

GUIDANCE NOTES AND REGULATORY REQUIREMENTS FOR INFORMED CONSENT IN RESEARCH DURING A PANDEMIC: COVID-19

INTRODUCTION¹

The climate of uncertainty during a pandemic may present barriers to the objective evaluation of research-related risks and benefits by Research Ethics Boards (REBs) and potential research participants. Accordingly, the informed consent process during the COVID-19 pandemic is of paramount importance to help insulate potential research participants from therapeutic misconceptions that may arise from uncertainty and fear when a proven treatment is lacking.

Informed consent is “the process in which a competent individual authorizes a course of action based on sufficient relevant information, without coercion or undue inducement” (WHO, 2016). Thus, informed consent procedures must clearly delineate the differences between research participation and critical clinical care procedures. Research participants must be informed that the experimental intervention might not benefit them and might even harm them.

The concept of informed consent is not only an ethical imperative when conducting research, it is codified within the context of Health Canada Regulated Clinical Trials. Health Canada, as a standing member of the International Council on Harmonization (ICH), is committed to the adoption and implementation of all ICH guidances. The ICH guidance are incorporated into the Canadian regulations, and as such, incorporated ICH guidances are law and not guidance.

Informed Consent Definition in the Health Canada Regulations

Informed consent is defined as a process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate (ICH E6, 1.28).

Potential participants in a clinical trial have the right to know the foreseeable risks or inconveniences and expected benefits that are part of the study they are thinking about joining [ICH E6, 4.8.10 (g) and (h)].

Informed consent is central to the conduct of high-quality research with integrity that maintains the public trust and upholds the core ethical principles of respect for persons, concern for welfare, and justice (TCPS 2, 2018). This guidance document outlines important considerations and regulatory requirements when obtaining participant consent during the COVID-19 pandemic in a manner that preserves these essential principles in a time of uncertainty.

¹ Adapted from the World Health Organization Guidance for Managing Ethical Issues in Infectious Disease Outbreaks.

GUIDANCE NOTE #1: ISOLATION

The separation from family, physicians, and other support systems during isolation and quarantine may prevent potential research participants from discussing the risks and benefits of research with someone they know and trust. This may lead to the potential for undue influence and power-over relationships, making it more difficult for research participants to feel empowered to decline an invitation to participate in research. When possible, research teams should be aware of neutral services available to those in isolation or quarantine such as, translation, medical, psychological and social services, which may be deployed to ensure informed consent is freely provided and research participants understand research procedures, risks, and benefits.

GUIDANCE NOTE #2: CAPACITY TO CONSENT

The ultimate choice of whether to participate in clinical research where there is an unproven experimental intervention must reside with the potential participant. The potential participant may not currently have the capacity to consent. If the patient is unconscious, cognitively impaired, or too sick to understand the information, proxy consent should be obtained from a substitute decision maker (SDM). If the participant regains capacity at a later date, their consent should also be sought at the earliest opportunity.

GUIDANCE NOTE #3: CONFIDENTIALITY

During a pandemic, the rapid sharing of information is essential to inform a global response to contain a disease. It is essential that researchers inform potential participants about the circumstances under which their personal information might be shared with public health authorities and other bodies as part of informed consenting procedures.

GUIDANCE NOTE #4: GENERAL GUIDANCE – PROCESS FOR OBTAINING CONSENT DURING A PANDEMIC

Potential participants should not be included in research without proper eligibility assessment and documented informed consent.

Due to the community spread of COVID-19, all researchers must carefully determine alternate consenting procedures that balance the need to prevent further transmission of the illness while also ensuring that the obligation to obtain prospective informed consent is met.

Currently all non-essential research procedures are suspended at British Columbia's Health Authorities to prevent disease transmission and maintain the ability of the health care system to respond to the COVID-19 pandemic.

In certain circumstances, an alteration of normal consent procedures (e.g., a waiver of consent) may be justified. Such alterations must be appropriately justified in the protocol and approved by the REB prior to implementation. Researchers should consult Article 3.8 Consent for Research in Individual Medical Emergencies of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans for further information on when such an alteration would be justifiable.

GUIDANCE NOTE #5: SPECIFIC GUIDANCE FOR HEALTH CANADA REGULATED TRIALS – PROCESS FOR OBTAINING CONSENT DURING A PANDEMIC

Applicable Regulations

The ICH Good Clinical Practice current version of the ICH guidance *Integrated Addendum to E6 (R1): Guideline for Good Clinical Practice E6(R2)* provides a unified standard on GCP. It became regulation in July 2001, the newest version of ICH E6(R2) was adopted by Health Canada in May 25, 2017 and fully implemented as of April 3, 2019. This applies to clinical trials for biologics, pharmaceuticals, radiopharmaceuticals, natural and non-prescriptive health products, combination products. GCP is cross-referenced in the Medical Device Regulations which applies to all Class II to IV devices including but not limited to test kits.

The Canadian Food and Drug Regulations (FDR) clearly establish that the sponsor has the overall responsibility for conducting a clinical trial in human subjects, including that the clinical trial be conducted in accordance with GCP [FDR C.05.010(a) to (j)].

Informed Consent Process

C.05.010 (h) written informed consent, given in accordance with the applicable laws governing consent, is obtained from every person before that person participates in the clinical trial but only after that person has been informed of:

(i) the risks and anticipated benefits to his or her health arising from participation in the clinical trial, and

(ii) all other aspects of the clinical trial that are necessary for that person to make the decision to participate in the clinical trial;

The risks and inconveniences should not outweigh the anticipated benefits when participating in a trial (ICH E6, 2.2). The rights, safety and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society (ICH E6, 2.3).

A clinical trial subject cannot be involved in any aspect of a clinical trial until he/she has gone through the ICF process, either in person or remotely, with a trial staff member (doctor, study nurse, clinical trial coordinator, etc.)

A qualified physician should be available to answer any medical questions that the subject may have regarding his/her participation in the study.

The original, and all amended ICFs and any other written information to be provided to subjects, must be approved by a REB prior to being presented to trial participants (ICH E6, 4.8.1).

Informed Consent Process Considerations for Qualified Investigators conducting COVID-19 Clinical Trials

For researchers conducting COVID-19 clinical trials, suggested considerations related to informed consent procedures include:

1. Documentation of any changes to the consent process should be maintained in the investigative site file and/or master study file. All documentation must be dated, signed with approval and clearly labelled with COVID-19 in the header.
2. Consent procedures should be approved by the REB and must be in compliance with Health Canada and the International Council for Harmonization. See references below.
3. To prevent transmission of COVID-19, written consent should be avoided, as shared pens and paper may be contaminated and Personal Protective Equipment (PPE) should be preserved for frontline health care workers' use. Potential solutions include;
 - a. consent obtained by electronic methods – This method could be considered if the technology is available. Electronic consent must be established in the environment and must meet the record keeping and validation requirements.
 - the system must be properly validated (ICH E6, 5.5.3), with documented procedures and appropriate training
 - all required elements (C.05.010(h); ICH E6, 4.8.10) must be present in the ICF
 - the information must be kept for 25 years [C.05.012(4)]
 - the process for obtaining informed consent using an electronic form should also be well detailed in an SOP
 - b. consent obtained orally by phone or videoconference – The research team obtains the participant's phone number and arranges a three-way call or video conference with the patient, an impartial witness, and if desired and feasible, additional participants requested by the patient, (e.g. next of kin). This process must be documented
 - c. consent obtained by email - consenting documents should be sent to participants/SDMs electronically by email for review, return with authorization/and witness and a return research team signed version for their records.
 - d. consent withdrawn by the participant – This may be done without written notification and should be documented by the research team in the participant notes section of the investigative site file.
4. The QI must have a written SOP in place for obtaining the informed consent or alternatively a quality deviation can be written on the existing SOP to describe the interim procedure that is in place. Procedural deviations must include: author, date, effective date, planned or unplanned deviation status, description of the deviation, impact on other procedures or forms and a dated authorization.

5. The clinical trial site personnel to whom the consenting process is delegated to by the Qualified Investigator, must be trained on the new process and have documented demonstrated skill in complying with the SOP or written Quality SOP deviation. (The training must be fully documented with assurances that the skills to perform the consenting process have been fulfilled)

6. The changing pandemic environment may impact the clinical trial. Participants should be made aware of important new information as soon as it becomes available, as it may affect their willingness to participate. The new information should be explained to the participant or the participant's legally acceptable representative in a timely manner, especially if the new information can have an immediate impact on the participant's health.

7. Health Canada expects that sponsors can demonstrate that the subject has understood the entire informed consent document(s).

8. In obtaining and documenting informed consent during the COVID-19 pandemic, the qualified investigator should still comply with the applicable regulatory requirement(s), and adhere to GCP and the ethical principles that have their origin in the Declaration of Helsinki (ICH E6, 4.8.1)

9. In emergency situations (As per section 4.8.15 of ICH E6), when prior consent of the subject is not possible, the consent of the subject's legally acceptable representative (as defined by provincial requirements), if present, should be requested. When prior consent of the subject is not possible, and the subject's legally acceptable representative is not available, enrolment of the subject should require measures described in the protocol and/or elsewhere, with documented approval by the REB, to protect the rights, safety and well-being of the subject, and to ensure compliance with applicable regulatory requirements.

The subject or the subject's legally acceptable representative should be informed about the trial as soon as possible and consent to continue and other consent as appropriate (see ICH E6, 4.8.10) should be requested.

Additional Note: *Additional guidance on the informed consent document and the process of obtaining the informed consent for Clinical Trials can be found through ICH E6 (section 4.8), the current version of the [Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans \(TCPS2 2018\)](#), in particular chapter 3, and/or obtained from the local REB approving the study.*

Record Keeping and Documentation

Record keeping including documentation of the informed consent must comply with regulatory requirements of section C.05.012 of the FDR. The collection and maintenance of clinical trial records, including the retention of records, is a critical component of any clinical trial. There is responsibility to ensure that trial information is recorded, handled and stored in a way that allows its accurate reporting, interpretation, and verification (ICH E6, 2.10). Documentation should follow 'ALCOAC' principles: *attributable, legible, contemporaneous, original, accurate and complete.*

Summary

Health Canada recommends that REBs overseeing clinical trials in Canada operate according to well established and recognized standards such including the ICH E6, the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2 2018) and provincially established standards and interpretive documents (Health Canada Guidance 0100).

References

Canadian Food and Drug Regulations

https://laws-lois.justice.gc.ca/eng/regulations/c.r.c.%2C_c._870/index.html

Amendment 1024 to the Food and Drug Regulations

<https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-clinical-practices/regulations/amending-food-drug-regulations-1024-clinical-trials.html>

Health Canada Guidance 0100

<https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-clinical-practices/guidance-documents/guidance-drugs-clinical-trials-human-subjects-gui-0100/document.html#c05010>

Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2) 2018.

[Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans \(TCPS2 2018\)](#)

World Health Organization. (2016). Guidance for managing ethical issues in infectious disease outbreaks. World Health Organization. <https://apps.who.int/iris/handle/10665/250580>