The Intensive Care Platform Trial (INCEPT)

The Netherlands



National appendix

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Version 1.1, 2026-04-01

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

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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
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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*
GCP: *Good Clinical Practice*
HRQoL: *health-related quality of life*
ICU: *intensive care unit*
INCEPT: *the Intensive Care Platform Trial*

3 | Screening, inclusion, and informed consent procedures

The following section contains specific procedures that apply for The Netherlands 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.

The Netherlands informed consent procedure

INCEPT facilitates rigorous assessment of interventions used in critically ill adults. *INCEPT* will primarily focus on interventions in common use where practice differs among clinicians, but other interventions may similarly be assessed on the platform.

Enrolment in *INCEPT* including all domains will occur without prior informed consent according to the criteria in the applicable EU regulation (No 536/2014) [1]:

- Critical illness requiring acute intensive care unit (ICU) admission constitutes a medical emergency requiring urgent treatment, including treatment with the interventions assessed in the domains in *INCEPT*.
- Participation in the trial and each domain has the potential to produce a direct clinically relevant benefit for the participant, as described for each domain in the domain-specific appendices.
- It is not possible to supply adequate information and obtain prior informed consent from the participant's representative within the therapeutic window, as the interventions assessed are required to be initiated urgently, as delays may negatively affect patient outcomes.
- It is required that the investigator(s) assessing eligibility are not aware of any previously expressed objections to trial participation; if so, the participant will be excluded according to the *"Informed consent following inclusion expected to be unobtainable"* exclusion criterion described in the core protocol.
- The platform trial and all relevant domains directly relate to the participant's medical condition (i.e., acute critical illness requiring ICU admission), because of which it is not possible to obtain prior informed consent from the participant or the participant's representative within the therapeutic window, and the platform trial and all relevant domains are of such a nature that they can only be conducted in emergency situations due to the clinical condition under study will always constitute an medical emergency.
- The platform and all relevant domains will generally pose minimal risk and burden on the participant in comparison with standard treatment of acute critical illness; if specific domains deviate from this criterion, this will be included and discussed in the domain-specific appendices.

First, participant's fulfilling all platform inclusion criteria, and no exclusion criteria will be screened and randomised to domains for which they fulfil all domain-specific eligibility criteria by trained trial staff. As soon as possible hereafter, informed consent for continuation in the platform trial (including all applicable domains) will be obtained from a legally designated representative (in The Netherlands the closest relative). All informed consents will be obtained by medical doctors or research nurses trained and certified in the trial protocol and follow all applicable regulations.

Eligible participants will be acutely admitted to the ICU, and due to their critical condition unable to provide consent before inclusion. In these cases, a representative of the participant (usually the closest relative) will be approached as soon as possible after inclusion. When the participant's representative is present, oral and written information will be given in person. Participant representatives will have sufficient time (at least 48 hours) to consider participation. If a participant's representative is not present in the hospital, the information letter will be given to the nurse and handled to the representative as soon as they visit the participant. The participant's representative will be given the opportunity to read the information letter, and to consider continued participation of the participant in *INCEPT.* The participant's representative will be given an opportunity to contact the medical doctor or research nurse either in person or by phone for further explanation on the study details. In case the relatives conclude that they have received sufficient information, the research nurse or medical doctor will obtain written informed consent.

Participants will be asked for informed consent as soon as possible hereafter. For participants, both oral and written information will be given preferably in person by a medical doctor or research nurse trained and certified in the trial protocol. If this is not possible (e.g., the participant has been discharged to another hospital that is not a participating site), we will inform and collect consent from the participant by sending the information letter by physical mail and ask them to contact the medical doctor or research nurse for additional explanation and eventually for signing informed consent.

All consenting parties will be provided with written and oral information about the platform trial (including all relevant domains) allowing them to make an informed decision about participation in the trial. Written information and the consent forms will be subject to review and approval by the applicable competent authorities (e.g., the relevant ethical committees). The written information material will be in modular format and consists of general information about *INCEPT* and additional information sheets about all relevant domains. The informed consent procedure will be common and simultaneous for all applicable domains, with explicit, written informed consent to each specific domain using separate informed consent forms, and with consent to one or more domains constituting consent to *INCEPT* including all elements that are common between domains. All consent forms will be signed by the consenting party and the medical doctor or research nurse who has provided trial information for the consenting party. We will emphasise that the consenting party has at least 48 hours to decide whether to give consent or not. The

consenting party can, at any time and without further explanation, withdraw consent to continued participation in the platform trial or specific domains.

Lack of informed consent from the participant's relative and the participant deceases
If the participant deceases before informed consent is obtained (due to rapid progression of critical illness), the consent procedure will be stopped. If the participant has been correctly included in the trial and reasonable attempts to identify relatives 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.

Trial personnel
The screening will be done by trained trial staff in collaboration with the treating medical doctor, who ultimately decides if a participant can be enrolled in the trial and one or more individual domains. When a candidate participant is identified, a member of the trained trial staff will screen the participant in the electronic case report form (eCRF). Collection of informed consent will be performed by medical doctors or research nurses 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 and research nurses with consent functions in the *INCEPT* 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 regulations. This follows the applicable regulations in the Netherlands.

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 Dutch national EQ-5D-5L national value set [3] for participants enrolled in The Netherlands to calculate EQ-5D-5L index values for the primary analyses.

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 The Netherlands with no country-specific adaptations and no additional collection or reporting of additional safety data.

6 | Other considerations

Insurance

Trial participants in The Netherlands are covered by the Dutch law according to *'Besluit verplichte verzekering bij medisch-wetenschappelijk onderzoek met mensen 2015'* [5].

7 | Summary of changes

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

Version 1.1, 2026-04-01:

- Updated to match core protocol version.

Version 1.0, 2025-12-08: 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. Off J Eur Union 2014. https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX%3A32014R0536 (accessed February 23, 2024).

[2] Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res 2011;20:1727–36. https://doi.org/10.1007/s11136-011-9903-x.

[3] Versteegh MM, Vermeulen KM, Evers SMAA, Wit GA de, Prenger R, Stolk EA. Dutch Tariff for the Five-Level Version of EQ-5D. Value in Health. 2016;19:343–52.

[4] EudraLex - EU Legislation. 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. EudraLex - Vol 10 - Clinical Trials Guideline 2017. https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en (accessed December 20, 2023).

[5] Besluit verplichte verzekering bij medisch-wetenschappelijk onderzoek met mensen 2015: https://wetten.overheid.nl/BWBR0035881/2022-01-01 (accessed November 17, 2023)