The Intensive Care Platform Trial (INCEPT)

Estonia



National appendix

National appendix version and date
Version 1.2 2026-09-02

Corresponding core protocol version and date
Version 1.5, 2026-04-01

Website: www.incept.dk

Applicable core protocol registration numbers
European Union Clinical Trials Information System (CTIS) EUCT number: 2024-516208-41-00.
ClinicalTrials.gov identifier: NCT06667999.
Universal Trial Number: U1111-1313-8171.

Table of contents

1 | Administrative information 3
1.1 | Protocol and national appendix structure 3
1.2 | National coordinating centre 3
2 | Abbreviations 4
3 | Screening, inclusion, and informed consent procedures 5
4 | Discontinuation and withdrawals 8
5.1 | EQ-5D-5L value set 9
5.2 | Safety outcomes 9
6 | Other considerations 10
7 | Summary of changes 11
8 | References 12

1 | Administrative information

1.1 | Protocol and national appendix structure

This is a national appendix to the *Intensive Care Platform Trial (INCEPT)* core protocol. Everything described in the version of the core protocol listed on the front page applies except where explicitly stated otherwise. This national appendix only covers details that are specific to this country and not otherwise covered by the *INCEPT* core protocol. The national appendix should be read along with the core protocol.

1.2 | National coordinating centre

National coordinating centre
Clinical Research Centre & Anesthesiology and Intensive Care Clinic
Tartu University Hospital
Puusepa tn 8, 50406 Tartu, Estonia
Phone: +37259000110
Email: hannakadri.laas@kliinikum.ee

A list of national coordinating investigators in all participating countries will be made available on the *INCEPT* website prior to first inclusion in each country and continuously updated.

2 | Abbreviations

CTIS: *Clinical Trials Information System*
eCRF: *electronic case report form*
EU: *European Union*
EUCT number: *European Union Clinical Trials Information System (CTIS) number*
ICU: Intensive care unit
GCP: *Good Clinical Practice*
HRQoL: *health-related quality of life*
INCEPT: *the Intensive Care Platform Trial*

3 | Screening, inclusion, and informed consent procedures

The following section contains specific procedures that apply for Estonia in addition to the generic principles outlined in the core protocol, including the use of a modular approach to the informed consent procedure with information only given for the domains that are relevant for a specific participant.

Estonian informed consent procedure

INCEPT facilitates the rigorous evaluation of interventions used in critically ill adults. The *INCEPT* platform trial primarily focuses on interventions that are already in common clinical use but for which practice varies between clinicians. However, other interventions may also be evaluated. Enrolment into *INCEPT*, including all trial domains, will occur without prior informed consent in accordance with the trial protocol and the criteria in the applicable EU Clinical Trials Regulation (No 536/2014) [1]. The justification for the use of emergency situation clinical trial procedures is provided in section 8.5 of the core protocol.

First, ICU patients fulfilling all platform inclusion criteria and none of the exclusion criteria will be screened and randomised to domains for which they meet all domain-specific eligibility criteria by trained trial staff.
Following enrolment, informed consent for continued participation will be sought without undue delay and during the participant's active trial period. Efforts to obtain informed consent will continue while trial-specific interventions are ongoing and consent remains relevant to continued participation. Once all trial-specific interventions applicable to the participant have been completed and the participant's active participation in the trial has ended, the study team will not continue to contact or trace the participant or their representative solely for the purpose of obtaining retrospective informed consent. This does not preclude obtaining consent from the participant if they regain decision-making capacity while they remain under active study follow-up. Informed consent for continuation in the platform trial will be obtained from the participant's representative, if the participant is unable to consent. Informed consent from the participant will be obtained as soon as he or she is physically and mentally capable of receiving information about the trial and providing written informed consent. All informed consent for continued participation in the platform trial (including all applicable domains) will be obtained by trained medical doctors. Both oral and written information will be provided to the participant or their representative, preferably in person at the study site. If this is not possible (e.g. the representative lives abroad or in-person communication would cause delays), information may be provided via telephone or video call. Written consent may only be provided in person at the study site. Alternatively, electronic consent may be provided during a video call. The identity of the participant or representative will be verified during the video call and the consent form will be electronically signed using an accepted electronic identification and signature method.

In all cases, the participant or their representative will be encouraged to read the information thoroughly and will be given sufficient time to consider participation and to ask questions before signing the informed consent form.

Lack of informed consent from the participant's representative

If information about the participant's legally appointed representative is not available after inclusion, the investigator will make reasonable efforts to determine whether such a representative exists and can be contacted.

Reasonable attempts shall include:

1. Review of readily available medical records and other information available at the time of enrolment to determine whether a legally designated representative has been documented.
2. Where feasible, enquiry with accompanying persons or known relatives regarding the existence and contact details of a legally designated representative.
3. If a legally designated representative is identified and contact details are readily available, at least two attempts to contact the legally designated representative by telephone or another immediately available means.

Attempts to identify or contact a legally designated representative must not delay clinically indicated treatment and shall be documented in the participant's medical records or other appropriate study documentation.

If a representative is not identified and the participant remains unable to consent themselves, the trial intervention(s) will be continued. All initiatives to identify the participant's representative will be documented in patient files, logs or similar.

Patient relatives will be informed of the trial. Informed consent will be sought from the participant as soon as they regain the capacity to provide consent.

Lack of informed consent from the participant's representative and the participant deceases

If the participant deceases before informed consent is obtained (e.g. due to rapid progression of critical illness, absence or unavailability of a representative, or inability to identify a representative), the consent procedure will be stopped. If the participant has been correctly included in the trial and reasonable attempts to identify representative and obtain their informed consent have been made, the collected data will be kept and analysed, and additional data from the electronic patient record may similarly be collected and analysed.

Withdrawal

In the event of withdrawal from a trial intervention by the participant or their representative, all trial-related interventions within the withdrawn domains will be discontinued. The participant will continue to receive the best available care as determined by the treating physician. Data collected up to the point of withdrawal will be retained and used for trial purposes.

Participants who withdraw from a trial intervention will be asked whether they consent to continued data collection from electronic health records and follow-up contact for assessments of cognitive function and health-related quality of life.
Participants who withdraw from the trial entirely will be asked whether they consent to continued data collection from electronic health records and follow-up contact. If they do not consent, no further data will be collected and no further follow-up contact will take place.

Informed consent process

All consenting parties will receive both written and oral information about the platform trial (including all relevant domains) to enable an informed decision regarding participation. All written information materials and consent forms will be reviewed and approved by the relevant competent authorities (e.g. ethics committees).
The written information will be provided in a modular format, consisting of:

- general information about *INCEPT*, and
- additional information sheets for each relevant domain.

The informed consent process will be conducted jointly for *INCEPT* and all applicable domains. Explicit written consent will be obtained for each specific domain using separate consent forms. Consent to one or more domains will constitute consent to *INCEPT*, including all elements common across domains.

Documentation of consent

All consent forms will be signed by the consenting party and the medical doctor who provided trial information, in two copies:

- one copy retained in the investigator's file,
- one copy provided to the participant or their representative.

All informed consent procedures will be conducted by medical doctors trained and certified in the trial protocol and in accordance with all applicable regulations.
Efforts to identify or contact the participant or their representative will be documented in the patient records, trial logs, or equivalent documentation.

Trial personnel

The screening will be done by trained trial staff in collaboration with the treating clinical doctor, who ultimately decides if a patient can be enrolled in the trial and individual domains. When a candidate patient is identified, a member of the trained trial staff will screen the patients in the electronic case report form (eCRF). Collection of informed consent will be performed by medical doctors who are trained and certified in the trial protocol. If questions arise during the informed consent procedure, coordinating trial staff (including the sponsor) can be reached through the 24-h trial hotline. All medical doctors with consent functions in the *INCEPT* platform trial will be trained and approved according to *Good Clinical Practice* (GCP) guidelines before engaging in the trial.

4 | Discontinuation and withdrawals

The core protocol outlines the procedure for handling discontinuations and withdrawals in *INCEPT* according to the applicable Danish and Estonian regulations as well as EU Clinical Trial Regulation 536/2014 [1]. This legislation also applies for Estonia.

5 | Outcomes and safety

5.1 | EQ-5D-5L value set

For the EQ-5D-5L instrument [2] used to assess health-related quality of life (HRQoL) at day 180, we will use the Danish EQ-5D-5L value set [3] for participants enrolled in Estonia to calculate EQ-5D-5L index values for the primary analyses, as no Estonian value set is currently available.

5.2 | Safety outcomes

The *INCEPT* core protocol outlines the handling of safety outcomes in *INCEPT* domains based on European Union (EU) regulations [4] for the assessment of safety outcomes for pharmacological interventions (investigational medicinal products); this procedure applies to Estonia with no country-specific adaptations and no additional collection or reporting of additional safety data.

6 | Other considerations

Insurance

Trial participants covered under the national health insurance system in Estonia, are covered under the healthcare provider's existing liability insurance and the national patient protection system in accordance with the Health Insurance Act ("*Ravikindlustuse seadus"*) and Medicinal Products Act ("*Ravimiseadus*") [5,6]. This coverage applies to harm resulting from medical treatment, including participation in clinical trials, in accordance with applicable national legislation.

For participants who are not covered under the national health insurance system, additional insurance will be arranged by the platform sponsor to ensure equivalent protection in case of trial-related injury or harm.

Participation in the trial will not result in any additional financial burden to the participant, and compensation for potential trial-related injury will be handled in accordance with applicable laws and insurance arrangements.

7 | Summary of changes

This section summarises all changes to the national appendix after initial submission for approval.

Version 1.2, 2026-09-02: The withdrawal procedure was clarified to distinguish between withdrawal from a trial intervention and withdrawal from the trial entirely, including the procedures for continued data collection and follow-up in each case. The remote informed consent procedure was further clarified to specify that electronic consent may be obtained during a video call, with verification of the participant's or representative's identity and use of an accepted electronic identification and signature method.

Version 1.1, 2026-08-16: It was clarified that remote informed consent may be obtained using an electronic signature, while written consent may be obtained in person at the study site. An explicit reference to the applicability of Estonian legislation was added. The consent procedure was revised to clarify that informed consent will be sought from the legally designated representative, rather than from a relative, and directly from the participant as soon as they regain the capacity to provide informed consent. The definition and documentation requirements for reasonable efforts to identify and contact a legally designated representative were clarified. The planned number of participants to be recruited in Estonia was also revised.

Version 1.0, 2026-06-29: first version submitted for approval.

8 | References

1. The European Parliament and the Council of the European Union. Regulation (EU) No 536/2014 of the European Parliament and of the Council. [Internet]. 2014 [cited 2023 Sep 21]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0536

2. Herdman M, Gudex C, Lloyd A, Janssen Mf, Kind P, Parkin D, Bonsel G, Badia X. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res. 2011 Dec;20(10):1727–36. doi:10.1007/s11136-011-9903-x

3. Jensen CE, Sørensen SS, Gudex C, Jensen MB, Pedersen KM, Ehlers LH. The Danish EQ-5D-5L Value Set: A Hybrid Model Using cTTO and DCE Data. Appl Health Econ Health Policy. 2021 Jul;19(4):579–91. doi:10.1007/s40258-021-00639-3

4. EudraLex - EU Legislation. EudraLex - Volume 10 - Clinical trials guidelines [Internet]. 2017 [cited 2023 Dec 20]. Risk proportionate approaches in clinical trials - Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use. Available from: https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en

5. Health Insurance Act (‘Ravikindlustuse seadus’) [Internet]. Riigikogu; [cited 2026 Jun 5]. Available from: https://www.riigiteataja.ee/en/akt/522042026001

6. Medicinal Products Act (‘Ravimiseadus’) [Internet]. Riigikogu; [cited 2026 Jun 5]. Available from: https://www.riigiteataja.ee/en/akt/508052026007