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Dear REC,

**SepTiC Trial Amendment AM010 (non-substantial NSA08)**

We are writing to you regarding the submission of a substantial amendment for the SepTiC Trial.

We have reviewed our recruitment and screening rates, and in conjunction with discussion and feedback from our independent Trial Steering Committee we would like to amend the inclusion and exclusion criteria of the trial. Therefore we are submitting an updated protocol v2.0. Both a clean and tracked changed version are included in the amendment and a summary of changes is provided below:-

SepTiC Protocol v2.0 12.08.2025\_TC  
SepTiC Protocol v2.0 12.08.2025\_Clean

- Additional inclusion criteria for the GM-CSF trial, clarification in 'or requiring two organ support' to include (i.e. two of vasopressors, renal replacement therapy, or non-invasive ventilation / continuous positive airway pressure / high flow nasal oxygen respiratory support)
- The following exclusion criteria for the trial have been removed:-
  - Not expected to survive 90 days, due to pre-existing chronic (end-stage) disease
  - Removing the following wording – 'A source of infection that will require a prolonged course of antibiotics, for greater than 21 days' and amending this to :- 'Being treated for infective endocarditis, osteomyelitis, hepatic or cerebral abscess, tuberculosis'

\*For change in protocol updates, please see supportive evidence from a TMG meeting and a review meeting with the funder:-

- SepTiC Trial Management Group Meeting Minutes 08May2025
- SepTiC\_17\_136\_02\_Meeting minutes\_20 June 2025\_FINAL
- Removing the MOCA-Blind questionnaire at 6 months from the secondary endpoint for the trial as discussed and agreed by the TMG.
  - See supportive evidence from discussion with TMG  
SepTiC TMG Email Confirmation\_Remove MOCA April 2025
- We would also like to submit a renewed insurance certificate for the trial

Please do not hesitate to contact us if you require any further information.

Yours sincerely

Janis

**Janis Best-Lane**

Clinical Trial Manager

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