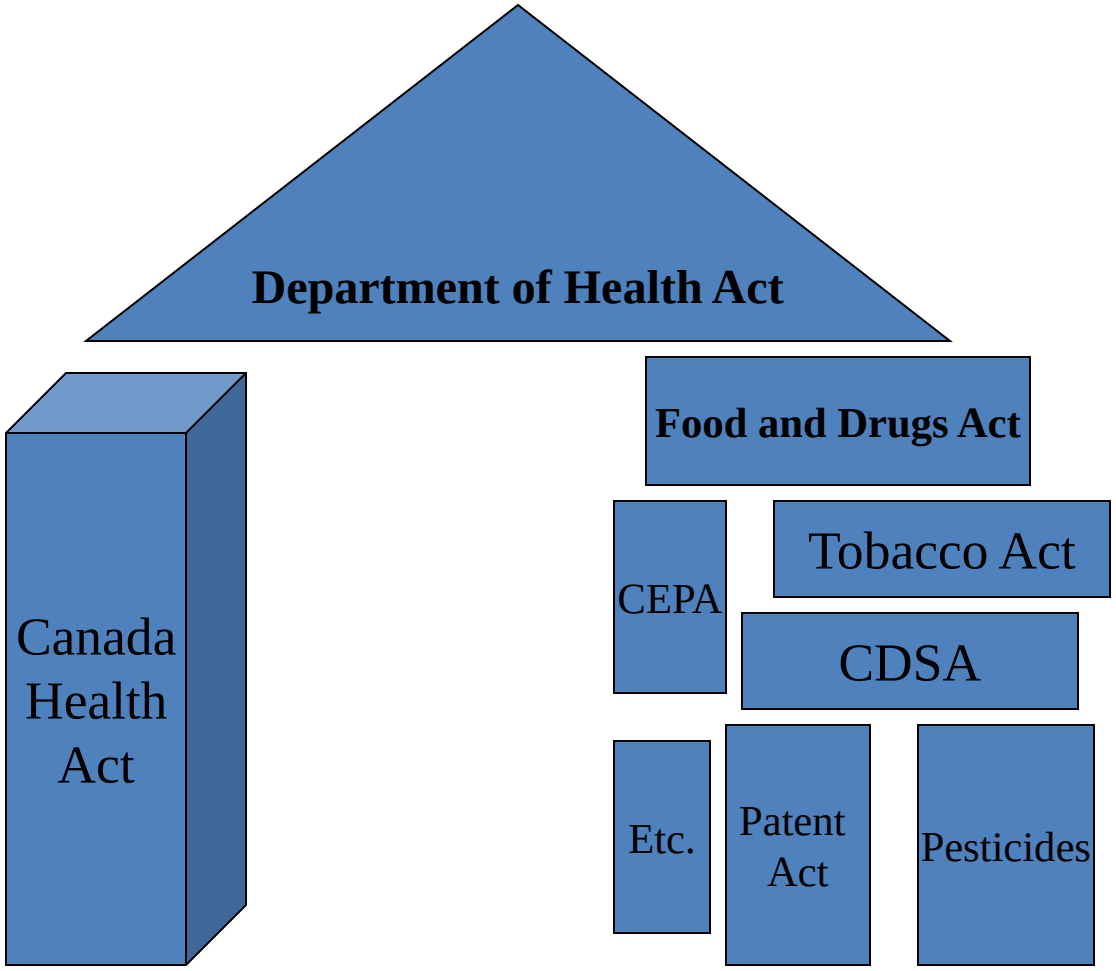
Canadian Clinical Trial Coordinating Centre

- 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 NNHPRegulations. (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

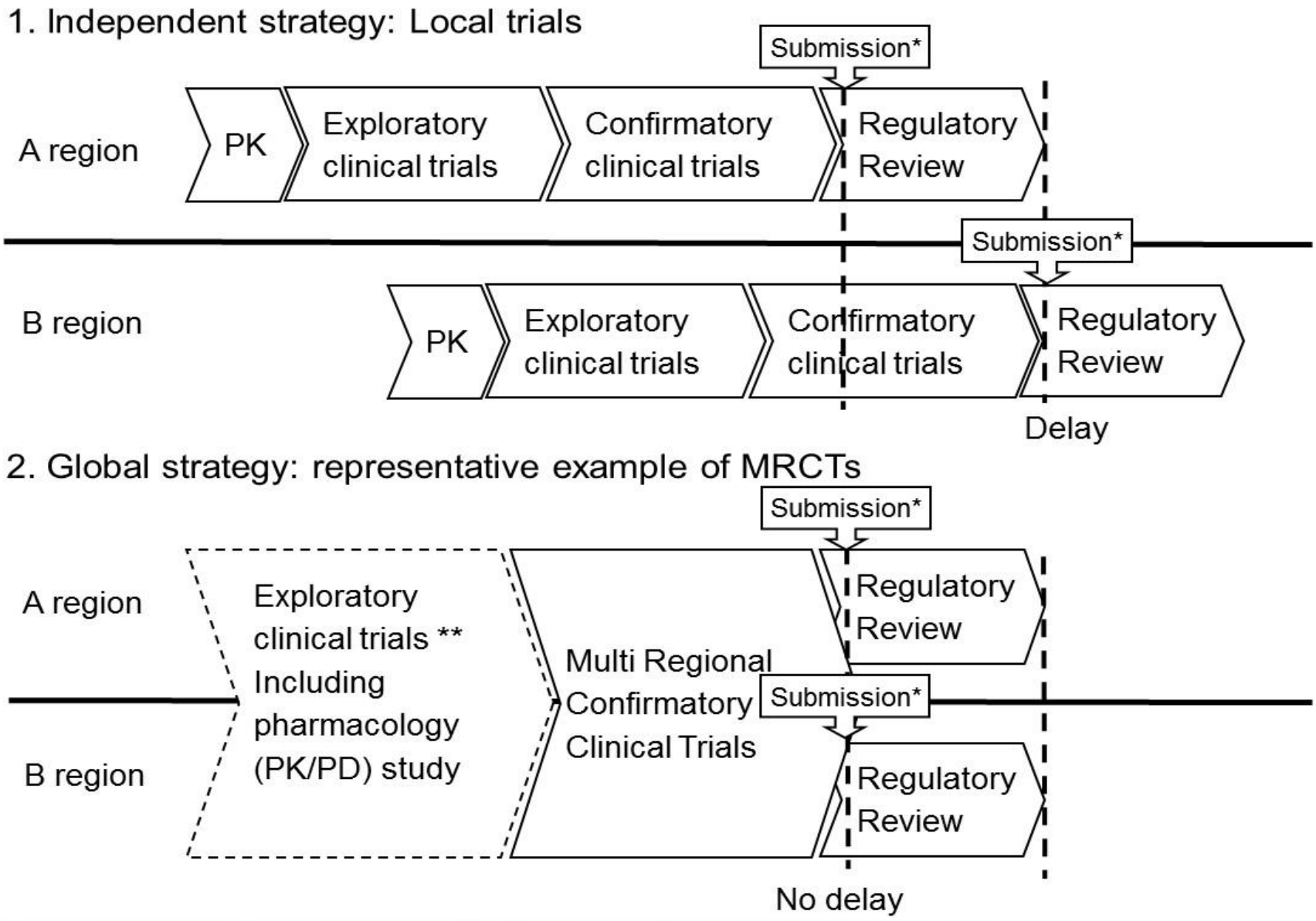
ICH E17 Multi-Regional Clinical Trials (MRCT)

- **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 Smarrt 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



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

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 ✶

Global Findings Site – GC Report 2018 V9

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 **C**oncern, **D**ebate or **I**nterest

- 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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