CLINICAL TRIALS ONTARIO

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July 4, 2021

Bureau of Policy, Science and International Programs
Therapeutic Products Directorate
Health Products and Food Branch
Health Canada
Ottawa, ON K1A 0K9

To Whom It May Concern:

This letter is in response to Health Canada's request for input called "*Consultation: Health Canada's Regulatory Modernization Initiative*." This submission has been prepared by Clinical Trials Ontario (CTO) with input from and on behalf of the organizations that appear after this letter's signature line. CTO is an independent not-for-profit organization established with support from the Government of Ontario. CTO's mandate is to work together with the clinical trials community, the public, and other partners to improve Ontario's clinical trials environment. Since 2012 we have been carrying out our mandate with one of our three strategic pillars being patient and public engagement. We believe engaging patients and the public is critical to improving the environment for clinical trials in Ontario (and Canada) and will result in better clinical trials, better experiences for trial participants, better physician-researcher experiences, and in the long run, a better health care system.

Along with this letter we have included our collective input and response to this consultation by answering the consultation questions that we feel are most appropriate to patients and the public, that is, those communities most represented by the signatories of this letter. To make our response approach straightforward, we have maintained the original consultation question numbering and wording as headings with our collective input and responses to these questions directly below them. We invite Health Canada to have a conversation with the signatories on this submission to further discuss the responses we have provided to further inform its next steps. CTO would be pleased to organize this virtual conversation in the coming months.

In closing, we appreciate the opportunity Health Canada has provided to submit this input to its Clinical Trials Regulatory Modernization Initiative. We look forward to continuing to work with the clinical trials community, including patients, patient organizations, and health charities to help bring their perspectives to the modernization of regulations of clinical trials in Canada.

Sincerely,

Susan Marlin, MSc
President and CEO

Dawn Richards, PhD
Director of Patient and Public Engagement

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And on behalf of:

BioCanRx
Brain Tumour Foundation of Canada
Canadian Arthritis Patient Alliance
Canadian Association of Psoriasis Patients
Canadian Breast Cancer Network
Canadian Cancer Survivor Network
Canadian Council of the Blind
Canadian PKU and Allied Disorders
Canadian Psoriasis Network
Canadian Skin Patient Alliance
Canadian Spondylitis Association
Colorectal Cancer Canada
Colorectal Cancer Resource & Action Network
Cystic Fibrosis Canada
Fighting Blindness Canada
Huntington Society of Canada
Life Saving Therapies Network
Myeloma Canada
Save Your Skin Foundation
Sickle Cell Awareness Group of Ontario
Skin Investigation Network (SkIN) Canada

/attachment follows

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Consultation Responses

Here we provide our collective response to questions posted at https://www.canada.ca/en/health-canada/programs/consultation-clinical-trials-regulatory-modernization-initiative/document.html.

1. *Please indicate which type of stakeholder you represent/identify with the most:*

   This response has been put together by Clinical Trials Ontario, an independent not-for-profit organization, and in collaboration with health charities, patient organizations, and two research networks.

2. *What describes your clinical trial activity (select all that apply):*

   Respondents involved in this submission primarily represent patient/participant and public perspectives, while two organizations involved are research networks that support clinical research.

3. *What health product line(s) do you or your organization represent or conduct trials for or are interested in? (select all that apply)*

   Respondents involved in this submission primarily represent patient/participant and public perspectives, while two organizations involved are research networks that support clinical research. Respondents are interested in clinical trials for drugs, medical devices and natural health products.

4. *Do you anticipate any benefits or impacts of the following proposals for your organization?*
   a. The agile life-cycle approach
   b. The single authorization for multiple products
   c. The risk-based approach
   d. The use of terms and conditions on a clinical trial authorization
   e. Decentralized trials

   The *agile life-cycle approach* would provide the opportunity for regulation of new types of innovative trial designs (e.g. basket trials, umbrella trials, platform trials) and future variations. Given that these types of clinical trials are very new and innovative, we are interested in learning more about how Health Canada plans to engage expertise to review these types of trials and to potentially train its staff in these areas. Providing Canadian participants with potential access to these types of clinical trials is important while ensuring participant safety.

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The *single authorization for multiple product types* may have the potential to increase efficiencies on a number of fronts for trials that include multiple health products from different categories (for example, drugs, natural health products and medical devices). Efficiencies related to streamlining the application, amendment, and authorization processes for these types of trials would potentially mean fewer delays in starting the trial and also equates to reducing the potential time for Canadians to access these health products.

The *risk-based approach* would stratify trials in to different categories based on potential risk (a term for which we would appreciate a formal definition) as determined by known information on products and therapies and hence their potential risk. As proposed, these changes would appear to have Health Canada focus its oversight and resources to areas with the greatest potential levels of risk, uncertainty and safety information. From a potential participant perspective, this would allow flexibility and efficiency of clinical trial start and conduct where the most is known about interventions (for example, when a well-known product of standard of care is involved).

For many individuals, *decentralized trials* may present an opportunity to more easily participate in clinical trials rather than traditionally-conducted clinical trials. From an equity perspective, decentralized clinical trials may help alleviate some burdens of participation and allow participants be part of studies no matter where they live in Canada (urban, rural, etc.) and while maintaining responsibilities related to their work, social, and family obligations, etc. Some of the signatories on this response have been involved in and are supportive of the Canadian Cancer Clinical Trials Network's Canadian Remote Access Framework for Clinical Trials (CRAFT), an effort in which we also know Health Canada is engaged. Further, in the winter of 2021, CTO engaged members of its College of Lived Experience (Ontarians who represent a range of lived experience; many of who live with conditions themselves or have loved ones who do) in a series of workshops about decentralized clinical trials, in which they expressed enthusiasm for what decentralized clinical trials may offer for potential participants. An important concept related to decentralized trials is the opportunity for choice in terms of participation, technology use, and potential site visits. Feedback also included that for site visits that might occur in one's own home, participant safety (with respect to having a stranger in the home) is also important.

5. Based on your experience and knowledge, would the proposals in the Consultation Paper meet Health Canada's goal of enabling innovative clinical trials in Canada?

From a potential participant perspective, the consideration of the approaches cited in question 4 above, represents a move to adopt new and more innovative approaches to clinical trials and their oversight, along with commitment to participant safety, in Canada.

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While the COVID-19 pandemic has necessitated a number of temporary changes to the conduct of clinical trials through two Interim Orders, the reflection on a potential more permanent change to clinical trials in Canada post-pandemic is appreciated. On many fronts, these proposed changes appear to increase efficiency and potentially streamline many aspects related to clinical trial operations and start up. They also outline a focus on ensuring participant safety based on known risks and risk-profiles of products/therapies.

6. Are there innovations or other future considerations that Health Canada should account for when modernizing the clinical trials framework?

Many organizations and regulators are encouraging work with patients as partners – either through their own work or through developing frameworks for others to consider and use for doing this. While Health Canada engages patients and the public through these types of formal submissions (and in other ways), we would encourage Health Canada to include language and guidance related to patient engagement with clinical trials and more formally in its own work. In the US, the FDA works collaboratively with patient organizations through its own initiatives such as the Patient Focused Drug Development initiative or through its work with the Clinical Trials Transformation Initiative (CTTI) related to Patient Group Engagement. In Europe, the European Medicines Agency has a website and framework dedicated to detailing its work and collaborations with patient organizations. We encourage Health Canada to look to its international regulator peers in the area of patient engagement – both in terms of its own work and in terms of encouraging the Canadian clinical trials community to engage with patient organizations and health charities.

We have submitted previously via Health Canada to calls for input from the International Council on Harmonisation (ICH) about their efforts related to patient engagement. As part of modernizing the clinical trials framework, we would appreciate Health Canada providing more guidance in this emerging area or in working with CTO and the signatories on this letter who have done significant work in this area. For example, many of the organizations contributing to this submission have been involved in work led by Colorectal Cancer Canada related to "Canadianizing" the CTTI Patient Pathways Model for drug development and approval. CTO also has a number of resources available on its website related to engaging patients as partners in the clinical trial process. CTO and many of the organizations that are signatories on this letter would be pleased to work with Health Canada in a collaborative manner on such guidance and would also be pleased for Health Canada to better highlight its support of ICH related work in this specific area, especially as ICH develops a framework related to patient engagement.

We wish to highlight that outside of decentralized clinical trials, there may be other important considerations about accessibility for participants for Health Canada and sponsors to consider. These may include ensuring that investigational products are fully accessible

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from the start with respect to individuals who live with sight loss or print or other disabilities. For example, in the investigational medical device area, this may include ensuring there is an audio option for participants (e.g. which provides an audible read-out to participants using the investigational device). With respect to other investigational products, it may include labeling and font size considerations.

9. Are there other areas where burden can be reduced that will better enable your organization to conduct clinical trials without compromising patient safety?

See our response to question 6 above related to engaging patients in the design and conduct of clinical trials.

10. Are there areas where Health Canada could go further in modernizing the Canadian clinical trials regulatory framework beyond what is proposed in the consultation paper?

As mentioned above in question 6, we encourage Health Canada to demonstrate a greater commitment to encouraging patient and public engagement. CTO has been working over the past 5 years on many resources to help enable this type of engagement, many of which have been created with other signatories on this submission, including:

- The Patient-Focused Medicines Development Patient Engagement Quality Guidance – part of a global initiative to help organizations developing medicines to better engage patients as partners
- Patient Partner and Investigator Decision Aids – developed in collaboration with Dr. Monica Parry (University of Toronto) and other team members, including patient partners, health charities and patient organizations, to facilitated engagement as or of patient partners on clinical trials teams.
- The Canadian Patient Group Pathway Model – led by Colorectal Cancer Canada, a "Canadianized" version of the CTTI Patient Group Pathway Model.

Some members of our community have previously engaged with Health Canada via its former Office of Consumer and Public Involvement (OCAPI), and wish to see Health Canada re-establish this type of Office. While the current open invitations to submit input to Health Canada are appreciated, Health Canada is encouraged to develop communications and approaches that are specific to engaging patients and the public in its work. These approaches would include ensuring that files and submissions are in plain language to encourage engagement and understanding of the topics at hand, and might include townhalls, webinars, specific communications, etc.. Other Canadian agencies such as CADTH and INESSS have formal processes to engage patients and patient organizations in their work. Tailored events, input opportunities, etc., provide Health Canada an opportunity to

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understand patient and public needs and perceptions, which may be very different from those of its other stakeholders.

We wish to draw attention to the fact that the signatories of this letter are invested in ensuring their communities have access to new safe and efficacious therapies in a timely manner. Health Canada is asked to consider how their efforts related to modernizing the Canadian clinical trials regulatory framework are part of the larger overall landscape of access to these new therapies for Canadians. While clinical trials are one part of this process, there are numerous other processes and agencies [such as the Canadian Agency for Drugs and Technologies in Health (CADTH), Institut national d'excellence en santé et services sociaux (INESSS), pan Canadian Pharmaceutical Alliance (pCPA), to name a few] that contribute to access to new therapies, and Health Canada is asked to work closely with the other agencies to continue to streamline or create more efficiencies in these processes where possible. We are currently aware of some of the work that is happening with CADTH on parallel scientific advice, and encourage more of this type of collaboration between agencies.

We wish to note the importance of the concept of harmonization across international regulatory agencies, for example, through efforts lead by the ICH or others. We know that Health Canada is part of ICH efforts and have contributed our input to them in the patient engagement space, and encourage Health Canada to continue these efforts. Other harmonisation across regulatory agencies is an important aspect to ensuring that different therapies become available to Canadians as well, and we encourage and support Health Canada's continued work in harmonising its processes with those of other international regulatory agencies.

We would like to see Health Canada working collaboratively with its stakeholders to develop a common definition of Real World Evidence (RWE). A consistent systematic approach and process for collection, analysis and interpretation is required. These all become more important as processes are put in place to modernize the clinical trials regulatory framework. Given that these concepts and processes related to RWE also impact others and other agencies, we encourage Health Canada to engage data custodians and groups that have done much foundational work in this space such as the CanREValue collaboration (in which we know Health Canada has been engaged). With respect to the concept of RWE, we also wish to draw Health Canada's attention to an initiative that many of the signatories of this submission have also been involved, the Declaration of Personal Health Data Rights in Canada, which highlights eleven rights with respect to personal health data provided for research (and other) purposes.

We wish to draw Health Canada's attention to the need to create innovative ways for physicians to access therapies that have already been approved for clinical trials, but for which their patients (who live with life-threatening diseases) may not qualify because of

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strict eligibility criteria. Health Canada facilitating a patient-centric approach for physicians to gain access to therapies would offer a mechanism for patients to access investigative therapies when they have no other options, without them being part of a clinical trial. This concept is similar to what the FDA calls the Right to Try, and we encourage Health Canada to explore this as an option for Canadians to gain additional access to therapies.

11. Do you see value in implementing a new policy and/or regulation for registration and reporting of results for clinical trials conducted in Canada, investigating drugs, medical devices and natural health products?

Registration and reporting of results for clinical trials conducted in Canada contribute to the transparency and trust that patients and the public have both in Health Canada as a regulator and in sponsors and investigators conducting clinical trials. Transparency is a critical factor in working with patients and the public.

Other regulatory agencies have policies and guidance on these specific areas of registration and reporting results. The FDA has issued guidance on these topics and has even more recently issued guidance on when fines may be imposed for failing to report clinical trial results on www.clinicaltrials.gov. The EMA has regulations about registration and reporting results, and this year, the EMA released its clinical trial registry and warrants that with few exceptions, clinical trial results must be available within one year of a clinical trial being completed. In fact, within the EMA regulations, the following is stated: "*The sponsor should submit a summary of the results of the clinical trial together with a summary that is understandable to a layperson, and the clinical study report, where applicable, within the defined timelines*." We support having summaries of clinical trials in language that the public understands and feel this approach builds trust and engages patients and the public with clinical trials. Below, in our response to this same question, we provide an example of resources CTO built with its community to facilitate creation of lay summaries of clinical trials results. It should also be noted that part of transparency is reporting results of clinical trials that meet their endpoints as well as clinical trials that do not meet their intended endpoints. In addition to being important from a transparency perspective, reporting of these results contributes to scientific and medical knowledge. We wish to emphasize that these summaries must be separate from scientific publications which frequently result from clinical trials. While these publications are important, their highly technical and scientific language and often paywalls are barriers to their widespread use by patients and the public.

It is important for Health Canada to consider that Canadians who are interested in clinical trials should be able to access a Health Canada hosted site to search for clinical trials, find information related to contacting those conducting the clinical trials on that site, and also be able to go back to that site to learn about the trial results. Canadians already face a number potential burdens related to clinical trials – finding appropriate information about clinical

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trials and their results should not be one of them. One might argue, especially given the profile of COVID-19 vaccines and Health Canada's very public presence related to their data reviews and approvals, Health Canada is a more obvious source than pre-pandemic for Canadians to go to find information on clinical trials. Furthermore, it may not be necessary for Health Canada to build its own registry and database *de novo* and our community supports the use of Health Canada's resources to take advantage of what is already working and publicly available as opposed to putting resources in to efforts to create new resources. CTO worked with patients, health charities and patient organizations to create and launch a Clinical Trials Finder. This database pulls relevant information from www.clinicaltrials.gov, and its menu of searchable options plus its 'notification/subscription feature' are the result of working collaboratively with patients, patient organizations and health charities. The Clinical Trials Finder is updated daily and has seen brisk traffic since it was launched.

Posting of clinical trial results are important and learning more about how this might be done most beneficially for Canadians could be the topic of collaboration between Health Canada and patient organizations, health charities and others. As an example, CTO has worked with patients, patient organizations and health charities to develop templates for sponsors and investigators to share clinical trial results back to participants who wish to receive this information. The Participant Experience Toolkit provides free, editable templates in multiple formats (and in both Official Languages) to make providing plain language result summaries back to participants as easy as possible on organizations conducting clinical trials.

With all of these efforts, Health Canada is encouraged to ensure all Canadians can access results and any clinical trials database. For example, ensuring that font size can be adjusted, there is a built-in screen reader, etc., will be important for accessibility. We also encourage Health Canada to ensure that search engines can index these resources so they are easy to find for Canadians who are looking for them.