

December 2025

Dear friends and colleagues,

EMPRESS status

To date, **181 patients** have been enrolled across 9 **active Danish ICUs** (Rigshospitalet, Aalborg, Kolding, Odense, Køge, Hillerød, Bispebjerg, Aarhus East and Aarhus North) – a huge thank you to all involved in securing such great progress!

At a glance:

Participants included to date: 179

Active sites: 9 (DK)

Next steps: initiation of additional Danish sites, and submission of application to get Sweden, Iceland and New Zealand approved.

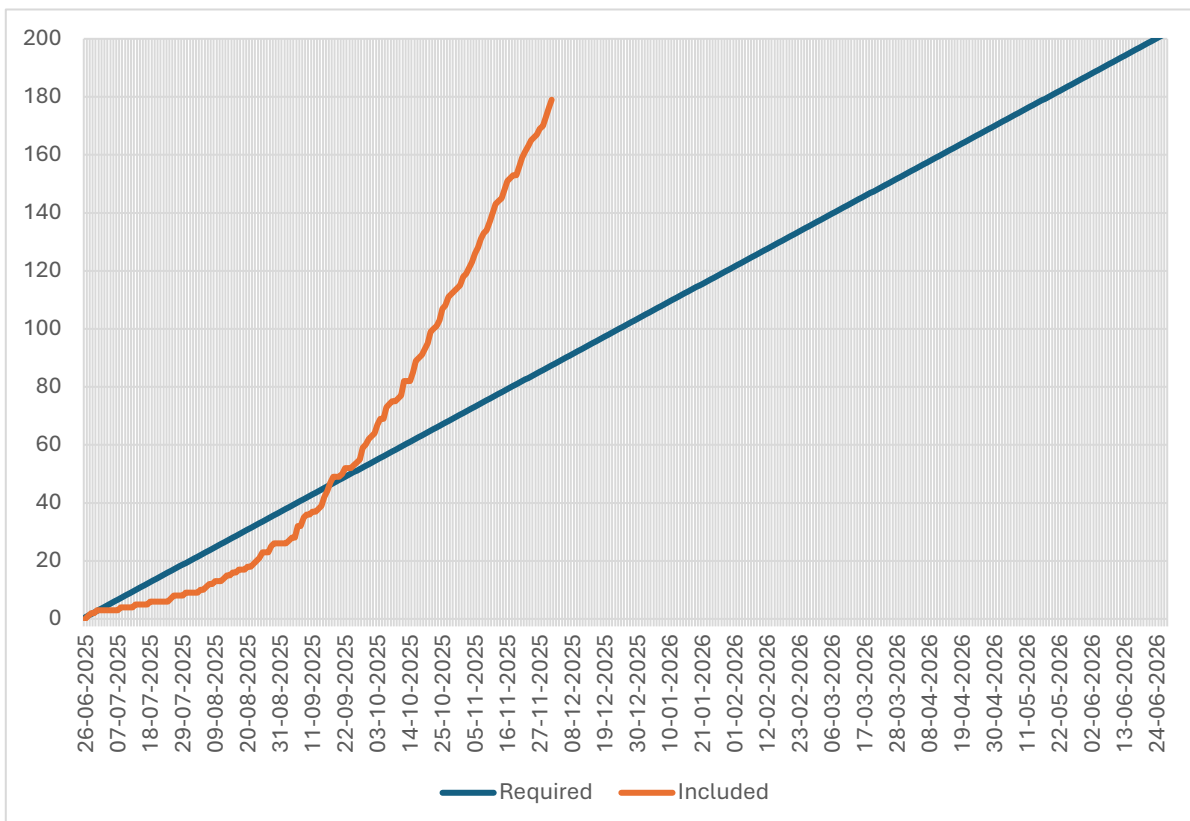


Figure 1: Participants included in EMPRESS since start of inclusion of the first participant (orange) versus the minimum requirement of 200 inclusions within a year to reach feasibility (navy)

Featured site of the month: Aalborg ICU

Bodil Steen Rasmussen writes the following:

We have an absolutely fantastic team, led by project nurse Anne-Marie Bunzel (on the right in the picture), in collaboration with project nurses Anne-Sofie Eriksen (at the back of the picture) and Jette Olsen (at the back on the left in the picture), as well as pre-course trainee Kristina Stamenkovic (at the front of the picture). The team continuously monitors the admitted patients, keeps track of informed consents, and ensures ongoing data entry.

The team is highly visible in the clinic and gives the clinical doctors a gentle daily nudge to make sure we include all potential patients and obtain consents in a timely manner.

In parallel, Kristina Stamenkovic is working on a quality assurance project focusing on the timely collection of consents – and this has shifted the process of obtaining consent from legal guardians and relatives from the doctors in the Research Unit to the clinical doctors.

We are proud of our team.

Bodil, Olav, Thomas and Jo



Swedish CTIS submission – international expansion underway

We are very pleased to share that the **EMPRESS application has been successfully submitted in CTIS to the Swedish authorities.** This marks an important step toward international expansion of the trial. The review process is now underway, and **conclusion of the process is expected by early February 2026.**

We would like to thank our Swedish collaborators and national PI **Frederik Sjövall** for the continued efforts in bringing EMPRESS to Sweden.



ICH GCP E6(R3) – what’s new, and what investigators need to know

The revised ICH GCP E6(R3) guideline has now been released, modernising GCP to better reflect risk-based, proportionate, and data-quality-focused clinical trial conduct. Compared with R2, R3 places greater emphasis on:

- Proportionality and critical-to-quality factors in trial design and oversight
- Risk-based monitoring and data management
- Clearer responsibilities for investigators and sponsors
- Participant protection in increasingly complex trial settings

To support implementation, we have shared a GAP analysis, allowing each site to identify and address local R2 → R3 changes.

All Site Investigators are kindly asked to:

1. Sign and archive the GAP analysis in the Site File.
2. **Review the provided R3 PowerPoint slides** (self-study)
3. **Complete the R3 certificate** after reviewing the material
4. Ensure the certificate is filed in the Investigator Site File

These steps help ensure that all EMPRESS sites remain aligned with current GCP requirements ahead of formal adoption.

Update: Registration of microbiology events

To ensure consistency, we have aligned how microbiological events should be recorded:

- **Day forms:** Register “Yes” on the **day the event is confirmed** (when the final microbiology result is available), not the sampling date. Only mark “Yes” on the first day of an event.
- **Baseline form:** For “*Positive bacterial cultures from usually sterile sites*”, registration must follow the **sampling date**, regardless of when the result becomes available.

Sites are kindly asked to **review earlier baseline entries** for this question and correct them if needed. If anything is unclear, please contact us at either 3545 0606 or empress@cric.nu.

Consent in acute settings – how does it work?

EMPRESS involves critically ill patients who are unable to provide informed consent at the time of enrolment. Therefore, the trial follows Danish regulations for emergency inclusion:

1. **Primary inclusion** must be performed by a trained clinician under the emergency provision
2. **Consent from a trial guardian** (forsøgsværge) should be obtained as soon as possible after inclusion and **needs to be obtained for all participants** (including deceased participants)
3. **Consent from relatives** should be obtained as soon as possible after inclusion and **needs to be obtained for all participants** (including deceased participants)
4. If the participant later regains capacity, informed consent must be reaffirmed directly with the participant **and generally cannot happen at the same timepoint as inclusion and randomisation is happening.**

This process ensures ethical and legal validity of enrolment while allowing timely initiation of life-saving treatment, i.e., empirical antibiotic therapy.

If you have any questions regarding documentation, please contact empress@cric.nu for templates and guidance.

eCRF updates & support

If you encounter issues of any kind (access, role permissions, edit checks, or unexpected queries), the hotline is open 24/7: +45 3545 0606 and we are available anytime at empress@cric.nu. When reporting, please include the participant ID (if applicable), the page name, and a screenshot without personal information—this helps us replicate and resolve potential issues within one cycle.

With collegial regards,

Nick Frørup Meier, Morten Hylander Møller, Anders Granholm, Maj-Brit Nørregaard Kjær and Team
EMPRESS

On behalf of the EMPRESS Coordinating group