Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)
Paediatric Intensive Care and Infection Control (PICnIC)

1. Is your project research?

(●) Yes ( ) No

2. Select one category from the list below:

( ) Clinical trial of an investigational medicinal product

( ) Clinical investigation or other study of a medical device

( ) Combined trial of an investigational medicinal product and an investigational medical device

(●) Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice

( ) Basic science study involving procedures with human participants

( ) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology

( ) Study involving qualitative methods only

( ) Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)

( ) Study limited to working with data (specific project only)

( ) Research tissue bank

( ) Research database

If your work does not fit any of these categories, select the option below:

( ) Other study

2a. Will the study involve the use of any medical device without a CE Mark, or a CE marked device which has been modified or will be used outside its intended purposes?

( ) Yes (●) No

2b. Please answer the following question(s):

a) Does the study involve the use of any ionising radiation? ( ) Yes (●) No

b) Will you be taking new human tissue samples (or other human biological samples)? (●) Yes ( ) No

c) Will you be using existing human tissue samples (or other human biological samples)? ( ) Yes (●) No

3. In which countries of the UK will the research sites be located?*(Tick all that apply)*

- [x] England
- [ ] Scotland
- [ ] Wales
- [ ] Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

- (•) England
- ( ) Scotland
- ( ) Wales
- ( ) Northern Ireland
- ( ) This study does not involve the NHS

4. Which applications do you require?

- [x] IRAS Form
- [ ] Confidentiality Advisory Group (CAG)
- [ ] Her Majesty's Prison and Probation Service (HMPPS)

5. Will any research sites in this study be NHS organisations?

(•) Yes ( ) No

5a. Are all the research costs and infrastructure costs (funding for the support and facilities needed to carry out research e.g. NHS Support costs) for this study provided by a NIHR Biomedical Research Centre, NIHR Collaboration for Leadership in Health Research and Care (CLAHRC), NIHR Patient Safety Translational Research Centre or Medtech and In Vitro Diagnostic Cooperative in all study sites?

Please see information button for further details.

( ) Yes (•) No

Please see information button for further details.

5b. Do you wish to make an application for the study to be considered for NIHR Clinical Research Network (CRN) Support and inclusion in the NIHR Clinical Research Network Portfolio?

Please see information button for further details.

(•) Yes ( ) No

The NIHR Clinical Research Network provides researchers with the practical support they need to make clinical studies happen in the NHS e.g. by providing access to the people and facilities needed to carry out research "on the ground".

If you select yes to this question, you must complete a NIHR Clinical Research Network (CRN) Portfolio Application Form (PAF) immediately after completing this project filter question and before submitting other applications. Failing to complete the PAF ahead of other applications e.g. HRA Approval, may mean that you will be unable to access NIHR CRN Support for your study.

6. Do you plan to include any participants who are children?

◉ Yes ○ No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

○ Yes ◉ No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

○ Yes ◉ No

9. Is the study or any part of it being undertaken as an educational project?

○ Yes ◉ No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

○ Yes ◉ No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

○ Yes ◉ No

Integrated Research Application System
Application Form for Other clinical trial or investigation

IRAS Form (project information)

Please refer to the E-Submission and Checklist tabs for instructions on submitting this application.

The Chief Investigator should complete this form. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting Help.

Please define any terms or acronyms that might not be familar to lay reviewers of the application.

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
Paediatric Intensive Care and Infection Control (PICnIC)

Please complete these details after you have booked the REC application for review.

REC Name:

REC Reference Number: **Submission date:**

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

A pilot cluster randomised clinical trial of the use of selective gut decontamination in critically ill children

A3-1. Chief Investigator:

	Title	Forename/Initials	Surname
	Dr	Nazima	Pathan
Post	University Lecturer and Consultant in Paediatric Intensive Care		
Qualifications	MBBS, BSc (Hons), PhD		
ORCID ID	0000 0002 9447 4252		
Employer	University of Cambridge		
Work Address	Paediatric Intensive Care, Department of Paediatrics Level 8, Addenbrookes Hospital Hills Road, Cambridge		
Post Code	CB2 0QQ		
Work E-mail	np409@medschl.cam.ac.uk		
* Personal E-mail			
Work Telephone	07941455497		
* Personal Telephone/Mobile			
Fax			

** This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*
A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?
This contact will receive copies of all correspondence from REC and HRA/R&D reviewers that is sent to the CI.

	Title	Forename/Initials	Surname
		Stephen	Kelleher
Address	Cambridge University Hopsitals		
	Hills Road		
	Cambridge		
Post Code	CB2 0QQ		
E-mail	research@addenbrookes.nhs.uk		
Telephone	01223217418		
Fax	01223348494		

A5-1. Research reference numbers. *Please give any relevant references for your study:*

Applicant's/organisation's own reference number, e.g. R & D (if available):	RG91998
Sponsor's/protocol number:	
Protocol Version:	1.0
Protocol Date:	21/11/2019
Funder's reference number (enter the reference number or state not applicable):	16/152/01
Project website:	

Registry reference number(s):
The UK Policy Framework for Health and Social Care Research sets out the principle of making information about research publicly available. Furthermore: Article 19 of the World Medical Association Declaration of Helsinki adopted in 2008 states that "every clinical trial must be registered on a publicly accessible database before recruitment of the first subject"; and the International Committee of Medical Journal Editors (ICMJE) will consider a clinical trial for publication only if it has been registered in an appropriate registry. Please see guidance for more information.

International Standard Randomised Controlled Trial Number (ISRCTN):
ClinicalTrials.gov Identifier (NCT number):

Additional reference number(s):

Ref.Number Description	Reference Number

A5-2. Is this application linked to a previous study or another current application?

◯ Yes ◉ No

Please give brief details and reference numbers.

2. OVERVIEW OF THE RESEARCH

To provide all the information required by review bodies and research information systems, we ask a number of

specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.

A6-1. Summary of the study. *Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. Where the research is reviewed by a REC within the UK Health Departments' Research Ethics Service, this summary will be published on the Health Research Authority (HRA) website following the ethical review. Please refer to the question specific guidance for this question.*

The PICnIC study will test if children in paediatric intensive care units (PICUs) can benefit from receiving a treatment called Selective Digestive Decontamination (SDD). SDD has been shown to improve survival in adults, however it is used less often in children. There is no high-quality evidence to inform SDD usage in children.

Finding this evidence is important because critically ill children are at a higher risk of hospital-acquired infections (HAIs). Bacteria in the digestive tract causes many of these infections. When someone is very unwell, the number of 'good' bacteria found in the digestive tract reduces. As a result, 'bad' bacteria levels may increase and spread to other organs. This can cause severe illnesses such as pneumonia and sepsis. SDDs stop the growth of these bacteria.

PICnIC will compare SDD with standard infection control procedures, such as good hand hygiene and non-touch techniques, in children admitted to PICU.

As large clinical trials are expensive and difficult to conduct, PICnIC is an 18-month feasibility study to check that the different parts, such as recruiting patients and delivering treatment, all run smoothly. We will also interview parents of participating children to ask them how they felt about their child being included. We will ask them about how they were approached and what outcome measures would be most important to them in a full trial. We will do the same thing with hospital staff working on the trial to find out how acceptable they found the trial processes.

PICnIC will include six PICUs and recruit up to 324 children. Children will be eligible if they are admitted to PICU and expected to be on a breathing machine for at least 48 hours. The study is funded by the National Institute of Health Research's Health Technology Assessment Programme.

A6-2. Summary of main issues. *Please summarise the main ethical, legal, or management issues arising from your study and say how you have addressed them.*

Not all studies raise significant issues. Some studies may have straightforward ethical or other issues that can be identified and managed routinely. Others may present significant issues requiring further consideration by a REC, HRA, or other review body (as appropriate to the issue). Studies that present a minimal risk to participants may raise complex organisational or legal issues. You should try to consider all the types of issues that the different reviewers may need to consider.

Purpose and design

The PICnIC study is an external pilot, parallel group, cluster-randomised clinical trial (cRCT) with integrated mixed-methods study. The cRCT will be conducted in mechanically-ventilated children implemented at the level of Paediatric Intensive Care Units. The mixed-methods study is designed to determine the feasibility of conducting a larger trial of SDD in paediatric intensive care through qualitative interviews with families and health care professionals regarding the processes and practices used.

Within the pilot trial, a cluster design will be used as SDD exerts an effect both on individual patients and the microbiological ecology of the unit. Individual patient randomisation, rather than unit randomisation, would not replicate the way SDD would be used in practice and would fail to evaluate the influence of SDD on antibiotic resistance. To be most efficacious, SDD should be introduced as early as possible in the admission and be administered as a unit-wide infection control measure. This is most feasible in a cluster design where the SDD treatment becomes standard practice for the duration of the trial.

Following a period of usual care, participating PICUs will be randomised to deliver SDD (intervention) or continue with usual care (control). We plan to start the intervention in all eligible patients as part of the PICUs infection control bundle for that period, initiation of the intervention is time sensitive. SDD is already in use in adult ICUs as routine practice. We plan to use routinely collected clinical data from PICAnet and other NHS databases.

The PICnIC study has been conceived and designed by experts in paediatric intensive care, health service research and clinical trials methodology and has been reviewed and approved by independent reviewers on behalf of the funder (National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme). Consultation with parents, PICU survivors and a young people's group has informed the design of the study and will continue to inform the conduct, management and dissemination of any of the study's findings. The prevention, identification and

treatment of HAIs has been identified as a priority by the James Lind Alliance. Furthermore, the Intensive Care Priority Setting Partnership group identified 'What is the best way to prevent, diagnose and treat hospital acquired infection (e.g. ventilator associated pneumonia, blood stream infections related to the use of invasive lines)?' as one of their top ten priorities.

Recruitment and consent

SDD has been shown to impact the rate of HCAIs in all patients within a unit, not just those receiving it. Because of this, it is essential to study both the patient-related direct effects (caused by the delivery of SDD to an individual patient) and the indirect effects of SDD (on all patients due to its impact on the ecology of the unit). To do this, a cluster-randomised design is the only feasible option for the study.
As such, the intervention will be given to all eligible patients in participating PICUs as part of their standard infection control practices; there will not be individual patient consent. SDD has been used safely in UK PICUs for many years and is widely adopted in other countries.

In order to effect the whole PICU, every eligible patient will receive the treatment during the study recruitment period. Posters will be displayed in the unit and we will proactively provide parents/legal representatives with information leaflets at an appropriate time, considering the burden on them at an already stressful time. The leaflet will highlight that parents can opt-out of continued data collection without this affecting their child's care. We will also make it clear that no patient identifiable information will be transferred as part of the study. Once their condition allows, age-appropriate information will be provided to children >8 years and assent will be sought.

Patients in the control arm of the trial and during the ecology surveillance periods will be recruited without consent as no intervention is being delivered.

The PICnIC study team have extensive experience of consent procedures within the PICU setting. This includes qualitative work within two National Institute of Health Research (NIHR) Health Technology Assessment programme funded research studies (FiSh, HTA 13/04/105, and FEVER, HTA 15/44/01) lead by Dr Kerry Woolfall. Dr Woolfall is a leading researcher in the field of paediatric critical care consent and is co-investigator on this study, contributing extensively to the design of the consent procedures. In total the FiSh and FEVER studies included interviews with 50 parents/guardians of former PICU patients to ascertain their views on emergency consent procedures (timings, information etc.) and the acceptability of research without prior consent within this population. The results of these studies have guided the development of the proposed consent procures within the PICnIC study.

Risks, burdens and benefits

Evidence from Randomised Clinical Trials (RCTs) and meta-analyses in adult intensive care patients has shown that the introduction of SDD reduces both mortality and ventilator-associated pneumonia (VAP). In addition to being beneficial to individual patients, it is apparent that SDD exerts an effect on the wider microbiological ecology of the unit in which it is delivered and may therefore impact the entire intensive care unit population, reducing incidence of HAI in both directly exposed and unexposed patients.

Although SDD has been shown to be beneficial in adults, it has not been routinely adopted into clinical practice due to concerns that its use may promote antimicrobial resistance. Whilst this could be conceived as a risk to study participants, data evaluating antimicrobial resistance are conflicting. Recent ecological studies conducted in adults, reported that SDD was associated with a reduction in antibiotic resistance rates. Antibiotic resistant will be monitored through the results of microbiological samples taken from study participants during recruitment and ecological surveillance periods.

Current evidence suggests SDD usage in PICU reduces the rate of HCAIs. However, a sufficiently powered trial of SDD has not been compared directly with modern infection control measures. It is therefore important to design a trial to address this gap in knowledge.

There are no foreseeable risks to either the healthcare professionals or the parents/legal representatives involved in the mixed methods study. Due to emotive nature of critical illness in children there is the risk that parents/legal representatives may find taking part in the study burdensome. The PICnIC study team have extensive experience designing and conducting interviews and surveys with parents/legal representatives of critically ill children and will ensure questions will be designed to limit stress or personal intrusion.

Confidentiality

Data collection will be limited to those data sufficient to address the objectives of the PICnIC study. No patient identifiable information will be transferred out of the local NHS sites.

A unique trial number will be generated for each patient recruited into the study in order to link PICnIC data. The link

between patient details and the trail number will only be accessible by local NHS teams.

As part of the trial's efficient design, additional data from enrolled participants will be collected via the Paediatric Intensive Care Audit Network (PICAnet). On admission patients are allocated a PICANet number which will be collected by the study team on the Case Report Form (CRF). The PICAnet numbers from all recruited patients across all sites will be provided to the PICAnet team who will then provide a custom secure data extract for each site. This data will remain anonymised and linked to participants trial number.

Conflict of interest

None

Use of tissue samples in future research

None

3. PURPOSE AND DESIGN OF THE RESEARCH

A7. Select the appropriate methodology description for this research. *Please tick all that apply*:

- ☐ Case series/ case note review
- ☐ Case control
- ☐ Cohort observation
- ☐ Controlled trial without randomisation
- ☐ Cross-sectional study
- ☐ Database analysis
- ☐ Epidemiology
- ☐ Feasibility/ pilot study
- ☐ Laboratory study
- ☐ Metanalysis
- ☐ Qualitative research
- ☐ Questionnaire, interview or observation study
- ☑ Randomised controlled trial
- ☐ Other (please specify)

A10. What is the principal research question/objective? *Please put this in language comprehensible to a lay person.*

The main objective of the trial is to determine whether it is feasible to conduct a study of SDD in critically ill children in paediatric intensive care.

A11. What are the secondary research questions/objectives if applicable? *Please put this in language comprehensible to a lay person.*

The secondary objectives of the pilot cRCT are to:

• Test the ability to randomise PICUs to either the intervention (SDD) or the control (usual care)
• Test the willingness and ability of health care professionals to screen and recruit eligible children
• Estimate the recruitment rate of eligible children
• Test adherence to the SDD protocol at intervention sites
• Test the procedures for assessing and collecting selected clinical and ecological outcomes and for adverse event reporting
• Assess the generalisability of the study results to all PICUs using PICANet

The objectives of the focus groups, telephone interviews and online survey of health care professionals in participating

PICUs and online survey of all PICUs are to:

• Assess the acceptability of (barriers to and enablers of) implementation of the SDD intervention and recruitment and consenting procedures
• Assess the acceptability of collecting data to assess the selected clinical and ecological outcomes
• Assess the acceptability of the SDD intervention and confirm interest in participation in a definitive trial in the wider PICU community

The objectives of the interviews and survey of parents/guardians of recruited children are to:

• Review and explore the acceptability of a definitive trial including the SDD intervention
• Test the acceptability of the recruitment and consenting procedures for the definitive trial, including all proposed information materials
• Review and explore selection of important, relevant, patient-centred, primary and secondary outcomes for a definitive trial

A12. What is the scientific justification for the research? *Please put this in language comprehensible to a lay person.*

Each year, around 20,000 children are admitted to Paediatric Intensive Care Units (PICUs) in the UK, accounting for 141,000 bed-days. During critical illness, the body has a reduced ability to fight infection. This, combined with invasive treatment procedures which decrease immunity, changes the balance of potentially harmful and normal bacteria in the mouth and stomach. This change can cause Healthcare Acquired Infections (HCAI) which may lead to severe illnesses such as pneumonia and sepsis. Whilst death in PICU is uncommon (<4%), around 7-14% of children will develop a HAI and they are recognised as an increasing public health problem.

Selective Decontamination of the Digestive tract (SDD) is an infection control strategy designed to prevent HAIs. This is done by applying a paste to the mouth and a liquid into the stomach, alongside other infection control techniques such as strict hand hygiene.

SDD is a common treatment in other countries, such as the Netherlands, and previous research studies conducted in adult intensive care have shown that SDD can be effective in reducing deaths. Additionally, research has shown that the effects of SDD may not be limited to the individual patient who receives the treatment but may benefit all patients admitted to the unit. However, there is limited evidence for its use in children.

In this study, we plan to undertake a randomised trial in six intensive care units to establish whether the effects of SDD can be tested in critically ill children in the UK.

A13. Please summarise your design and methodology. *It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.*

The PICnIC study is a pilot, parallel group cluster randomised clinical trial (cRCT) that includes an integrated mixed-methods study. We will discuss the cRCT and mixed-methods separately. The whole study has designed as a miniature version of a potential definitive cRCT and will test feasibility and the study procedures.

cRCT

Participating sites will undergo an 8-week baseline period of usual care, during which sites will be randomised to either continuing usual care (control) or delivering SDD (intervention) in the second 8-week period. There will be a two-week transition period between the delivery of usual care and starting the intervention. The trial is unblinded, SDD will become usual practice for participating PICUs randomised to deliver the intervention.

There will be three one-week observational ecological assessments over the course of the study: pre-trial; during the transition period; post-trial.

Eligible patients will be:
1. Age >37 weeks (corrected gestational age) and ≤ 18 years
2. Receiving mechanical ventilation expected to last at least 48 hours
All patients admitted to the study PICU during the ecological surveillance weeks will be included, regardless of their ventilation status.

The intervention will be started in all eligible patients as it will form part of the standard infection control strategy in the participating PICU. In addition to usual care, the follow SDD regimen will be adopted:

1. A six-hourly topical, application of a pea-sized (0.5g) amount of paste to the mouth
2. A six-hourly administration of liquid given via the existing feeding tube into the stomach via the nose. The amount of liquid given will vary based on the child's age between half a teaspoon – 2 teaspoons (2.5ml – 10ml)
Treatment will be given 30 minutes before feeds, where feeding is not continuous. This dosing regimen is based on that in use in a UK PICU for a period of over 10 years. The intervention will start in all eligible patients within 6 hours of the child fulfilling the inclusion criteria. It will continue until the patient is extubated or for 30 days, whichever is sooner.

Readmitted patients will continue to receive the intervention, as it will form part of the standard care bundle but would not be counted as a separate enrolment.

Per standard practice, routine surveillance swabs will be taken from all patients on admission. Additional surveillance swabs will then be taken twice-weekly until discharge (or on the day of discharge for admission durations less than 7 days). Samples taken will be:

1) Respiratory
2) Urine
3) Stool or rectal
4) Wound (where present)

Data collection will be restricted to data required to address the objectives. Where possible, data will be obtained from standard data collection via PICAnet to maximise efficiency. A number of additional data points will be collected to inform possible outcomes for a definitive trial (duration of invasive mechanical ventilation, days alive and free of mechanical ventilation censored at 30 days, infectious episodes during PICU admission, total antibiotic usage in PICU, duration of PICU stay and hospital stay, mortality at PICU discharge and 30-days post-randomisation).

Adverse events will be monitored and reported up to 30 days post-randomisation.

Mixed Methods study

Health Care Professionals

All health care professionals currently working in a UK PICU will be invited to take part in an online survey. Additionally, focus groups will be held with healthcare professionals from two of the participating PICUs, with opportunities for telephone interviews for those unable to attend the group.

These will explore health care professionals' views on:

• acceptability of the trial design including selection of, and adherence to, the SDD intervention;
• acceptability of recruitment and deferred consent procedures in the trial; and
• acceptability of the overall trial procedures.

Parents/Guardians

The parents/guardians of each recruited child will be asked to complete a short, anonymous questionnaire which will seek their experiences of:

• recruitment and emergency consent;
• content and format of the PIS;
• decision-making in the PICU setting; and
• acceptability of the overall trial procedures.

Parents/guardians will also be invited to take part in a more detailed telephone interview. Interviews will be completed until data saturation (anticipated to be 15-25 based on previous studies).

A14-1. In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?

- [x] Design of the research
- [x] Management of the research
- [ ] Undertaking the research
- [ ] Analysis of results

- [x] Dissemination of findings
- [ ] None of the above

Give details of involvement, or if none please justify the absence of involvement.
The involvement of patients and their families has been integral to the design of PICnIC. Consultation has been undertaken with parents, PICU survivors, and a young people's group about the proposed study. Their views have contributed to the choice of outcomes and informed the study design.

Two contributors including, a former long-stay PICU patient, and, a mother who has first-hand experience of the difficulties of ventilator-associated pneumonia, are co-applicants on the grant proposal. They have contributed to the study design and, in particular, the consent procedures. We discussed at length that the intervention represents a PICU-wide infection control strategy for which specific consent would not typically be sought. We also discussed the collection of routine data vs. research specific data.

These contributors will be members of the Trial Management group to help guide the ongoing management of the trial. A further PPI member, with experience as a parent of a long-stay PICU patient, will sit on the Trial Steering Committee. The trial team at ICNARC CTU are working with all PPI members to help them contribute meaningfully to study discussions.

The mixed-methods study increases patient and public involvement through the research delivery phases, providing feedback on the trial processes to inform a larger study.

4. RISKS AND ETHICAL ISSUES

RESEARCH PARTICIPANTS

A15. What is the sample group or cohort to be studied in this research?

Select all that apply:

- [ ] Blood
- [ ] Cancer
- [ ] Cardiovascular
- [ ] Congenital Disorders
- [ ] Dementias and Neurodegenerative Diseases
- [ ] Diabetes
- [ ] Ear
- [ ] Eye
- [ ] Generic Health Relevance
- [ ] Infection
- [ ] Inflammatory and Immune System
- [ ] Injuries and Accidents
- [ ] Mental Health
- [ ] Metabolic and Endocrine
- [ ] Musculoskeletal
- [ ] Neurological
- [ ] Oral and Gastrointestinal
- [x] Paediatrics
- [ ] Renal and Urogenital
- [ ] Reproductive Health and Childbirth

- ☐ Respiratory
- ☐ Skin
- ☐ Stroke

Gender:	Male and female participants
Lower age limit: 38	Weeks gestational age
Upper age limit: 18	Years

A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).

Pilot cRCT:

Age >37 weeks (corrected gestational age) and ≤ 18 years
Receiving mechanical ventilation expected to last at least 48 hours

Mixed methods study:

Online survey/telephone interviews: All health care professionals working in a PICU within the UK
Focus Groups: All health care professionals working in the two PICUs selected for focus groups
Survey/telephone interviews: Parents/legal representatives of all recruited patients

A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).

Known allergy, sensitivity or interaction to polymyxin E, tobramycin, or nystatin
Known to be pregnant
Death perceived as imminent

RESEARCH PROCEDURES, RISKS AND BENEFITS

A18. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. *These include seeking consent, interviews, non-clinical observations and use of questionnaires.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days)
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Focus group/telephone interviews	1		60	Focus groups with around 8 health care professionals will be conducted at one intervention site and one control site by the PICnIC study team. Up to ten telephone interviews will be conducted with health care professionals at these sites who are unable to attend the focus groups.
Staff survey at participating sites	1		30	All staff involved in the PICnIC pilot study will be invited to complete an online survey of their experiences of taking part in the study,
Nationwide online staff surverys	1		30	Research active health care professionals across all UK PICUs will be invited to complete an online survey to assess the acceptability of the intervention and study design.
Patient survey/interviews	1		30-60	Following consent procedures all parents/legal representatives of children enrolled in the PICnIC study will be asked to complete an anonymous questionnaire or take part in a telephone interview within 4 weeks of their child's admission. This will be

conducted by members of the PICnIC study team.

A19. Give details of any clinical intervention(s) or procedure(s) to be received by participants as part of the research protocol. *These include uses of medicinal products or devices, other medical treatments or assessments, mental health interventions, imaging investigations and taking samples of human biological material. Include procedures which might be received as routine clinical care outside of the research.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days).
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
SDD Intervention - administration of SDD suspension and SDD paste	~20		10	Administration of study drug 4 times daily for duration of mechanical ventilation (typically 5 days)
Collection of microbiological samples	2		10	Twice-weekly Samples to be collected from patients in accordance with the PICnIC protocol by clinical staff deemed qualified to do so by the hospital.

A20. Will you withhold an intervention or procedure, which would normally be considered a part of routine care?

○ Yes ◉ No

A21. How long do you expect each participant to be in the study in total?

Given the nature of the study, all data collection is censored at 30 days. The average length of a PICU stay in the UK is 3-4 days.

A22. What are the potential risks and burdens for research participants and how will you minimise them?

For all studies, describe any potential adverse effects, pain, discomfort, distress, intrusion, inconvenience or changes to lifestyle. Only describe risks or burdens that could occur as a result of participation in the research. Say what steps would be taken to minimise risks and burdens as far as possible.

SDD is a licensed drug which has been in use for more than 30 years. It is used as standard within some adult ICUs in the UK and was standard practice in a PICU for many years. It also represents routine practice throughout some countries in Northern Europe. Those recruited to the trial face minimal risks associated with participation.

Additional samples will be taken from patients during the ecological surveillance periods. As the patients in the study are mechanically ventilated children, it is expected that they will be heavily sedated thus not conscious of any pain or discomfort. Staff will incorporate sample collection into normal routines thus minimising the emotional burden on parents of witnessing additional procedures.

The oral paste can have a poorly tolerated bitter taste, however, again, it is not expected that patients would experience this due to sedation and pain relief.

All patients with a documented allergy to any of the components will be excluded. There is a small risk of an undocumented allergy which would be reported to the MHRA per standard practice.

Whilst there is no explicit risk to parents/guardians from taking part in the mixed methods study, we acknowledge that the topics covered will be emotive for some. Prompts and questions will be designed to reduce any distress or personal intrusion. Parents/guardian will be able to withdraw from the conversation/study at any point without giving a reason. Participants will be signposted to referral agencies where the interviewer feels this is appropriate.

A23. Will interviews/ questionnaires or group discussions include topics that might be sensitive, embarrassing or upsetting, or is it possible that criminal or other disclosures requiring action could occur during the study?

◉ Yes ○ No

If Yes, please give details of procedures in place to deal with these issues:

The study team are aware that critical illness in children in an emotive topic and that there is the potential for parents/legal representatives to find this topic upsetting or stressful. The PICnIC study team have extensive experience designing and conducting interviews that include sensitive topics and all questions and prompts will be designed to minimise any potential stress or burden on the participants.

Focus groups/interview/surveys of health care professionals during the study are not predicted to contain sensitive or emotive topics or any disclosures requiring action.

A24. What is the potential for benefit to research participants?

Whilst there will be no suggestion of therapeutic superiority of SDD to parents/guardians when compared to standard infection control practices, SDD has been shown to reduce the incidence of ventilator-associated pneumonia in children. Larger trials in adults have shown that SDD increases survival rates. As such, participants in the intervention arm have the potential for benefit.

A25. What arrangements are being made for continued provision of the intervention for participants, if appropriate, once the research has finished? *May apply to any clinical intervention, including a drug, medical device, mental health intervention, complementary therapy, physiotherapy, dietary manipulation, lifestyle change, etc.*

The intervention is only provided to intubated patients in the PICU, there is no requirement for continued provision.

A26. What are the potential risks for the researchers themselves? *(if any)*

None

RECRUITMENT AND INFORMED CONSENT

In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.

A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used?*For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).*

Potential participants will be identified by the participating site's clinical and research team who will assess if the inclusion and none of the exclusion criteria have been met based on the patient's medical history and notes. Patients will be monitored for eligibility during their PICU stay by the site teams.

Participants for the mixed-method study will be identified directly from parents approached for consent or from the PICnIC site research teams.

A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?

◉ Yes ○ No

Please give details below:

Patient data will be reviewed during the screening and enrolment process by the local clinical and research teams who are bound by the standard duty of confidentiality.

A27-3. Describe what measures will be taken to ensure there is no breach of any duty of confidentiality owed to patients, service users or any other person in the process of identifying potential participants.*Indicate what steps have been or will be taken to inform patients and service users of the potential use of their records for this purpose. Describe the arrangements to ensure that the wishes of patients and service users regarding access to their records are respected. Please consult the guidance notes on this topic.*

Patient data which may be identifiable will only be seen by the local, direct healthcare team. This data will be kept within the NHS hospital or database and anonymised before it leaves the participating site.

All staff confirming eligibility will be required to be listed on the PICnIC Delegation Log and approved by the site's Principal Investigator(s).

No identifiable information will be passed to any individual outside of the direct health care team.

Patient identifiable information from any aspect of the mixed methods study will not be passed on to members outside of the PICnIC team.

A27-4. Will researchers or individuals other than the direct care team have access to identifiable personal information of any potential participants?

○ Yes ◉ No

A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?

○ Yes ◉ No

A29. How and by whom will potential participants first be approached?

Children admitted to PICU are facing a life-threatening emergency and it is understood that their parents may struggle to provide informed consent at this time. Approaches will be delayed until an appropriate time. A member of the research team will provide study information to patients/family members during recovery, giving them the opportunity to ask questions and opt-out of the use of trial specific data.

Information will be displayed in the PICU family/waiting room.

Mixed Methods study

All parents/guardians will be invited to complete a short, anonymous questionnaire and/or take part in a telephone interview by the local PICnIC team. It will be made clear that declining to participate will not affect their child's care in anyway.

Healthcare professionals will be sent email invitations to participate in the qualitative research, identified either locally or from the Paediatric Intensive Care Society's mailing list.

A30-1. Will you obtain informed consent from or on behalf of research participants?

○ Yes ◉ No

If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.

If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

If you are not obtaining consent, please explain why not.

The medicine used within the study is a standard, licensed treatment used in clinical practice, these are used without specific consent. All eligible patients will receive the treatment as part of the unit's standard infection control

procedures for the duration of the trial.

Posters will be displayed prominently within the units and leaflets will be provided explaining that a trial is taking place in the PICU. Local NHS research team staff will be available to answer any questions the parents may have, and we would encourage this approach to be supported by the child's assigned nurse. The leaflets will include details of how to obtain further information and clear guidance on how to request their child's data is not included in the data analysis. This is an established method within PICUs and is used to inform patients of data collection for PICANet.

Mixed methods study

Parents/legal representatives will be supplied with the questionnaire to complete or a link to the online version. It will be made clear that these are optional and will not affect their child's care, thus consent is implicit in their participation. If they wish to participate in telephone interviews, further information will be supplied in the form of an information leaflet.

Site staff will be supplied with written information via the initial invitation, supplemented by additional information if they agree to take part. Written consent will be sought from participants at the start of the focus group.

Please enclose a copy of the information sheet(s) and consent form(s).

A30-2. Will you record informed consent (or advice from consultees) in writing?

(●) Yes ( ) No

A31. How long will you allow potential participants to decide whether or not to take part?

Families will be given as much time as needed to consider participation. They will be able to opt-out of the use of their healthcare information until the time the study database is locked for final analysis. Contact information for the study teams will be clearly stated in the written information to afford patients this opportunity.

As the intervention will be part of the infection control policy, it will continue as normal in the PICU unless the family request for it to stop.

A32. Will you recruit any participants who are involved in current research or have recently been involved in any research prior to recruitment?

(●) Yes
( ) No
( ) Not Known

If Yes, please give details and justify their inclusion. If Not Known, what steps will you take to find out?

As SDD will form part of the standard care at the unit, co-enrolment into other studies will be allowed where there is no clash with the study's aims.

We will follow the "co-enrolment to critical care studies and trials in the United Kingdom" - a guidance document 2012 produced by the Intensive Care Society and consider the burden of possible co-enrolment on the patient and family.

Details of any co-enrolment will be documented on the PICnIC Trial Screening Log.

A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or written information given in English, or who have special communication needs?*(e.g. translation, use of interpreters)*

As per routine practice, hospital translation services will be used if the parents/legal representatives do not understand oral or written information in English.

For the qualitative components, as we are unable to conduct interviews in any languages other than English, we are unable to include participants who do not speak English.

A34. What arrangements will you make to ensure participants receive any information that becomes available during the course of the research that may be relevant to their continued participation?

All information received of any importance will be passed through the Principal Investigator at the site. Patient information sheets will be updated as required.

Any relevant studies will be monitored from clinical trial databases. The Chief Investigator will inform the both the Trial Steering Committee and the Data Monitoring and Ethics Committee of any relevant new data

CONFIDENTIALITY

In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data capable of being linked to a participant through a unique code number.

Storage and use of personal data during the study

A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)?*(Tick as appropriate)*

- [x] Access to medical records by those outside the direct healthcare team
- [ ] Access to social care records by those outside the direct social care team
- [x] Electronic transfer by magnetic or optical media, email or computer networks
- [x] Sharing of personal data with other organisations
- [ ] Export of personal data outside the EEA
- [x] Use of personal addresses, postcodes, faxes, emails or telephone numbers
- [ ] Publication of direct quotations from respondents
- [ ] Publication of data that might allow identification of individuals
- [ ] Use of audio/visual recording devices
- [x] Storage of personal data on any of the following:
  - [x] Manual files (includes paper or film)
  - [x] NHS computers
  - [ ] Social Care Service computers
  - [ ] Home or other personal computers
  - [ ] University computers
  - [x] Private company computers
  - [ ] Laptop computers

Further details:
ICNARC CTU will require access to patient's medical notes for monitoring visit(s) to ensure the quality of the data collection and consenting procedure.

Names and addresses will be collected, by necessity, from parents/guardians who wish to take part in a telephone questionnaire. Consent will be obtained for these contact details to be held by the PICnIC study team and used to arrange and conduct the interview.

Publication of direct quotes from participants may be necessary to report the results of the qualitative research, these will be anonymised.

Audio recordings of interviews and focus groups are necessary for transcription and analysis purposes. Transcription will be completed by a professional transcription company and files will be deleted once anonymised and check for

accuracy.

A37. Please describe the physical security arrangements for storage of personal data during the study?

All personal identifying data will be kept on NHS computers following appropriate safeguards. Only pseudonymised data will be kept on other computers.

At the ICNARC CTU, all personal data collected will be stored on a secure web-based data entry system housed at Red Technology. This is a specialist eCommerce hosting provider and all data centre buildings include proximity access control and digital CCTV to control physical access to equipment. These data are transferred to servers at ICNARC via a site-to-site IPsec VPN between ICNARC and Red Technology (VPN access is unidirectional from ICNARC to Red Technology).

Data are processed and stored on a server located in a secure, locked, air-conditioned room at ICNARC. Access to this room is restricted to authorised staff only. Access to both the web portal (by NHS and ICNARC staff) and ICNARC servers (by ICNARC staff) is restricted to authorised personnel only (permissions are attached to user names which requires a secure password).

Data are not encrypted on the servers due to the logical and physical office security in place, however, data are encrypted at the point they are stored on backup tapes. Physical office security includes a Grade 3 Red Care intruder detection system that has been supplied, installed and is maintained by ADT Fire and Security Plc. Staff are also required to sign in and out of the office at all times. All visitors are notified to building security by ICNARC staff in advance

Data destruction will be carried out in compliance with the Research Governance Framework and we work with suitably qualified contractors for both electronic and paper record destruction. For example, data stored at ICNARC are removed via a sector by sector wipe of the hard drive prior to physical destruction of the hard drive. Darik's Boot and Nuke is used to perform multiple passes of Mersenne Twister using DoD Short. This automatically and completely deletes the contents of any hard disk that it detects, making it an appropriate utility for bulk or emergency data destruction

A38. How will you ensure the confidentiality of personal data?*Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.*

Each PICnIC participant will be allocated a unique study number which will be used in all communications about the patient.

NHS staff are bound by the standard duty of confidentiality. All staff employed by ICNARC sign a contract, which incorporates a confidentiality clause and the consequences of breaching confidentiality are covered in our Disciplinary Procedure.

At the University of Liverpool, a unique identifier code for each interview participant will be generated based upon date of birth and a researcher-derived participant number (e.g.15/09/1978/01). The digital audio recordings of the interviews and focus groups are likely to contain details that could identify participants. They will be securely uploaded to a professional transcription company. Once transcribed, they will be anonymised and checked against original files for accuracy. Interview and focus group files will be labelled with a unique identity number, encrypted and held on password protected University of Liverpool desktop computers. All results will be presented in a way that does not attribute information to individuals.

A40. Who will have access to participants' personal data during the study? *Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.*

The data generated by the study will be analysed by appropriately qualified members of the PICnIC team within the ICNARC office in London and the University of Liverpool. Access to data will be restricted to members of the study team.

The principal means of study specific data collection will be electronic via a password protected website. Only pseudonymised data will be uploaded to this database.

Folders will be provided for the local research team to file any paper documents. This will be stored in secure, locked cabinets with access limited to authorised persons.

Storage and use of data after the end of the study

A41. Where will the data generated by the study be analysed and by whom?

The data generated by the study will be analysed by appropriately qualified members of the study team within the ICNARC office in London, England.

The qualitative evaluation will be conducted by appropriately qualified members of the PICnIC study team based at the University of Liverpool.

A42. Who will have control of and act as the custodian for the data generated by the study?

	Title	Forename/Initials	Surname
	Dr	Nazima	Pathan
Post	University Lecturer and Consultant in Paediatric Intensive Care		
Qualifications	MBBS, BSc, PhD		
Work Address	University of Cambridge		
	Hills Road		
	Cambridge		
Post Code	CB2 OQQ		
Work Email	np409@medschl.cam.ac.uk		
Work Telephone	07941455497		
Fax			

A43. How long will personal data be stored or accessed after the study has ended?

- ○ Less than 3 months
- ○ 3 – 6 months
- ◉ 6 – 12 months
- ○ 12 months – 3 years
- ○ Over 3 years

A44. For how long will you store research data generated by the study?

Years: 15
Months:

A45. Please give details of the long term arrangements for storage of research data after the study has ended. *Say where data will be stored, who will have access and the arrangements to ensure security.*

In line with Standard Operating Procedures for ICNARC CTU, all central essential documents will be archived for 15 years after the end of the trial. Once this period has passed, arrangements will be made for its confidential destruction.

INCENTIVES AND PAYMENTS

A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?

○ Yes ◉ No

A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

○ Yes ◉ No

A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

○ Yes ◉ No

NOTIFICATION OF OTHER PROFESSIONALS

A49-1. Will you inform the participants' General Practitioners (and/or any other health or care professional responsible for their care) that they are taking part in the study?

○ Yes ◉ No

If Yes, please enclose a copy of the information sheet/letter for the GP/health professional with a version number and date.

PUBLICATION AND DISSEMINATION

A50. Will the research be registered on a public database?

The UK Policy Framework for Health and Social Care Research sets out the principle of making information about research publicly available. Furthermore: Article 19 of the World Medical Association Declaration of Helsinki adopted in 2008 states that "every clinical trial must be registered on a publicly accessible database before recruitment of the first subject"; and the International Committee of Medical Journal Editors (ICMJE) will consider a clinical trial for publication only if it has been registered in an appropriate registry. Please see guidance for more information.

◉ Yes ○ No

Please give details, or justify if not registering the research.
The trial will be registered with ISRCTN via CPMS

Please ensure that you have entered registry reference number(s) in question A5-1.

A51. How do you intend to report and disseminate the results of the study?*Tick as appropriate:*

☑ Peer reviewed scientific journals
☐ Internal report
☑ Conference presentation
☑ Publication on website
☐ Other publication
☐ Submission to regulatory authorities
☐ Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
☐ No plans to report or disseminate the results

☐ Other (please specify)

A52. If you will be using identifiable personal data, how will you ensure that anonymity will be maintained when publishing the results?

All analysis, quantitative and qualitative, will be performed on anonymised data.

A53. Will you inform participants of the results?

◉ Yes ○ No

Please give details of how you will inform participants or justify if not doing so.
Results will be disseminated to those hospitals and made publicly available via the NIHR, University of Cambridge and ICNARC. Participants and their parents/legal representatives will be informed in the PIS as to where they will be able to see the study results.

5. Scientific and Statistical Review

A54. How has the scientific quality of the research been assessed?*Tick as appropriate:*

☑ Independent external review
☐ Review within a company
☐ Review within a multi−centre research group
☐ Review within the Chief Investigator's institution or host organisation
☐ Review within the research team
☐ Review by educational supervisor
☐ Other

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:
The trial has been reviewed by the NIHR Health Technology Assessment programme which commissioned the trial after advertising a priority call for research into SDD in paediatric critical illness.

For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.

For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.

A56. How have the statistical aspects of the research been reviewed?*Tick as appropriate:*

☑ Review by independent statistician commissioned by funder or sponsor
☐ Other review by independent statistician
☐ Review by company statistician
☐ Review by a statistician within the Chief Investigator's institution
☐ Review by a statistician within the research team or multi−centre group
☐ Review by educational supervisor
☐ Other review by individual with relevant statistical expertise
☐ No review necessary as only frequencies and associations will be assessed – details of statistical input not required

In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

	Title	Forename/Initials	Surname
		Aninymous	Reviewer
Department	Health Technology Assessment (HTA) Programme		
Institution	National Institute for Health Research (NIHR)		
Work Address			
Post Code			
Telephone			
Fax			
Mobile			
E-mail			

Please enclose a copy of any available comments or reports from a statistician.

A57. What is the primary outcome measure for the study?

Acceptability of the intervention to health care professionals and to parents/guardians(assessed by exploring willingness to recruit and acceptability of consent process)

A58. What are the secondary outcome measures?*(if any)*

- Adherence to the SDD intervention (assessed by proportion of eligible children allocated to the intervention that receive SDD)
- Estimation of recruitment rate
- Understanding of potential patient-centred primary and secondary outcome measures for the definitive cRCT

A59. What is the sample size for the research? *How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.*

Total UK sample size:	324
Total international sample size (including UK):	324
Total in European Economic Area:	324

Further details:
Pilot cRCT: We aim to recruit 324 participants across the 6 participating sites over an 18 week recruitment period

Mixed-methods study: focus groups (n=2) and telephone interviews (n=~10) with staff in participating PICUs; online survey with staff in all UK PICUs; and surveys (n=~100) and telephone interviews (until data saturation is reached, n=~15-25 based on previous studies) with parents/guardians.

A60. How was the sample size decided upon? *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

Data from PICANet indicate that during the period 1 January 2015 to 31 December 2015, 13,036 children admitted to 28 UK PICUs (9 per PICU per week) received invasive ventilation for a median of 3 calendar days (interquartile range 2 to 6 days). Based on this, an average of approximately 4.5 children per PICU per week receive invasive ventilation for 48 hours or more, and the average anticipated recruitment rate for the pilot cRCT is 3 children per PICU per week. The total anticipated sample size is therefore 324 children, of which 90 would receive the SDD intervention. Assuming an intracluster correlation coefficient (ICC) of 0.05 (average ICC for binary process measures in implementation studies, reported by the Health Services Research Unit at the University of Aberdeen), this sample size would enable rate parameters (recruitment, adherence, follow-up) with an observed value of 80% or greater to be estimated with a precision of ±10% or less.

A61. Will participants be allocated to groups at random?

○ Yes ◉ No

A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

Descriptive analysis will be conducted to assess the objectives of PICnIC. It is noted that obtaining reliable estimates of between-cluster variation (e.g. ICC) from pilot cRCTs is problematic, and likely to require pilots that are almost as large as the definitive trial. We propose to address this limitation by nesting the pilot cRCT-based estimates within wider routine data collection from PICANet. For each potential outcome that can be addressed from the routine data, we will compare trial-based estimates of its characteristics with estimates based on all potentially eligible children in both participating PICUs and in all UK PICUs. Furthermore, it should be noted that as a feasibility study, individual outcomes measures should be considered as just one of several assessment steps.

Interviews and focus groups will be transcribed, checked and anonymised as the study progresses. QSR NVivo software will be used to assist in the organisation and indexing of qualitative data. Whilst analysis will be informed by the constant comparison approach of grounded theory, the focus will be modified to fit with the criterion of catalytic validity, whereby findings should be relevant to future research and practice (in particular, the design of the potential definitive cRCT).

6. MANAGEMENT OF THE RESEARCH

A63. Other key investigators/collaborators. *Please include all grant co−applicants, protocol co−authors and other key members of the Chief Investigator's team, including non-doctoral student researchers.*

	Title	Forename/Initials	Surname
	Dr	David	Harrison
Post	Head Statistician		
Qualifications	PhD, MA, BA		
Employer	Intensive Care Audit & Research Centre		
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	London		
	London		
Post Code	WC1V 6AZ		
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Work Email	david.harrison@icnarc.org		

	Title	Forename/Initials	Surname
	Professor	Brian	Cuthbertson
Post	Department Chief		
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Title	Forename/Initials	Surname
Professor	Lyvonne	Tume

Post	Associate Professor in Child Health
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Title	Forename/Initials	Surname
Dr	Rob	Shulman

Post	Lead Pharmacist - Critical Care
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Title	Forename/Initials	Surname
Dr	Kerry	Woolfall

Post	Research Fellow
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Employer	University of Liverpool
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Post Code	L69 3BX
Telephone	01517944634
Fax	
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Title	Forename/Initials	Surname
Dr	John	Pappachan

Post	Consultant in Anaesthesia and Paediatric Intensive Care
Qualifications	BM BCh
Employer	University Hospital Southampton NHS Foundation Trust

Work Address	Southampton Children's Hospital Tremona Road Southampton
Post Code	SO16 6YD
Telephone	
Fax	
Mobile	
Work Email	jvp@soton.ac.uk

Title	Forename/Initials	Surname
Mr	Paul	Mouncey

Post	Head of Research
Qualifications	MSc, BSc
Employer	Intensive Care National Audit & Research Centre
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Post Code	WC1V 6AZ
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Fax	
Mobile	
Work Email	paul.mouncey@icnarc.org

Title	Forename/Initials	Surname
Dr	Estee	Torok

Post	Clinician Scientiest Fellow and Senior Research Associate (Microbiology)
Qualifications	PhD, MBBS, BA
Employer	University of Cambridge
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Post Code	CB2 0QQ
Telephone	
Fax	
Mobile	
Work Email	et317@medschl.cam.ac.uk

Title	Forename/Initials	Surname
Professor	Kathryn	Rowan

Post	Director of Scientific and Strategic Development
Qualifications	PhD, MSc, BSc
Employer	Intensive Care National Audit & Research Centre
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Post Code	WC1V 6AZ
Telephone	02072699277
Fax	
Mobile	
Work Email	kathy.rowan@icnarc.org

Title Forename/Initials Surname

Post
Qualifications
Employer
Work Address

Post Code
Telephone
Fax
Mobile
Work Email

A64. Details of research sponsor(s)

A64-1. Sponsor

Lead Sponsor

Status:
- (●) NHS or HSC care organisation
- ( ) Academic
- ( ) Pharmaceutical industry
- ( ) Medical device industry
- ( ) Local Authority
- ( ) Other social care provider (including voluntary sector or private organisation)
- ( ) Other

Commercial status: Non-Commercial

If Other, please specify:

Contact person

Name of organisation	Cambridge University Hospitals NHS Foundation Trust and University of Cambridge
Given name	Adam
Family name	Loveday
Address	Hills Road
Town/city	Cambridge
Post code	CB2 0QQ
Country	
Telephone	01233245151
Fax	
E-mail	research@addenbrookes.nhs.uk

A65. Has external funding for the research been secured?

Please tick at least one check box.

- [x] Funding secured from one or more funders
- [ ] External funding application to one or more funders in progress
- [ ] No application for external funding will be made

What type of research project is this?

- (•) Standalone project
- ( ) Project that is part of a programme grant
- ( ) Project that is part of a Centre grant
- ( ) Project that is part of a fellowship/ personal award/ research training award
- ( ) Other

Other – please state:

Please give details of funding applications.

Organisation	National Institute of Health Research
Address	Evaluation Trials and Studies Coordinating Centre
	University of Southampton
	Enterprise Road, Southampton
Post Code	SO16 7NS
Telephone	02380595586
Fax	
Mobile	
Email	netscomms@nihr.ac.uk

Funding Application Status: (•) Secured ( ) In progress

Amount: 519,652.40

Duration
Years: 1
Months: 6

If applicable, please specify the programme/ funding stream:

What is the funding stream/ programme for this research project?
Health Technology Assessment

A66. Has responsibility for any specific research activities or procedures been delegated to a subcontractor (other than a co-sponsor listed in A64-1) ? *Please give details of subcontractors if applicable.*

(•) Yes ( ) No

Name:

Type of organisation:
( ) NHS ( ) Academic ( ) Commercial (•) Other

Please give further details of sub-contractor and main areas of delegated responsibility: Intensive Care National Audit & Research Centre

A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?

○ Yes ◉ No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.

A68-1. Give details of the lead NHS R&D contact for this research:

	Title	Forename/Initials	Surname
	Dr	Adam	Loveday
Organisation	Cambridge University Hospitals NHS Foundation Trust		
Address	Hills Road		
	Cambridge		
Post Code	CB2 0QQ		
Work Email	adam.loveday@addenbrookes.nhs.uk		
Telephone	01223348455		
Fax			
Mobile			

Details can be obtained from the NHS R&D Forum website: http://www.rdforum.nhs.uk

A68-2. Select Local Clinical Research Network for NHS Organisation identified in A68-1:

Eastern

For more information, please refer to the question specific guidance.

A69-1. How long do you expect the study to last in the UK?

Planned start date: 01/11/2019
Planned end date: 30/04/2021
Total duration:
Years: 1 Months: 5 Days: 30

A70. Definition of the end of trial, and justification in the case where it is not the last visit of the last subject undergoing the trial (1)

Last patient discharge (censored at 30 days)

A71-1. Is this study?

◯ Single centre
◉ Multicentre

A71-2. Where will the research take place? *(Tick as appropriate)*

☑ England
☐ Scotland
☐ Wales
☐ Northern Ireland
☐ Other countries in European Economic Area

Total UK sites in study

Does this trial involve countries outside the EU?
◯ Yes ◯ No

A72. Which organisations in the UK will host the research?*Please indicate the type of organisation by ticking the box and give approximate numbers if known:*

☐ NHS organisations in England 6
☐ NHS organisations in Wales
☐ NHS organisations in Scotland
☐ HSC organisations in Northern Ireland
☐ GP practices in England
☐ GP practices in Wales
☐ GP practices in Scotland
☐ GP practices in Northern Ireland
☐ Joint health and social care agencies (eg community mental health teams)
☐ Local authorities
☐ Phase 1 trial units
☐ Prison establishments
☐ Probation areas
☐ Independent (private or voluntary sector) organisations
☐ Educational establishments
☐ Independent research units
☐ Other (give details)

Total UK sites in study: 6

A73-1. Will potential participants be identified through any organisations other than the research sites listed above?

◯ Yes ◉ No

A74. What arrangements are in place for monitoring and auditing the conduct of the research?

Recruitment
The Chief Investigator will delegate recruitment of participants at the study research sites to the local Principal Investigators. This may be further delegated to local research nurses and investigators. Details of delegation will be recorded in delegation logs. The local Principal Investigators will ensure adequate local training of all staff involved in the study.

Management
Management and monitoring of the study will be delegated by the study Sponsor to the ICNARC CTU. The progress of the study will be monitored and supervised by the Trial Steering Committee. At least 75% of the members will be independent (including the Chair).

Site monitoring
All participating sites must agree to allow study-related monitoring and audits by providing direct access to source data/documents, as required. Informed consent from parents/legal representatives for this will also be obtained. Frequency of monitoring visits will be outlined in the PICnIC Pilot Study Monitoring Plan and will consist of all sites visited at least once to monitor recruitment and compliance with the study protocol. Additional on-site monitoring visits may be scheduled where there is evidence or suspicion of non-compliance by a site to important aspect(s) of the study requirements.

A75-1. What arrangements will be made to review interim safety and efficacy data from the trial? Will a formal data monitoring committee or equivalent body be convened?

In line with standard practice, an independent Data Monitoring and Ethic Committee (DMEC) will be convened made up of experts in clinical trials, biostatistics and paediatric intensive care medicine. Their role will be to provide oversight to ensure the rights and safety of patients involved in the study are protected. which will include experienced paediatric intensive care medicine clinicians and statistician(s). All members of the DMEC will remain independent from the study and the Trial Steering Committee and will operate in accordance with the DAMOCLES Charter.

If a formal DMC is to be convened, please forward details of the membership and standard operating procedures to the Research Ethics Committee when available. The REC should also be notified of DMC recommendations and receive summary reports of interim analyses.

A75-2. What are the criteria for electively stopping the trial or other research prematurely?

The study may be terminated at any time at the request of the Trial Steering Committee, independently of, or in consultation with, the Data Monitoring and Ethics Committee. Assessment of trial data can be requested at any time. As the intervention is already in use, it is not expected that early stopping of the trial would be recommended unless circumstances are exceptional.

A76. Insurance/ indemnity to meet potential legal liabilities

***Note:* in this question to NHS indemnity schemes include equivalent schemes provided by Health and Social Care (HSC) in Northern Ireland**

A76-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? *Please tick box(es) as applicable.*

Note: Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the arrangements and provide evidence.

- [x] NHS indemnity scheme will apply (NHS sponsors only)
- [ ] Other insurance or indemnity arrangements will apply (give details below)

Please enclose a copy of relevant documents.

A76-2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research? *Please tick box(es) as*

applicable.

Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.

☐ NHS indemnity scheme will apply (protocol authors with NHS contracts only)

☑ Other insurance or indemnity arrangements will apply (give details below)

The University Insurance Section has advised that subject to the study being approved by the relevant Ethics Committees there should be no difficulty in arranging insurance cover for negligent and non-negligent harm to research subjects under the University's Clinical Trials and/or Human Volunteer Studies policy

Please enclose a copy of relevant documents.

A76-3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research?

Note: Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.

☑ NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)

☐ Research includes non-NHS sites (give details of insurance/ indemnity arrangements for these sites below)

Please enclose a copy of relevant documents.

A77. Has the sponsor(s) made arrangements for payment of compensation in the event of harm to the research participants where no legal liability arises?

○ Yes ◉ No

Please enclose a copy of relevant documents.

A78. Could the research lead to the development of a new product/process or the generation of intellectual property?

○ Yes ◉ No ○ Not sure

Part B: Section 5 – Use of newly obtained human tissue(or other human biological materials) for research purposes

1. What types of human tissue or other biological material will be included in the study?

Sputum/secretions from the endotracheal tube, urine, stool/rectal swabs and (if present) wound swabs will be taken from all enrolled patients during the recruitment period at admission and twice weekly until discharge. Samples will be repeated on the day of discharge for patients with a length of stay of <7 days.

These same samples will be taken from all patients admitted to a participating PICU during the trials three distinct ecology surveillance period. Similarly, these will be taken twice weekly until discharge with samples being repeated on the day of discharge for patients with a length of stay of <7 days. In addition to reporting of microbiological cultures from routine clinical care the purpose of collection and analysis of these samples is to monitor changes in antibiotic resistance rates.

2. Who will collect the samples?

Samples will be collected by trained health care professionals working in the participating PICU at the designated time points.

3. Who will the samples be removed from?

- [x] Living donors
- [ ] The deceased

4. Will informed consent be obtained from living donors for use of the samples? *Please tick as appropriate*

In this research?

◯ Yes ◉ No

In future research?

◯ Yes ◉ No ◯ Not applicable

If answering No in either case, please justify:

Patients will be given the opportunity to opt out of further sample collection and the use of study specific data

6. Will any tissues or cells be used for human application or to carry out testing for human application in this research?

◯ Yes ◉ No

8. Will the samples be stored: *[Tick as appropriate]*

In fully anonymised form? *(link to donor broken)*

◉ Yes ◯ No

In linked anonymised form? *(linked to stored tissue but donor not identifiable to researchers)*

◯ Yes ◯ No

In a form in which the donor could be identifiable to researchers?

◯ Yes ◯ No

9. What types of test or analysis will be carried out on the samples?

10. Will the research involve the analysis or use of human DNA in the samples?

◯ Yes ◉ No

11. Is it possible that the research could produce findings of clinical significance for donors or their relatives?

◯ Yes ◉ No

12. If so, will arrangements be made to notify the individuals concerned?

○ Yes ○ No ◉ Not applicable

13. Give details of where the samples will be stored, who will have access and the custodial arrangements.

The samples will be stored under the custodianship of the chief investigator, Dr Nazima Pathan, at the sponsor site for a period of three years following informed parental consent. Any samples remaining at the end of the study will be discarded (as per Q14).

14. What will happen to the samples at the end of the research? *Please tick all that apply and give further details.*

☐ Transfer to research tissue bank

(If the bank is in England, Wales or Northern Ireland the institution will require a licence from the Human Tissue Authority to store relevant material for possible further research.)

☐ Storage by research team pending ethical approval for use in another project

(Unless the researcher's institution holds a storage licence from the Human Tissue Authority, or the tissue is stored in Scotland, or it is not relevant material, a further application for ethical review should be submitted before the end of this project.)

☐ Storage by research team as part of a new research tissue bank

(The institution will require a licence from the Human Tissue Authority if the bank will be storing relevant material in England, Wales or Northern Ireland. A separate application for ethical review of the tissue bank may also be submitted.)

☐ Storage by research team of biological material which is not "relevant material" for the purposes of the Human Tissue Act

☑ Disposal in accordance with the Human Tissue Authority's Code of Practice

☐ Other

☐ Not yet known

Please give further details of the proposed arrangements:

PART B: Section 7 - Children

1. Please specify the potential age range of children under 16 who will be included and give reasons for carrying out the research in this age group.

Any child over 37 weeks corrected gestational age

2. Indicate whether any children under 16 will be recruited as controls and give further details.

The same patient population will be included in control and intervention sites.

3-2. Please describe the arrangements for seeking informed consent from a person with parental responsibility and/or from children able to give consent for themselves.

Individual patient consent will not be sought as the study intervention will represent 'usual care' for the duration of the study. Posters and leaflets will be prominently displayed around the unit. The leaflets will give clear guidance on how to opt-out of data collection. Local NHS research staff will be on hand to answer questions the family may have, supported by the child's assigned nurse.

4. If you intend to provide children under 16 with information about the research and seek their consent or agreement, please outline how this process will vary according to their age and level of understanding.

An age appropriate PIS and assent form will to be provided to children once they have recovered – these will be for children 8-11 years and 12 and over.

The local research team which will consist of experienced paediatricians and paediatric nurse who possess extensive experience in providing information to children in age appropriate ways. The team will discuss the PIS with the child and provide the opportunity to ask any questions about the research study. If the child has yet to regain capacity but is likely to do so after discharge parents/legal representatives will be provided with the age appropriate PIS to take home for discussion following recovery.

The following link to an animation (https://youtu.be/_Fs1yUxeBFQ) which describes what happens when children are included in research without prior consent will be included in the age-appropriate PIS. The animation is based on the findings from 'The Childrens Voices project' which explored the views of 16 children aged 7-15 about research without prior consent.

Copies of written information sheet(s) for parents and children, consent/assent form(s) and any other explanatory material should be enclosed with the application.

PART C: Overview of research sites

Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites. *For further information please refer to guidance.*

Investigator identifier	Research site		Investigator Name	
IN1	◉ NHS/HSC Site ○ Non-NHS/HSC Site		Forename Middle name Family name Email Qualification (MD...) Country	Nazima Pathan np409@medschl.cam.ac.uk MB BS, PhD UNITED KINGDOM
	Organisation name	CAMBRIDGE UNIVERSITY HOSPITALS NHS FOUNDATION TRUST		
	Address	ADDENBROOKES HOSPITAL HILLS ROAD CAMBRIDGE CAMBRIDGESHIRE		
	Post Code	CB2 0QQ		
	Country	ENGLAND		
IN2	◉ NHS/HSC Site ○ Non-NHS/HSC Site		Forename Middle name Family name Email Qualification (MD...) Country	Peter Davis peter.davis@uhbristol.nhs.uk MB ChB UNITED KINGDOM
	Organisation name	UNIVERSITY HOSPITALS BRISTOL NHS FOUNDATION TRUST		
	Address	MARLBOROUGH STREET BRISTOL AVON		
	Post Code	BS1 3NU		
	Country	ENGLAND		
IN3	◉ NHS/HSC Site ○ Non-NHS/HSC Site		Forename Middle name Family name Email Qualification (MD...) Country	John Pappachan john.pappachan@uhs.nhs.uk Ma MBBChir FRCA UNITED KINGDOM
	Organisation name	UNIVERSITY HOSPITAL SOUTHAMPTON NHS FOUNDATION TRUST		
	Address	MAILPOINT 18 SOUTHAMPTON GENERAL HOSPITAL		

	TREMONA ROAD SOUTHAMPTON HAMPSHIRE
Post Code	SO16 6YD
Country	ENGLAND

IN4

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Organisation name	THE NEWCASTLE UPON TYNE HOSPITALS NHS FOUNDATION TRUST
Address	FREEMAN HOSPITAL
	FREEMAN ROAD
	HIGH HEATON NEWCASTLE-UPON-TYNE TYNE AND WEAR
Post Code	NE7 7DN
Country	ENGLAND

Forename	Grace
Middle name	
Family name	Williamson
Email	grace.williamson@nuth.nhs.uk
Qualification (MD...)	MD
Country	UNITED KINGDOM

IN5

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Organisation name	BIRMINGHAM WOMEN'S AND CHILDREN'S NHS FOUNDATION TRUST
Address	STEELHOUSE LANE
	BIRMINGHAM WEST MIDLANDS
Post Code	B4 6NH
Country	ENGLAND

Forename	Kevin
Middle name	
Family name	Morris
Email	kevin.morris@bch.nhs.uk
Qualification (MD...)	MB BS
Country	UNITED KINGDOM

PART D: Declarations

D1. Declaration by Chief Investigator

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.

2. I undertake to fulfil the responsibilities of the chief investigator for this study as set out in the UK Policy Framework for Health and Social Care Research.

3. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.

4. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.

5. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.

6. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.

7. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.

8. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.

9. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 2018.

10. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:

    - Will be held by the REC (where applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
    - May be disclosed to the operational managers of review bodies, or the appointing authority for the REC (where applicable), in order to check that the application has been processed correctly or to investigate any complaint.
    - May be seen by auditors appointed to undertake accreditation of RECs (where applicable).
    - Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.
    - May be sent by email to REC members.

11. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 2018.

12. I understand that the main REC or its operational managers may share information in this application or supporting documentation with the Medicines and Healthcare products Regulatory Agency (MHRA) where it is relevant to the Agency's statutory responsibilities.

13. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the Health Research Authority (HRA) together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after the issue of the ethics committee's final opinion or the withdrawal of the application.

Contact point for publication*(Not applicable for R&D Forms)*

HRA would like to include a contact point with the published summary of the study for those wishing to seek further information. We would be grateful if you would indicate one of the contact points below.

- ◯ Chief Investigator
- ◯ Sponsor
- ◯ Study co-ordinator
- ◯ Student
- ◯ Other – please give details
- ◯ None

Access to application for training purposes *(Not applicable for R&D Forms)*

Optional – please tick as appropriate:

☐ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

This section was signed electronically by Dr Nazima Pathan on 30/01/2020 20:00.

Job Title/Post:	University Lecturer and Consultant In Paediatric Intensive Care
Organisation:	Cambridge University
Email:	np409@cam.ac.uk

D2. Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the co−sponsors by a representative of the lead sponsor named at A64-1.

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.

2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.

3. Any necessary indemnity or insurance arrangements, as described in question A76, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.

4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.

5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.

6. The responsibilities of sponsors set out in the UK Policy Framework for Health and Social Care Research will be fulfilled in relation to this research.

   Please note: *The declarations below do not form part of the application for approval above. They will not be considered by the Research Ethics Committee.*

7. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

8. Specifically, for submissions to the Research Ethics Committees (RECs) I declare that any and all clinical trials approved by the HRA since 30th September 2013 (as defined on IRAS categories as clinical trials of medicines, devices, combination of medicines and devices or other clinical trials) have been registered on a publically accessible register in compliance with the HRA registration requirements for the UK, or that any deferral granted by the HRA still applies.

This section was signed electronically by Dr Adam Loveday on 03/02/2020 11:47.

Job Title/Post:	Research Governance Coordinator
Organisation:	Cambridge University Hospitals NHS FT
Email:	adam.loveday@addenbrookes.nhs.uk