Health Canada Santé Canada

Canada

Conducting Clinical Trial Inspections During the Pandemic

Clinical Trial Compliance Program

Regulatory Operations and Enforcement Branch

Health Canada/Government of Canada

June 16, 2022

YOUR HEALTH AND SAFETY... OUR PRIORITY.

Objectives

- Overview of the Health Canada Clinical Trial Compliance Program (CTCP)
- COVID-19 impact and the management of clinical trials (CT) conducted in Canada during the COVID-19 pandemic
- Update on CTCP inspections (overview of the remote/hybrid/on-site inspection approach in Canada)
- Key lessons learned
- Future CTCP plans

CTCP mandate under the *Food and Drugs Act*

- Promotes and verifies compliance of drug clinical trials (CT) against the *Food and Drugs Act* and its associated Regulations.

  - Particularly Part C, Division 5: “Drugs for Clinical Trials Involving Human Subjects” which include the principles of Good Clinical Practices (GCP) to:

    - Protect subjects enrolled in clinical trials; (reduce risks to subjects enrolled in clinical trials and strengthen the protection of rights and safety of trial participants); and

    - Increase confidence that the data collected and subsequently submitted to Health Canada is valid.

- Authority to inspect under Section 23 of the *Food and Drugs Act.*

Health Canada – Clinical Trial Compliance Program (CTCP)

CTCP scope and activities

- Inspection of on-going trials at qualified investigator (QI) sites.
- System-based inspections of sponsors, CROs & SMOs (cyclical inspection approach).
- Bioequivalence trial inspections (clinical and lab sites), open/active or closed.
- CT inspections in support of a drug submission, in Canada or at a foreign site.
- For-cause inspection: compliance verification (and investigations)
- Compliance readiness inspections (COVID-19 related trials)
- International collaboration/coordination
- Compliance promotion: publication of guidance documents and delivering training sessions at stakeholders events.

Impacts of the pandemic

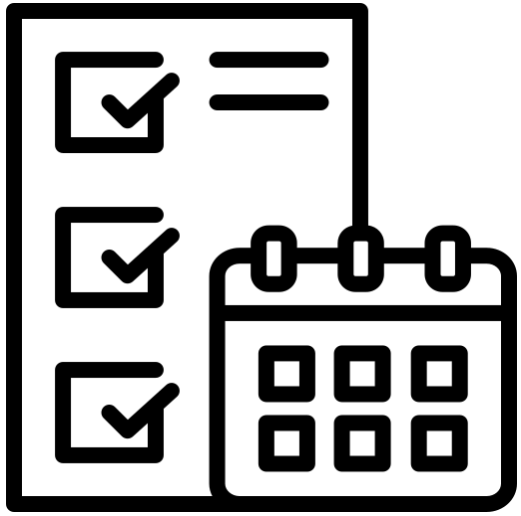
- The regulated parties most impacted were qualified investigator (QI) sites that are mainly hospital or clinic-based.

- The program limited hospital/clinic on-site inspections since:
  - some sites becoming COVID-19 centres
  - travel restrictions, physical distancing of both regulatees and regulators made it challenging to continue with on-site inspections.

- The conduct of clinical trials (CTs) at QI sites was also impacted.

During the pandemic

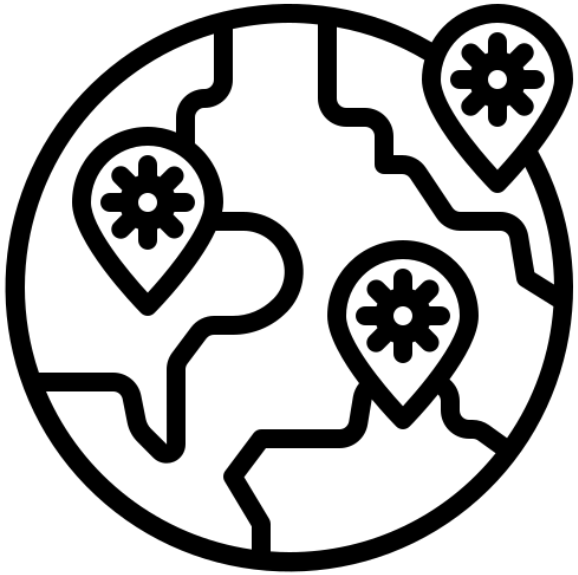
- CTCP continued to maintain regulatory oversight by conducting:
  - Compliance verifications (e.g. complaints)
  - Regular outreach & response to inquiries
  - Compliance monitoring projects
  - Update and review of quality documentation
  - Advancing initiatives
  - Remote inspections



During the pandemic

Continued participation in international committees and branch working groups:

- **PIC/S**
  International collaboration/consultation on pandemic inspection approaches
- **Digital Transformation**
  e.g., International Coalition of Medicines Regulatory Authorities (ICMRA)
- **CT Interim Order**
- **Notice to Stakeholders** (management of CTs during the pandemic)
- **Clinical Trial Modernization**



During the pandemic (continued)

Adaptations and/or new activities & their impacts

- CT Interim Order (IO) 1, CT IO 2, transitions regulations and associated guidance documents.
    - IO 1 and 2 provides a more flexible authorization and implementation pathway for the clinical trials of drugs and medical devices used to diagnose, treat, mitigate or prevent COVID-19 in people.
    - The provisions of IO No. 2 expired on May 3, 2022 and is replaced by the Transition Regulations, which came into force on February 27, 2022.
    - The Regulations maintain the flexibilities set out by the interim order until the framework established through the Clinical Trials Modernization Initiative is in place.

During the pandemic (continued)

Adaptations and/or new activities & their impacts

- Adapted compliance promotion activities heavily focused on adjustments in the conduct of CTs during the pandemic.
  - Enabled regulated parties to continue their operations and ensured safety requirements continued to be met while allowing flexibilities where possible.
- Developed and implemented compliance readiness inspections (CRI) for COVID-19 CTs.
  - Regulated parties better prepared to meet requirements before starting trial and reduced likelihood of non-compliance.

During the pandemic (continued)

Adaptations and/or new activities & their impacts (continued)

- Engaged our international partners to discuss their approaches, alternatives and to share practices.
  - acquired best practices and identified suitable approach
- Developed and implemented a phased approach for remote inspections during the pandemic, with a view to inform future transformation.
  - enabled oversight over certain regulated parties while on-site inspections were challenging
- Not all regulated parties can accommodate a remote inspection due to:
  - paper-based business documents (i.e., records)
  - limited IT capabilities

Management of CTs during the COVID-19 pandemic

Health Canada is aware of the impact of the pandemic on the conduct of clinical trials, including the need for:

- participants to self-isolate
- deployment of healthcare personnel involved in clinical trials to other duties during this public health emergency, resulting in delays in completing certain tasks

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Canada.ca > Coronavirus disease (COVID-19) > COVID-19 health product industry

Interim Order No. 2 Respecting Clinical Trials for Medical Devices and Drugs Relating to COVID-19

Whereas the Minister of Health believes that immediate action is required to deal with a significant risk, direct or indirect, to health, safety or the environment;

Therefore, the Minister of Health, pursuant to subsection 30.1(1) [a] of the *Food and Drugs Act* [b], makes the annexed *Interim Order No. 2 Respecting Clinical Trials for Medical Devices and Drugs Relating to COVID-19*.

Ottawa, May 3, 2021

Patricia Hajdu
Minister of Health

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Canada.ca > Departments and agencies > Health Canada > Drugs and health products > Drug products > Drug product announcements

Management of clinical trials during the COVID-19 pandemic: Notice to clinical trial sponsors

From: Health Canada
Updated: May 6, 2021

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Overview

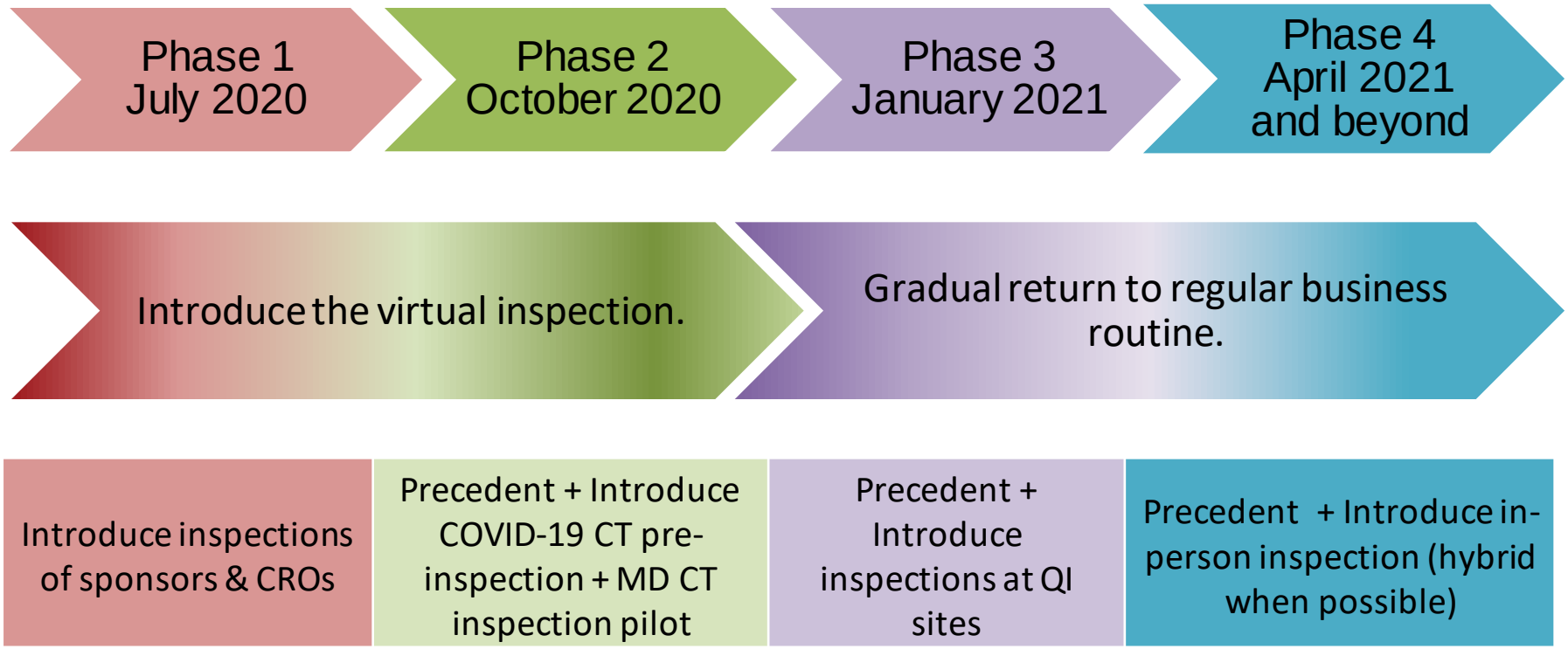
Management of CT during the COVID-19 pandemic (continued)

- Several compliance promotion events to help the industry to adjust.
- Provide guidance when written consent is not possible at the time. *electronic consent or non-written informed consent (verbal)*
- Dialogue with regulated parties to ensure the on-going safety of trial participants.

- Guidance and additional flexibility for shipping clinical trial investigational products (IP) directly to participants.
- Guidance on virtual visits. *alternative methods for safety assessments if participants will not be able to come to the investigational sites as specified in the study protocol.*
- Guidance on protocol deviations.
- Guidance on monitoring. *remote monitoring, central monitoring of clinical trials (ICH E6) and/or amending the monitoring plan*

CTCP remote inspection approach

- CTCP developed and implemented a remote inspection approach to adapt to the pandemic situation and to minimize the impact of the COVID-19 pandemic on its everyday activities.



CTCP remote inspections: benefits & challenges

Benefits

- Increased flexibility - inspectors could manage own inspection schedule, with no travel or exposure to COVID-19.
- Enabled continued oversight over regulated parties.
- Some cost savings (no travel expenses).

Challenges

- Challenges with the use IT for both the department and regulated parties

  For example to ensure secure sharing of information.
- Inability to pick up on non-verbal cues/body language which can re-direct the inspection to identify areas of non-conformances.
- Limited equipment made it difficult to navigate multiple documents and cross reference information.

CTCP: remote inspections – lessons learned

- There is value in adopting elements of remote inspections post-pandemic; including conducting hybrid inspections.
- Adequate computer equipment and effective applications for communication and file sharing are essential to the success and efficiency of remote inspections.
- Remote inspections are not the best approach for the following types of inspection activities:
  - QI sites often times are not IT enabled
  - source documents with personal & confidential medical data are paper based at most of these sites
  - limited IT tools and platforms for reviewing source documents that contain confidential personal information

Looking towards the future for CTCP

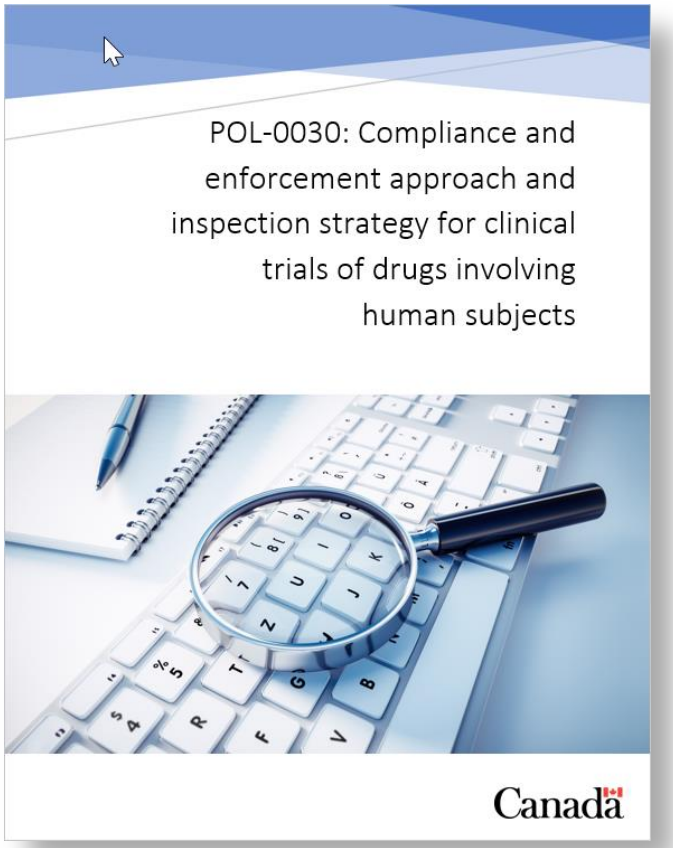
- Prioritization exercise for sites to inspect this fiscal year and modality of inspection to be explored.
  - A hybrid inspection model is being used this fiscal year to identify best options by type of regulated party and/or type of inspection.
  - Resume on-site inspections once possible: priority will be given to establishments that could not be inspected remotely during the pandemic.
  - Expansion of scope for compliance readiness inspections (not just COVID-19 trials).

Looking towards the future for CTCP (2022-2023 and beyond)

- Incorporation of medical devices investigational testing (MDIT) and natural health products (NHP) inspections into CTCP's inspection program cycle.
- System-based inspections (sponsor/CROs/SMOs) cyclical approach – 5 year cycle.
- Amendments to the *Food and Drug Regulations*, the *Medical Devices Regulations* and the *Natural Health Products Regulations.*
- Proposed CT modernization regulations for public comments.
    - Canada Gazette I (CGI)
- Publication of the final regulatory amendments for the CT modernization.
    - Canada Gazette II (CGII)

Other important information – POL-0030

- Final version of POL-0030 (v3): Compliance and enforcement approach and inspection strategy for clinical trials of drugs involving human subjects was published on HC's website in November 2021.



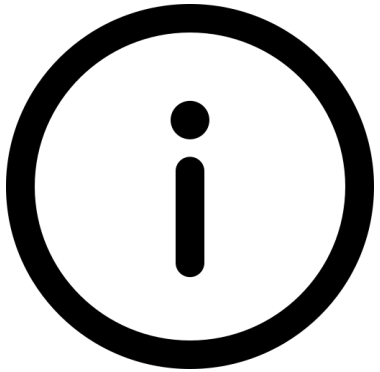
Other important information – GUI-0043

- The final version of GUI-0043 will be published in the summer of 2022.
- HC collected feedback from stakeholders on December, 2021.

Other important information

The regulatory initiative about alignment of CT records retention timelines (from 25 years to 15 years) for all CTs of drugs (and NHPs) involving human subjects was announced online on April 1, 2021 and has been implemented on February 11, 2022:

https://www.canada.ca/en/health-canada/services/clinical-trials/notice-period-reduced-keeping-records-drugs-natural-health-products.html



The publication of the regulatory proposal in the Canada Gazette (CG), Part II was expected in fall 2021.

Other important information

- “Health Canada's Clinical Trials Regulatory Modernization Initiative” (consultation from May 20, 2021 to July 4, 2021)

  - Information can be found on the consultation webpage: https://www.canada.ca/en/health-canada/programs/consultation-clinical-trials-regulatory-modernization-initiative/document.html

  - A reference to the consultation paper, which outlines key policy proposals for the modernization of Canada’s clinical trials regulatory framework: https://www.canada.ca/en/health-canada/corporate/about-health-canada/legislation-guidelines/acts-regulations/forward-regulatory-plan/plan/modernization-regulation-clinical-trials.html

- A “What we heard” report summarizing the discussions and comments received was published February 2022.

THANK YOU!

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Further information available online at:
www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-clinical-practices.html

Questions?