HEALTH SCIENCES AUTHORITY

REGULATORY GUIDANCE

06 NOV 2020

CLINICAL TRIALS GUIDANCE

ELECTRONIC CONSENT

GN-IOCTB-14 Rev. No. 001

HSA
Health Sciences Authority

PREFACE

This document is intended to provide general guidance. Although we have tried to ensure that the information contained here is accurate, we do not, however, warrant its accuracy or completeness. The Health Sciences Authority (HSA) accepts no liability for any errors or omissions in this document, or for any action / decision taken or not taken as a result of using this document. If you need specific legal or professional advice, you should consult your own legal or other relevant professional advisers.

In the event of any contradiction between the contents of this document and any written law, the latter should take precedence.

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SUMMARY OF AMENDMENTS

This section is not applicable.

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1. INTRODUCTION

1.1. Purpose

The purpose of this document is to provide guidance to sponsors and investigators on electronic consent (i.e. e-consent).

Please note that references to trial participants in this guidance also apply to legal representatives of trial participants who are minors or adults lacking capacity.

1.2. Background

1.2.1. **Overview of informed consent requirements**

Informed consent is a fundamental ethical and legal requirement in clinical trials. Freely given informed consent should be obtained from every trial participant prior to clinical trial participation.

The ICH[1] Good Clinical Practice (GCP) guidelines define informed consent as a process by which a trial participant voluntarily confirms his/her willingness to participate in a clinical trial after having been informed about all aspects of the clinical trial that are relevant to the trial participant's decision to participate.

The investigator is responsible for obtaining informed consent from the trial participant prior to clinical trial participation. The informed consent form serves as a tool to encourage open discussion between the investigator and the trial participant, and to document the consent. The investigator should ensure that adequate information about the clinical trial is provided to the trial participant for the trial participant to understand and voluntarily make an informed decision about clinical trial participation.

[1] International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

The informed consent process often continues beyond obtaining the trial participant's initial consent at the time of enrollment, and may involve providing additional information as the clinical trial progresses.

1.2.2. **Electronic consent (e-consent)**

Traditionally, paper-based informed consent forms have been personally signed and dated by the investigator, trial participant and impartial witness (where applicable) once the trial participant is agreeable to participate in a clinical trial. However, sponsors and investigators are increasingly embracing digital transformation by using e-consent to provide potential trial participants with information to decide on clinical trial participation and to document informed consent.

E-consent refers to the use of electronic systems and processes to:

(i) convey information related to the clinical trial to obtain informed consent; and/or

(ii) document informed consent, via electronic signature / digital signature, using an electronic device such as a smartphone, tablet or computer.

E-consent may supplement the traditional paper-based approach or where appropriate, replace it. However, it is important to note that e-consent should not replace the informed consent discussion between the investigator, trial participant and impartial witness (where applicable).

E-consent offers a number of potential benefits, including:

(i) Improving, assessing and reinforcing the trial participant's understanding of the clinical trial;

(ii) Increasing work efficiencies for sponsors and investigators;

(iii) Improving quality through version control, audit trails and reduced non-compliances; and

(iv) Complementing risk-based monitoring through centralized monitoring and remote monitoring of informed consent processes etc.

Conversely, e-consent may pose certain challenges, including:

(i) Increasing costs, resources and time required to set up and maintain electronic systems;

(ii) Unfamiliarity and lack of experience of investigators and institutions in using e-consent platforms;

(iii) Reluctance in embracing digital transformation due to limited experience and discomfort by some populations of trial participants (e.g. illiterate / elderly / poor eyesight / impaired motor skills);

(iv) Possible incompatibilities with institutional policies for data protection, electronic signatures or digital signatures; and

(v) Needing to develop business continuity plans in the event of system failure or maintenance.

Regardless of the mode of informed consent implemented for clinical trials, sponsors and investigators should ensure the following:

(i) Rights, safety, well-being and privacy of trial participants are safeguarded;

(ii) Data security, confidentiality, reliability, integrity and quality are assured;

(iii) Basic principles of informed consent (i.e. information, comprehension and voluntariness) are assured;

(iv) Regulatory provisions for informed consent as specified in the applicable clinical trials regulations and ICH E6 GCP guidelines are complied with.

1.3. Scope

This guidance applies to clinical trials regulated by HSA, namely:

(i) Clinical trials of Therapeutic Products that are subject to the requirements for a Clinical Trial Authorisation (CTA) or a Clinical Trial Notification (CTN);

(ii) Clinical trials of Medicinal Products that are subject to the requirements of a Clinical Trial Certificate (CTC).

2. GENERAL CONSIDERATIONS FOR E-CONSENT

2.1. What are the regulatory requirements for e-consent?

2.1.1. Sponsors and investigators must comply with the regulatory requirements for informed consent as specified in the applicable clinical trials regulations and ICH E6 GCP guidelines.

2.1.2. Additionally, sponsors and investigators must comply with the Personal Data Protection Act (PDPA) for regulatory requirements on the collection, use and disclosure of personal data; and the Electronic Transactions Act (ETA) for regulatory requirements on the use of electronic signatures and digital signatures.

2.2. Is HSA approval required for the e-consent system?

2.2.1. HSA approval is not required for the e-consent system. However, sponsors and investigators should notify the Health Sciences Authority (HSA) of their e-consent system prior to implementation.

2.2.2. It is recommended that the following be submitted to HSA in the clinical trial application:

(i) Screen shots and/or demonstration video of the e-consent system;

(ii) E-consent materials that will be presented to trial participants (e.g. videos, web sites etc.) to convey information specifically related to the clinical trial;

(iii) Proposed e-consent process;

(iv) Measures in place to safeguard trial participant privacy and data security, confidentiality, reliability, integrity and quality for the e-consent system;

(v) Measures in place to safeguard trial participant privacy and data confidentiality during centralised monitoring / remote monitoring (if applicable).

2.2.3. Sponsors and investigators should notify HSA of subsequent changes to the e-consent system that may significantly impact trial participant privacy and data security, confidentiality, reliability, integrity and quality. Such changes should be submitted to HSA as amendment applications.

2.3. What information should be provided in the e-ICF?

2.3.1. Sponsors and investigators must ensure that the electronic informed consent form (e-ICF) contains all the elements of an informed consent form, as specified in the applicable clinical trials regulations and ICH E6 GCP guidelines.

2.3.2. The language should be as non-technical as practical and understandable to the potential trial participant, and conveyed in a manner that minimizes the possibility of coercion or undue influence regarding the trial participant's decision to participate in a clinical trial.

2.3.3. The e-ICF should be appropriate for the intended audience, taking into consideration the trial participant's age, language, and comprehension level.

2.4. How can the trial participant's understanding of the information presented in the e-ICF be enhanced, assessed and reinforced?

2.4.1. Sponsors and investigators may use the following interactive tools to enhance, assess and reinforce the trial participant's understanding of the e-ICF:

(i) Section views to allow content to be viewed in separate sections;

(ii) Electronic media such as diagrams, images, graphics, audio, video, narrations, websites etc.;

(iii) Glossaries to provide definitions to certain terminologies;

(iv) Call out boxes to reinforce key ideas in 1-2 sentences;

(v) Flags for trial participants to identify sections that require further clarifications;

(vi) Comment boxes for trial participants to document questions;

(vii) Self-assessment checklists or short questions about the clinical trial to assess trial participant's understanding of the information presented; and/or

(viii) Section-based attestation to allow trial participants to acknowledge understanding of specific sections.

2.4.2. Regardless of whether interactive tools are used, it is often the face-to-face communication between the investigator and the potential trial participant that will be the most effective way of improving potential trial participants' understanding of what is involved.

2.5. Who is responsible for obtaining e-consent?

2.5.1. The investigator, who is a qualified practitioner and delegated to obtain informed consent, is responsible for obtaining e-consent from the trial participant. He/she should conduct the informed consent discussion with the trial participant prior to personally signing the e-ICF.

2.6. Where should e-consent be obtained?

2.6.1. The e-consent may be obtained either:

(i) At the trial site where both the investigator and trial participant are present; or

(ii) Remotely via audio / video calls, where the investigator and trial participant are at different locations (i.e. remote consent). Refer to Section 2.11 for additional information on remote consent.

2.7. How should the informed consent discussion be conducted?

2.7.1. The purpose of the informed consent discussion is to ensure that the investigator has provided adequate information about the clinical trial to the trial participant for the trial participant to understand and voluntarily make an informed decision about clinical trial participation. Simply providing a potential trial participant with this information (whether by paper or electronic means) would not be adequate as the informed consent discussion requires a two-way communication in real time between the investigator and the trial participant.

2.7.2. The study staff should be trained on navigating the e-consent system. Training documentation should be maintained on file. Similarly, trial participants should be trained or given written instructions on navigating the e-consent system.

2.7.3. Sponsors and investigators should ensure that the correct version of the e-ICF that has been approved by the IRB and HSA (where applicable) has been uploaded into the e-consent system.

2.7.4. An impartial witness should participate in the informed consent discussion if the trial participant is unable to read or sign/date the informed consent form.

2.7.5. A translator should participate in the informed consent discussion if the trial participant is unable to communicate with the investigator in the same language.

2.7.6. The investigator should conduct the informed consent discussion in a conducive environment, respecting the privacy of the trial participant and confidentiality of the information being discussed. There should be no coercion or undue influence.

2.7.7. The trial participant should be given ample time and opportunity to ask questions about the clinical trial to decide on clinical trial participation. All questions should be answered in a satisfactory manner.

2.7.8. In situations where it may not be appropriate to use the e-consent for certain study populations (e.g. illiterate / elderly / poor eyesight / impaired motor skills), investigators should have the option to use paper-based or electronic informed consent methods completely or partially throughout the informed consent process. In such circumstances, it may be appropriate for investigators or study personnel to assist subjects in using the e-consent technology, such as navigating through the e-consent or clicking on the electronic media.

2.8. How should e-consent be documented?

2.8.1. E-consent may be documented on a hard copy or electronically.

2.8.2. In situations where information relating to the clinical trial is conveyed using electronic systems and processes, and the consent is documented on a hard copy, the hard copy of the informed consent form may be printed out for all relevant parties to personally sign and date. The study team may then upload the copy of the signed informed consent form in the e-consent system, as required.

2.8.3. In situations where information relating to the clinical trial is conveyed using electronic systems and processes, and the consent is documented electronically, all relevant parties may personally sign the e-consent via secure electronic signatures, in accordance with the Electronic Transactions Act (ETA). The e-consent system should also capture the date when the e-consent had been signed.

2.8.3.1. In accordance with the Electronic Transactions Act (ETA), an electronic signature (i.e. e-signature) is considered a secure electronic signature if it can be verified, through the application of a prescribed security procedure or a commercially reasonable security procedure agreed to by the parties involved, that the signature is:

(i) unique to the person using it;
(ii) capable of identifying such a person;
(iii) created in a manner or using a means under the sole control of the person using it; and
(iv) linked to the electronic record to which it relates in a manner such that if the record is changed, the electronic signature would be invalidated.

2.8.3.2. The ETA is intended to be technologically neutral and thus does not prescribe the specific technology to be used for secure electronic signatures.

2.8.3.3. In general, the secure e-signature that is adopted for the clinical trial should ensure that you can verify:

(i) that the persons who signed are who they say they are;
(ii) that the consent form they signed has not been altered; and
(iii) when the signatures were applied.

2.8.3.4. The following are examples of secure e-signatures that are considered to be acceptable for clinical trials:

(i) Signing using a finger / stylus on a touch screen if consent is conducted via face-to-face or video call where the identity of the trial participant can be verified;

(ii) Ticking a checkbox or clicking 'I accept' button via an electronic system or process that can uniquely identify the trial participant;

(iii) Digital signature.

It is not recommended to paste a digital image of a manuscript signature.

2.8.4. The investigator should document the e-consent process in the trial participant's source documents. Information on the protocol reference, informed consent date, informed consent process and provision of a signed copy of the informed consent form should be documented.

2.9. How should a copy of the e-ICF be provided?

2.9.1. The trial participant should receive a signed copy of the e-ICF.

2.9.2. The investigator may provide a soft copy or hard copy of the signed e-ICF to the trial participant.

2.9.2.1. If a soft copy of the signed e-ICF is provided to the trial participant, the investigator should consider sending it in a file format that allows limited and secure access and prevents unauthorised editing of the signed e-ICF.

2.9.2.2. If a hard copy of the signed e-ICF is provided to the trial participant, it is acceptable to exclude the interactive tools used to enhance, assess and reinforce understanding of the clinical trial

from the hard copy of the signed e-ICF. If the copy provided includes hyperlinks to information on the internet, the hyperlinks should be maintained and information should be accessible until study completion. The information in these hyperlinks should be included in any printed paper copy, if one is provided.

2.10. What should be done when new information becomes available?

2.10.1. When new information becomes available during the clinical trial, investigators should re-consent the trial participant if the new information may affect the trial participant's willingness to continue trial participation.

2.10.2. Sponsors and investigators may have the flexibility to use paper and electronic consent methods independently or in combination throughout the clinical trial.

2.11. What are additional considerations if e-consent is conducted remotely via audio / video calls (i.e. remote consent)?

2.11.1. Investigators may consider the following if e-consent is conducted remotely:

(i) Consult the institution (e.g. IT department) on the acceptable telemedicine software to be used for remote consent;

(ii) Ensure that the informed consent discussion is conducted in a secure manner, and adequate measures are in place to safeguard trial participant privacy and data confidentiality;

(iii) Provide a copy of the e-ICF to the trial participant to read before the informed consent discussion;

(iv) Verify the identity of the trial participant during the remote consent discussion (e.g. by checking an official photo identification);

(v) Ensure that all parties personally sign the e-ICF. The e-consent system should also capture the date when the e-ICF had been signed.

(vi) Document details of the remote consent process in the trial participant's source documents;

(vii) Retain the signed copy of the e-ICF (signed by all parties) on site in a manner that has secure and limited access and prevents unauthorised editing. The trial participant should also be provided a signed copy of the e-ICF in a similar manner.

2.11.2. If e-consent is used remotely for enrollment of new trial participants, an impartial witness should participate in the informed consent process regardless of whether the trial participant is unable to read or sign/date the ICF. The role of the impartial witness in this case would be to ensure that the identity of the potential trial participant has been verified and consent has been freely given.

2.11.3. If it is not possible to verify that the trial participant has personally signed the e-ICF (e.g. during an audio call), it would be recommended for all parties to sign the e-ICF via secure electronic signatures that uniquely identify the parties signing. Hence, it would not be recommended for all parties to sign the e-ICF using finger / stylus on a touch screen.

2.12. What are the additional considerations for privacy and data protection?

2.12.1. Prior to implementation, investigators should consult their institutions (e.g. IT department) to ensure that the e-consent system is in line with institutional policies for data protection and electronic / digital signatures.

2.12.2. Sponsors and investigators should ensure that e-consent system has secure and limited access and audit trail.

2.12.3. The personal data of the trial participant (e.g. name and email address of the trial participant) should be encrypted within the e-consent system. A reasonable and appropriately equivalent measure may be utilised if encryption is not possible. The sponsor and any third party should not have access to the personal data of the trial participant throughout the clinical trial and even after study completion.

2.12.4. In situations where the trial participant is required to create an account to access the e-consent system, the investigator should ensure that the personal data of the trial participant (e.g. name and email address) is not provided to the sponsor or other third parties due to privacy and confidentiality concerns.

2.12.5. Access to the e-consent system should be provided during monitoring, audits and inspections.

2.13. What are the additional considerations for centralised monitoring or remote monitoring of the e-consent system?

2.13.1. Sponsors are responsible for monitoring the e-consent system. Traditionally, this is done via on-site monitoring visits by a monitor. However, these may be supplemented with centralised monitoring or remote monitoring.

2.13.2. Sponsors and investigators should ensure the following for centralised monitoring or remote monitoring of the e-consent system:

(i) Build protection against potential issues that may lead to breach of confidentiality;

(ii) Identify areas of training and best security practices; and

(iii) Consider restricting access to data fields that may identify trial participants.

2.13.3. Monitors should not have any access to the personal data of the trial participant during centralised monitoring or remote monitoring. As it will not be possible to verify the identity of the trial participant through centralised or remote monitoring, sponsors should ensure that monitors verify the identities of the trial participants during on-site monitoring visits.

3. REFERENCES

(i) Health Products (Clinical Trials) Regulations
(ii) Medicines (Clinical Trials) Regulations
(iii) Personal Data Protection Act (PDPA)
(iv) Electronic Transactions Act (ETA)
(v) FAQs on the Electronic Transactions Act (ETA)
(vi) IMDA Guide to Adopting Electronic Signature Solutions
(vii) FDA Guidance on Use of Electronic Consent, Questions and Answers, Guidance for Institutional Review Boards, Investigators, and Sponsors - Dec 2016
(viii) MHRA Joint Statement on Seeking Consent by Electronic Methods
(ix) Transcelerate E-consent Implementation Guidance – Version 1.0

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