GUIDANCE FOR SPONSORS ON THE USE OF ELECTRONIC INFORMED CONSENT IN INTERVENTIONAL CLINICAL TRIALS IN BELGIUM

Document history:	
Supersedes:	*1.0*
Changes compared to superseded version:	*Section Informing the participant:* - *The right of the participant to refuse should be mentioned in the e-ICF.* - *Sentence added "It should be clearly mentioned in the (e-)ICF whether this interview occurs via a video conference or via a physical meeting."* *Section Signing the consent form:* - *The biometric e-signature is removed since this is not in accordance with GDPR.*

This guidance document (version 1.0) is developed by a working group (WG ICF) consisting of representatives of BAREC (Belgian Association of Research Ethics Committees), pharma.be (the Belgian association of the innovative (bio)pharmaceutical industry) and patient organizations, and was coordinated by the CT-College at the FPS Health, Food chain safety and Environment. The changes made to version 1.0 were requested by the College Board.

In general, the electronic Informed Consent Form (e-ICF) must at least provide the same information as the paper version. It can be an added value, as it can respond to the individual needs of the participant. The use of interactive video's and multimedia components may make the information of the ICF more digestible (Ref. 1). Some restrictions, however, should be taken into account and are mentioned below. These restrictions are also valid for the re-consent process.

In the text below, with the term "Informed consent form (ICF)" both the informative part (information leaflet) as the signature part (consent form) of the document is meant.

INFORMING THE PARTICIPANT

- Even when the sponsor provides electronic methods for informing the participant of a clinical trial, the latter has the **right to refuse and ask the investigator for a physical consent process with a paper version** of the ICF. This right should be mentioned in the e-ICF.

- Informing the participant in advance via electronic means (e.g. by e-mail, via an internet portal, …) should never replace a personal face-to-face interview with the investigator. This interview may, however, also be organized via a video conference, not a phone call. It should be clearly mentioned in the (e-)ICF whether this interview occurs via a video conference or via a physical meeting.

- In case the participant is informed via video conference, a statement must be added to the consent part of the ICF in which the participant declares he/she has understood all information given via the video conference and has had the opportunity to ask questions.

- A **trial site** always has the **right to refuse** an electronic information process, *i.e.* via video conference, with their participants.

SIGNING THE CONSENT FORM

- Identical to the signing of the paper version of the ICF, the signing of the e-ICF can only happen once the interview (face-to-face or by video conference) with the investigator has been performed. The investigator always signs the ICF last.

- The **participant** has the **freedom to choose** to give his/her consent by signing electronically (via e-ICF) or by signing a paper version of the (e-)ICF (Ref. 2).

- A **trial site** always has the **right to refuse** the electronic signing of the ICF by their participants.

- If the participant has the option to sign the ICF via electronic methods, this method has to be adapted according to the considered trial and the context of the consent process and adapted to the patient needs. E-signatures could involve participant's handwritten signature using a finger or a stylus under the condition that there is a table trail which makes it possible to demonstrate that the person making the electronic signature was indeed the participant (e.g. the check of the ID document of the person). This is a particular application for phase 1 trials during which participants are required to show official ID at every visits. If such a verification of the identity is **not** performed, an **advanced** or a **qualified electronic signature as defined in the eIDAS regulation** (Ref. 3) should be used as they uniquely identify the individual signing. Be aware that:
    - only a qualified electronic signature has the equivalent legal effect of a handwritten signature (eIDAS, art 25. §2.). Signatures via e-ID (Ref. 4) or itsme® (Ref. 5) are qualified electronic signatures.
    - the advanced signature should comply with the defined requirements as described in the article 26 of the eIDAS Regulation that give guarantees of the identification of the individual signing.

  More information is available on the website of the FPS Economy (Ref. 6).

- After signing of the e-ICF by both parties, the participant and the investigator, it must be ensured that the document/PDF is locked to avoid editing after signing. The properties of the electronic document/PDF must be audit trailed, to ensure traceability of when it was signed and locked.

ACCESS TO e-ICF AFTER SIGNING

- *Access by the participant:*
  If the participant and the investigator have signed the ICF via electronic methods, the participant will still receive a **printed** version and/or **electronic locked copy** of the signed and dated e-ICF.

- *Access by the clinical trial site:*
  The clinical trial site should have access to the ICF as a PDF of the signed document or as the e-signed PDF in order to archive it electronically on site for at least 25 years after the end of the trial.

SUBMISSION DOSSIER

- All documents and materials have to be submitted **in a format that allows to see how it will be provided to the participant** (including logos, images, photos, colours, videos, link to the web-based presentations, etc.) in order to allow the evaluating Ethics Committee to assess the e-ICF and the method used to obtain the electronic signature. As it should always be possible to print the ICF on paper, a PDF of the ICF needs to be provided as well.

- **Note**: For phase 1 trial sites that use a **standardized** e-ICF environment for different healthy volunteer trials, the e-consent materials template (including standard process flow, logos, images, photos, colours, videos, etc) will be submitted for Ethics Committee approval for the first trial using this informed consent process (Ref. 7). After Ethics committee approval of this e-consent materials template, for each following trial using the same standard templates, the submission dossier may only contain the trial specific (e-consent) materials of the ICF and the PDF of the entire ICF (including all information provided to the participant).

- The electronic informed consent process must incorporate procedures to ensure that electronic documents can be archived appropriately and that all versions of the approved e-ICF can be retrieved easily.

GDPR

- The e-ICF is to be **GDPR compliant** and e-ICF process **GCP compliant**. If the ICF is signed electronically, the sponsor will not be able to trace the identity of the participant. The persons that have access to the identity to verify the quality of the trial (the personnel designated by the sponsor, monitors and auditors, and people or organisations providing services for or collaborating with the sponsor , inspectors of competent health authorities worldwide, an independent audit group, people designated by the Ethics Committee) must be subject to professional secrecy or a confidentiality agreement.

- The electronic storage place of the signed e-ICF must be separate from the other results of the trial and under the responsibility of the investigator.

This guidance will be adapted in the future if deemed necessary, in function of new technologies being developed.

REFERENCES

[1] Informed Consent, N. Engl. J Med 376, 9, 856-867.

[2] Art.7. § 1. of the law of 21 July 2016 on the implementation and supplementation of Regulation (EU) No 910/2014.

[3] eIDAS regulation No 910/2014 of the European Parliament and of the council of 23 July 2014 on electronic identification and trust services for electronic transactions in the internal market and repealing Directive 1999/93/EC.

[4] FAQ N° 35 of the document with "Frequently asked questions on the trust services" to be found on the website of the FPS Economy, version 30/01/2018:
https://economie.fgov.be/sites/default/files/Files/Online/FAQ-vertrouwensdiensten.pdf or
https://economie.fgov.be/sites/default/files/Files/Online/FAQ-services-de-confiance.pdf

[5] The list of qualified trust services in Belgium is published each 4 months on the website of the FPS Economy (https://economie.fgov.be/nl/themas/online/elektronische-handel/elektronische-handtekening-en) and on the Trusted List Browser of the European Commission (https://webgate.ec.europa.eu/tl-browser/#/tl/BE/7)

[6] Website of the Federal Public Service of Economics, Electronic signature and other trust services:
https://economie.fgov.be/nl/themas/online/elektronische-handel/elektronische-handtekening-en

[7] With the first trial using this consent process, the first trial submitted in the CTR Pilot project and using this consent process is meant.