

Dr Les Gelling
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East of England – Cambridge South REC
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The Old Chapel
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31 January 2019

Dear Dr Gelling

Study title: **FIRST-line support for Assistance in Breathing in Children (FIRST-ABC): A master protocol of two randomised trials to evaluate the non-inferiority of high flow nasal cannula (HFNC) versus continuous positive airway pressure (CPAP) for non-invasive respiratory support in paediatric critical care**

REC reference: **19/EE/0185**

IRAS number: **260536**

Amendment number: **1**

I wish to seek a substantial amendment for the above study. This main purpose of this amendment is to 1) update the protocol. We have also taken the opportunity to add the additional age-appropriate Pediatric Quality of Life Inventory (Peds-QL) questionnaires and to update the Health Services Questionnaire that will be used as part of the six month follow-up (detailed in points 2) and 3) below).

1) We propose updating the protocol as follows:

- a. FIRST-ABC is a master protocol comparing two modes of non-invasive respiratory support (High Flow Nasal Cannula (HFNC) versus Continuous Positive Airway Pressure (CPAP)). Therefore, patients in which a clinical decision is made to start a different form of non-invasive respiratory support are not eligible. This message is reinforced in study training materials however some sites have requested this be added as exclusion criteria for clarity amongst their teams. We have therefore added '*Clinician decision to start other form of non-invasive respiratory support (i.e. not HFNC or CPAP)*' as an exclusion criterion.
- b. In light of the higher than expected recruitment rate in the step-down RCT, no formal interim analysis will be performed. Safety data (counts and percentages of adverse events by arm, and a line listing of SAEs) will be available for scrutiny by the DMEC, by the end of the internal pilot stage. There are no changes to the planned interim analysis of the step-up RCT. This approach has been agreed with the DMEC.
- c. We have also taken the opportunity to make minor administrative changes to the protocol and have updated and corrected the algorithms for HFNC and

CPAP (unfortunately these algorithms are created in a software program that does not have a 'tracked changes' function).

- 2) We had added the further age-appropriate versions of the Peds-QL questionnaire which are used as part of the six-month follow-up.
- 3) We have reviewed the content of the health services questionnaire and improved the response options, reducing the burden of text on each of the pages.

Please find enclosed the following supporting documents:

- FIRST-ABC Master Protocol v1.2 dated 9 December 2019 (tracked and changed versions)
- Peds-QL 2-4 years v1.0 dated 16 December 2019
- Peds-QL 5-7 years v1.0 dated 16 December 2019
- Peds-QL 8-12 years v1.0 dated 16 December 2019
- Peds-QL 13-18 years v1.0 dated 16 December 2019
- FIRST-ABC Health Services Questionnaire dated 21 January 2020 (tracked and changed versions)

Please do not hesitate to get in touch if you require any further information to consider this substantial amendment.

I look forward to hearing from you.

Yours sincerely



Alvin Richards-Belle
Trial Manager

Copy to: Dr Padmanabhan Ramnarayan, Chief Investigator
Dr Jenny Rivers, Sponsor Contact