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Research Ethics Coordinator,

13th February 2025

Dear Sir/Madam,

Re: EVIS Study

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| --- | --- |
| **Study title:**  **REC Reference:** | **EVIS - Early vasopressors in Sepsis**  **22/SS/0009** |
| **Protocol number:** | **GN20AE342** |
| **EudraCT number:** | **2021-006886-39** |
| **IRAS project ID:** | **307862** |
| **Amendment:** | **Substantial Amendment 10** |

Please find enclosed documents pertaining to a Substantial amendment for the EVIS Trial.

The EVIS Trial Team following the submission of the previous Substantial amendment (SA09) on the 20th of December 2024, received communication from the HRA on the 31st of December 2024 that the updated wording submitted in the SA09 EVIS main PIS/ICFs (V4.0) and the Sub-Study Consent Form and PIS (V2.0) was not compliant with GDPR.

In response, the EVIS Trial team updated this wording using the newly released HRA GDPR guidance and submitted V5.0 – 09.01.25 of the main EVIS PIS/ICFs and V3.0 – 09.01.25 of the Sub-Study Consent Form and PIS back to the HRA on the 10th of January 2025. The HRA accepted the proposed changes on the 13th of January 2025, and sent this on to the NRS & REC to be included in the review of SA09. Due to a staff absence these documents were missed, and not incorporated in to the RECs review of SA09. Therefore, the favourable opinion for SA09 issued on the 15th of January 2025 approved the superseded documents, but not the current versions.

Following discussion with the REC it was advised that the updated documents should be submitted separately in a Non-Substantial amendment. However, during the development of the amendment, previously missed errors in the EVIS protocol were identified, and therefore Substantial protocol changes have also been included in this amendment in order to address this.

The principle changes submitted in SA10 are as follows:

1. **Minor updates to the EVIS PIS/ICF’s (V5.0)**
2. To include additional wording for participants regarding the processing of participant data to comply with the HRA guidance and transparency wording for all Sponsors released on the 23rd of October 2024.
3. **Minor Changes to the EVIS Sub-Study Consent Form & PIS (V3.0) for the Qualitative Research in the context of the Early Vasopressors in Sepsis (EVIS) Trial imbedded EVIS Process Evaluation**
4. To include additional wording for participants regarding the processing of participant data to comply with the HRA guidance and transparency wording for all Sponsors released on the 23rd of October 2024.
5. **Minor Changes to the EVIS GP Letter (V2.0)**

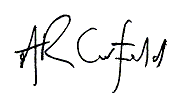
(A). To update the GP letter to provide the new primary outcome as the way in which clinical effectiveness is measured.

(B). To provide the new follow up period to match the protocol changes submitted in SA09.

1. **Substantial Changes to the EVIS Trial Protocol (V5.0):**
2. Revised time point of evaluation for the Health outcomes i.e. the collection of re-admission data 30 & 90 days post randomisation instead of post discharge.
3. **Non-Substantial Changes to the EVIS Trial Protocol (V5.0):**
4. Administrative updates: versioning.
5. Correction of identified errors in time points for various end points. Updated the Schedule of Assessments, Study Visits, Objectives and Outcome Measures and Appendix C to ensure consistency in each section in regard to the time points specified for data collection for each end point.
6. Updated the description of the health economics evaluation to provide further information regarding the data used, and how this is being collected.

Thank you for considering this application.

Yours sincerely,



Dr Alasdair Corfield

The following additional documents are provided in support of this application:

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|  | **Document Name** | **Version** | **Date** |
| 1. | EVIS\_Amendment\_Tool\_GN20AE342\_307862\_SA10\_13\_02\_25 | V1.6 | 13/02/2025 |
| 2. | EVIS PIS ICF Personal Legal Rep (Eng, Wales & NI) V5.0 - 09.01.25 CLEAN | V5.0 | 09/01/2025 |
| 3. | EVIS PIS ICF Personal Legal Rep (Eng, Wales & NI) V5.0 - 09.01.25 TC | V5.0 | 09/01/2025 |
| 4. | EVIS PIS ICF Prof Legal Rep (Eng, Wales, NI) V5.0 - 09.01.25 CLEAN | V5.0 | 09/01/2025 |
| 5. | EVIS PIS ICF Prof Legal Rep (Eng, Wales, NI) V5.0 - 09.01.25 TC | V5.0 | 09/01/2025 |
| 6. | EVIS PIS ICF Prof Legal Rep (Scotland) V5.0 - 09.01.25 CLEAN | V5.0 | 09/01/2025 |
| 7. | EVIS PIS ICF Prof Legal Rep (Scotland) V5.0 - 09.01.25 TC | V5.0 | 09/01/2025 |
| 8. | EVIS PIS ICF Recovered Capacity (Eng, Wales & NI) V5.0 - 09.01.25 CLEAN | V5.0 | 09/01/2025 |
| 9. | EVIS PIS ICF Recovered Capacity (Eng, Wales & NI) V5.0 - 09.01.25 TC | V5.0 | 09/01/2025 |
| 10. | EVIS PIS ICF Recovered Capacity (Scotland) V5.0 - 09.01.25 CLEAN | V5.0 | 09/01/2025 |
| 11. | EVIS PIS ICF Recovered Capacity (Scotland) V5.0 - 09.01.25 TC | V5.0 | 09/01/2025 |
| 12. | EVIS PIS Summary V5.0 - 09.01.25 CLEAN FINAL | V5.0 | 09/01/2025 |
| 13. | EVIS PIS Summary V5.0 - 09.01.25 TC FINAL | V5.0 | 09/01/2025 |
| 14. | EVIS PIS ICF V5.0 - 09.01.25 CLEAN FINAL | V5.0 | 09/01/2025 |
| 15. | EVIS PIS ICF V5.0 - 09.01.25 TC FINAL | V5.0 | 09/01/2025 |
| 16. | EVIS PIS ICF WA & Guardian (Scotland) V5.0 - 09.01.25 CLEAN | V5.0 | 09/01/2025 |
| 17. | EVIS PIS ICF WA & Guardian (Scotland) V5.0 - 09.01.25 TC | V5.0 | 09/01/2025 |
| 18. | EVIS Sub-Study CF\_V3.0; 09.01.25 CLEAN FINAL | V3.0 | 09/01/2025 |
| 19. | EVIS Sub-Study CF\_V3.0; 09.01.25 TC FINAL | V3.0 | 09/01/2025 |
| 20. | EVIS Sub-Study PIS\_V3.0; 09.01.25 CLEAN FINAL | V3.0 | 09/01/2025 |
| 21. | EVIS Sub-Study PIS\_V3.0; 09.01.25 TC FINAL | V3.0 | 09/01/2025 |
| 22. | EVIS GP Letter V2.0 03.02.25 CLEAN FINAL | V2.0 | 03/02/2025 |
| 23. | EVIS GP Letter V2.0 03.02.25 TC FINAL | V2.0 | 03/02/2025 |
| 24. | EVIS Protocol V5.0 – 13.02.25 CLEAN FINAL | V5.0 | 13/02/2025 |
| 25. | EVIS Protocol V5.0 – 13.02.25 TC FINAL | V5.0 | 13/02/2025 |
| 26. | EVIS Protocol V5.0 13 Feb 25 Schedule of Assessments | V5.0 | 13/02/2025 |
| 27. | EVIS Summary of Protocol Changes V5.0 to V4.0 13 Feb 25 | V5.0 | 13/02/2025 |