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)
PRISM

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
- [x] Scotland
- [x] 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 review bodies are you applying to?

- [ ] HRA Approval
- [x] NHS/HSC Research and Development offices
- [ ] Social Care Research Ethics Committee
- [x] Research Ethics Committee
- [ ] Confidentiality Advisory Group (CAG)
- [ ] National Offender Management Service (NOMS) (Prisons & Probation)

For NHS/HSC R&D offices, the CI must create Site-Specific Information Forms for each site, in addition to the study-wide forms, and transfer them to the PIs or local collaborators.

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

(•) Yes ( ) No

5a. Are all the research costs and infrastructure costs for this study provided by an NIHR Biomedical Research Centre, NIHR Biomedical Research Unit, NIHR Collaboration for Leadership in Health Research and Care (CLAHRC) or NIHR Research Centre for Patient Safety & Service Quality in all study sites?

( ) Yes (•) No

If yes and you have selected HRA Approval in question 4 above, your study will be processed through HRA Approval.

If yes, and you have not selected HRA Approval in question 4 above, NHS permission for your study will be processed through the NIHR Coordinated System for gaining NHS Permission (NIHR CSP).

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 (CRN) Portfolio? Please see information button for further details.

(•) Yes ( ) No

If yes, you must complete a NIHR Clinical Research Network (CRN) Portfolio Application Form immediately after completing this project filter and before submitting other applications. If you have selected HRA Approval in question 4 above your study will be processed through HRA Approval. If not, NHS permission for your study will be processed through the NIHR Coordinated System for gaining NHS Permission (NIHR CSP).

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

NHS/HSC R&D Form (project information)

Please refer to the Submission and Checklist tabs for instructions on submitting R&D applications.

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)
PRISM

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

Prevention of Respiratory Insufficiency after Surgical Management (PRISM) Trial:
A pragmatic randomised controlled trial of continuous positive airway pressure (CPAP) to prevent respiratory complications and improve survival following major abdominal surgery

A3-1. Chief Investigator:

	Title	Forename/Initials	Surname
	Professor	Rupert	Pearse
Post	Professor of Intensive Care Medicine		
Qualifications	BSc(Hons) MBBS MD FRCA FFICM		
Employer	Queen Mary University of London		
Work Address	Adult Critical Care Unit, Royal London Hospital London		
Post Code	E1 1BB		
Work E-mail	r.pearse@qmul.ac.uk		
* Personal E-mail			
Work Telephone	+442035940346		
* Personal Telephone/Mobile			
Fax	+442035943140		

** 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
	Mr	Richard	Haslop
Address	Adult Critical Care Research Office, Room 14, Central Tower		
	Royal London Hospital		
	London		
Post Code	E1 1BB		
E-mail	r.haslop@qmul.ac.uk		
Telephone	0203 59 40352		
Fax	020 7882 7276		

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):	10443
Sponsor's/protocol number:	10443
Protocol Version:	1.4
Protocol Date:	18/08/2015
Funder's reference number:	

Project website: www.prismtrial.org

Registry reference number(s):
The Department of Health's Research Governance Framework for Health and Social Care and the research governance frameworks for Wales, Scotland and Northern Ireland set out the requirement for registration of trials. 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.*

Far from being replaced by new drug therapies, surgical treatments are offered to more patients than ever before. In particular, older patients with serious medical problems are more likely to undergo surgery today than 20 years ago. In

a technical sense, surgery and anaesthesia are very safe, yet high-risk patients frequently develop medical complications, especially following major abdominal surgery. These complications have a lasting human and financial cost which may be avoidable. Surgery and anaesthesia have a number of harmful effects on the lungs, and respiratory complications such as pneumonia, are amongst the most important in terms of frequency and severity. However, current standard treatments like physiotherapy and supplemental oxygen do not always prevent complications from developing.

Several small clinical trials have shown that continuous positive airways pressure (CPAP) can reduce respiratory complications after major abdominal surgery. CPAP is a method of supporting breathing using slightly pressurised air, usually delivered using a tight-fitting facemask. This can make it easier for patients to breathe, and may help them recover more quickly from the effects of surgery and anaesthesia, so avoiding complications such as pneumonia. CPAP has been widely used for many years in the treatment of patients with various types of breathing problems and can be delivered safely on hospital wards or even in the patient's home. However, a lack of robust evidence from large-scale clinical trials has prevented the routine use of CPAP for patients after abdominal surgery.

We propose to recruit 4800 patients into an international, randomised controlled trial to determine whether CPAP immediately after major abdominal surgery can reduce the number of patients who develop serious respiratory complications.

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, R&D office 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.

There are few significant issues with the proposed trial.

Consent
We will only recruit patients with capacity to consent. Patients will be approached before surgery, and in the great majority of cases this will be in the pre-operative assessment clinic several days before surgery. This is preferable both for the patient and the investigators. However, some patients will arrive in hospital on the morning of surgery having not attended a pre-operative assessment clinic. Provided that all reasonable efforts have been made to identify a potential participant at least 24 hours in advance of surgery, they will still be eligible for recruitment within a shorter time frame if this has not proved possible.

Risks, burdens and benefits
CPAP has been used routinely in NHS hospitals for many years. It is likely that many patients enrolled in this trial will benefit. The treatment has an excellent safety record, and all eligible hospitals already employ trained staff to administer CPAP to other patient groups according to well established protocols. CPAP is even used by patients at home to treat sleep apnoea.

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.*

To determine whether the use of continuous positive airway pressure (CPAP) immediately following surgery reduces the incidence of pneumonia, re-intubation or death within 30 days of major elective abdominal surgery compared to usual care.

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

To determine whether routine CPAP reduces other types of complications after surgery. These include infections, the need for mechanical support of breathing, the duration of time spent in the critical care unit, duration of hospital stay, re-admission to hospital within 30 days of surgery and death within one year of surgery. We will also determine the safety and tolerability of routine CPAP following surgery.

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

Approximately 310 million surgical procedures are carried out worldwide each year. After surgery more than seven million patients develop complications with one million deaths. Estimates of postoperative mortality range from 1 to 4% depending on the population sampled and the type of surgical procedure. However, it is clear that mortality and morbidity following surgery is greater in high-risk populations, where patients have pre-existing medical conditions, are elderly or undergoing a major abdominal procedure.

Major abdominal surgery is associated with significant adverse changes in respiratory function. Anaesthesia can cause reduced lung capacity and cause abnormally low levels of oxygen in the blood, while surgery can restrict breathing, damage muscles involved with breathing and cause collapse or closure of the lung. These factors interact with pre-existing lung disease and pain following surgery to create a significant risk of pneumonia and respiratory failure, which may result in death. Evidence from one study suggests that the risk of death within 30 days of surgery is increased from 1% to 27% in patients with respiratory failure.

Continuous positive airway pressure (CPAP) is a non-invasive method of supporting breathing. The patient breathes slightly pressurised air whilst inhaling and exhaling. It is delivered via a facemask, helmet or nasal device by experienced nurses with minimal supervision by a doctor. The findings of several trials have demonstrated that CPAP can prevent respiratory complications in high-risk patients following major surgery. However, all of the previous clinical trials have been relatively small and therefore lacking in statistical power. Whilst the results of these trials suggest that postoperative CPAP has some benefit, there has yet to be a large multicentre trial to evaluate clinical effectiveness. The several trials of CPAP in the abdominal surgery population have shown encouraging results, but there has been limited translation to clinical practice. More robust evidence is needed to justify the changes to patient care after surgery, and as a result the preventative use of CPAP after major abdominal surgery has not been introduced to routine practice in most healthcare systems. There is a clear need for a large clinical trial to address this uncertainty.

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.*

Study design
Randomised controlled trial with open study group allocation

Patients
We will recruit patients scheduled for elective major, open, abdominal surgery

Randomisation

Randomisation will occur after the participant has provided informed consent but before the surgical procedure is due to start. It will occur on the day of surgery when surgery is confirmed. Participants will be centrally allocated to treatment groups (1:1) by a computer generated dynamic procedure (minimisation) with a random component. Minimisation will be performed by country, surgical procedure category and planned use of epidural anaesthesia. The surgical procedure categories are: resection of colon, rectum or small bowel; resection of liver, pancreas or gall bladder; resection of stomach (non-obesity surgery); obesity surgery; vascular procedure; or other intra-peritoneal procedure.

Trial intervention
The trial intervention period will commence immediately after the completion of surgery and continue for four hours. After four hours, CPAP will be continued or discontinued at the clinician's discretion. Patients in the usual care group will be managed by clinical staff according to local policy and guidelines. It is considered good practice for postoperative patients to receive oxygen via facemask or nasal cannulae.

Data collection
Patients will be assessed at screening, where the trial inclusion/exclusion criteria will be checked. Pre-operatively, demographic information, medical history, height/weight and quality of life will be assessed and the patient will be randomised. 24 hours post-operatively, intraoperative information, CPAP use and adverse events will be assessed. On hospital discharge, there will be a review of the medical notes, days of ICU and hospital will be checked and adverse events will be assessed. 30 days and one year after randomisation, investigators will review the patient's medical record to assess specific postoperative complications and treatments for postoperative complications and contact the patient by telephone to conduct a brief interview and assess quality of life. To facilitate the health economic analysis, in terms of hospital episode data, and in cases where the participant is un-contactable during the follow-up period, we will request hospital episode statistics and mortality data from the HSCIC for UK participants or equivalent national database for other participating countries. Prospective consent for ONS/HES data linkage will be sought before enrolment into the trial.

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
- [x] Undertaking the research
- [x] 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 study protocol has also been reviewed by the Royal College of Anaesthetists Patient and Public Involvement group.

The PRISM study group includes two patient representatives who have helped us to develop all patient facing documentation. They will be involved throughout the study from design through to dissemination.

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
- [x] Generic Health Relevance
- [ ] Infection
- [ ] Inflammatory and Immune System
- [ ] Injuries and Accidents
- [ ] Mental Health
- [ ] Metabolic and Endocrine
- [ ] Musculoskeletal
- [ ] Neurological
- [ ] Oral and Gastrointestinal
- [ ] Paediatrics
- [ ] Renal and Urogenital
- [ ] Reproductive Health and Childbirth
- [ ] Respiratory
- [ ] Skin
- [ ] Stroke

Gender:	Male and female participants
Lower age limit: 50	Years
Upper age limit:	Years

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

1. Aged 50 years or over

2. Undergoing elective major, open, abdominal surgery

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

1. Inability or refusal to provide informed consent

2. Anticipated requirement for invasive or non-invasive mechanical ventilation for at least four hours after surgery as part of routine care

3. Pregnancy or obstetric surgery

4. Previous enrollment in PRISM trial

5. Participation in a clinical trial of a treatment with a similar biological mechanism or related primary outcome measure

6. Clinician refusal

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
Informed consent	1	0	15 minutes	Appropriately trained member of the research team
EQ-5D questionnaire	3	0	5 minutes	Appropriately trained member of the research team
Telephone follow-up	2	0	5 minutes	Appropriately trained member of the research 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
Continuous positive airway pressure intervention	1	0	4 hours	Appropriately trained member of clinical staff as part of the patient's direct clinical care team

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?

After informed consent, the study period will begin. Postoperative follow up will continue until one year after the date of randomisation.

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.

Previous research suggests that the treatment we are investigating will benefit the majority of patients. The risks of this study to patient health are very small. Continuous positive airway pressure is routinely used to support the breathing of patients with long-term breathing problems and is considered very safe. In a small number of cases CPAP may cause side effects, for example discomfort around pressure areas (eg nose), claustrophobia and oro-nasal dryness. The trial intervention will only be administered by trained clinical staff according to local hospital policies in an appropriate clinical area.

Adverse events will be assessed by the Data Monitoring and Ethics Committee (DMEC) and the Trial Management Group (TMG) using serious adverse event report assessment. The DMEC is independant of the trial team and comprises of two clinicians with experience in undertaking clinical trials and a statistician. The DMEC will perform a single interim analysis as it sees fit. The trial will be terminated early if there is evidence of harm in the intervention

group or if recruitment is futile.

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

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

The findings of several trials have demonstrated the efficacy of CPAP as a preventative treatment for high-risk patients following abdominal surgery by reducing the incidence of postoperative pulmonary complications.

The information learned from this trial is likely to result in safer surgery for future patients.

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.*

Any further treatment will be decided by the treating clinician.

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

None anticipated.

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).*

Patients will be identified and approached by a member of the research team before surgery. Potential participants will be screened by research staff at the site having been identified from pre-admission clinic lists, operating theatre lists and by communication with the relevant nursing and medical staff. Members of the research team are considered part of the patient's direct clinical care team.

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:
Members of the research team, who also form part of the patient's direct clinical care team, at the participating sites will have access to patient records as part of their medical care and will use these records to screen for potentially eligible patients. Patients who consent to enter the trial are informed that staff from the research team, the sponsor (and its representatives), relevant regulatory authorities, or from the NHS Trust/Health Board may require access to their full medical records for monitoring and auditing purposes.

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.*

The paper data collection sheets will be stored securely in a locked cupboard and handled only by members of the research team. They are familiar will handling and storage of personal data and work in accordance with Good clinical Practice Guidance and the Data Protection Act. Computer security is maintained through user names and frequently updated passwords and back up procedures are in place.

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?

The majority of potential participants will be approached regarding involvement in the trial at a pre-admission clinic appointment or in the admissions unit prior to surgery. Where this is not possible, potential participants may be approached by their own doctor or nurse, followed by a telephone call with one of the research team to discuss participation in the trial further. Each member of the research team has experience in obtaining informed consent and is Good Clinical Practice trained.

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.

Written informed consent will be obtained by a member of the local research team after the participant has had the opportunity to read a participant information sheet, ask questions and consider their participation. If they wish to participate they will then sign the patient consent form. Each member of the research team has experience in obtaining informed consent and is GCP trained.

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

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?

Where possible participants will be approached in advance of their surgical procedure in order to provide them with an information sheet to read days in advance. However, it is inevitable that a small number of eligible patients will arrive in hospital on the day of surgery without having previously attended pre-operative assessment clinic. Where it was not possible to approach the patient before the day of surgery, these patients will still be eligible to participate in the trial provided appropriate efforts had been made to approach them at an earlier stage.

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?

We will recruit patients who are currently enrolled in other trials as long as the trial does not have a similar biological mechanism or related primary outcome measure. However, we will only ask such participants to take part after careful consideration of the total burden of research participation.

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)*

Where necessary a translator will be used to take consent. In each centre there are many healthcare professionals who can assist in this respect.

A33-2. What arrangements will you make to comply with the principles of the Welsh Language Act in the provision of information to participants in Wales?

Effort will be made to enrol all eligible patients into the trial. If local interpreters are not available at the hospital and fully informed consent is not deemed possible, the patient would not be considered for the study.

Individual sites may translate patient information sheets and consent forms according to local needs but these will also need to be back-translated. Translations and back translations should be submitted for ethics approval prior to being used at site.

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?

The intervention will last only four hours. It is extremely unlikely that new safety information will arise during the intervention period. Nonetheless, should this situation arise, participants will be informed and asked if they wish to discontinue the intervention. If the subjects wish to continue in the trial they will be formally asked to sign a revised approved patient information sheet and consent form.

A35. What steps would you take if a participant, who has given informed consent, loses capacity to consent during the study? *Tick one option only.*

- ( ) The participant and all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.
- ( ) The participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant.
- ( ) The participant would continue to be included in the study.
- ( ) Not applicable – informed consent will not be sought from any participants in this research.
- (●) Not applicable – it is not practicable for the research team to monitor capacity and continued capacity will be assumed.

Further details:

Patients will not have capacity during surgery but the intervention does not commence until surgery has ended. CPAP is not effective unless the patient is conscious and able to cooperate with clinical staff who administer the treatment.

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
- [ ] 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
  - [x] University computers
  - [ ] Private company computers
  - [ ] Laptop computers

Further details:
The research team will have access to the medical records in order to record the preoperative and postoperative outcome data. Paper (case report forms) CRFs will be stored in a locked NHS office.

Some coded data will be stored on NHS password protected computers.

University computers will not be used to store patient identifiable information under any circumstances.

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

Data will be transcribed on to the paper CRF prior to entry on to the secure PRISM data entry web portal. Submitted data will be reviewed for completeness and consistency by authorised users within the study group. Submitted data will be stored securely against unauthorised manipulation and accidental loss since only authorised users at site, the Sponsor organisation or at Queen Mary University of London (host of the data entry portal) will have access. Desktop security is maintained through user names and frequently updated passwords. Data back-up procedures are in place. Storage and handling of confidential trial data and documents will be in accordance with the Data Protection Act 1998 (UK).

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.*

All data will be pseudo−anonymised or coded wherever possible. To facilitate linkage to national databases for the collection of follow-up data, patient identifiable data will be collected and entered on to the secure data entry web portal. Data will be stored and handled in accordance with the Data Protection Act 1998 (UK) or equivalent legislation for a particular country or site. In the event that patient identifiable data needs to be transferred between authorised users, this will occur by email from @nhs.net to @nhs.net accounts in the UK or equivalent secure email transfer other countries. The data will be stored and kept for a maximum of 20 years as per trust policy.

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.*

Only members of the research team and R&D staff for the purpose of audit and monitoring will have access to the patients' personal data on the data sheets during the study. Consent will be sought for this.

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?

Trial data will be analysed by a statistician at Queen Mary University London.

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

	Title	Forename/Initials	Surname
	Professor	Rupert	Pearse
Post	Professor of Intensive Care Medicine		
Qualifications	MBBS BSc FRCA MD FFICM		
Work Address	Adult Critical Care Unit		
	The Royal London Hospital		
	Whitechapel		
Post Code	E1 1BB		
Work Email	r.pearse@qmul.ac.uk		
Work Telephone	02035940352		
Fax	02035940352		

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

If longer than 12 months, please justify:
20 years in line with local policy.

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

Years: 20
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.*

The data will be archived for 20 years in accordance with local standards and Queen Mary University, London procedures for quality & assurance. Accessed by members of the research study team.

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.

A49-2. Will you seek permission from the research participants to inform their GP or other health/ care professional?

◉ Yes ○ No

It should be made clear in the participant's information sheet if the GP/health professional will be informed.

PUBLICATION AND DISSEMINATION

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

The Department of Health's Research Governance Framework for Health and Social Care and the research governance frameworks for Wales, Scotland and Northern Ireland set out the requirement for registration of trials. 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.
ISRCTN registration
Protocol will be published
Statistical analysis plan will be published

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?

Only summary data will be presented. No individual patient will be identified.

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.
A copy of the scientific report will be available to any participant who requests it.

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 proposal has undergone internal and external peer review.

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
	Mr	Brennan	Kahan
Department	Pragmatic Clinical Trials Unit		
Institution	Queen Mary University of London		
Work Address	58 Turner St London		
Post Code	E1 2AB		
Telephone			
Fax			
Mobile			
E-mail	b.kahan@qmul.ac.uk		

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

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

Composite endpoint of pneumonia, endotracheal re-intubation or death within 30 days of randomisation.

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

- Pneumonia within 30 days of randomisation
- Endotracheal re-intubation within 30 days of randomisation
- Death within 30 days of randomisation
- Postoperative infection within 30 days of randomisation
- Mechanical ventilation (invasive or non-invasive) within 30 days of randomisation
- All-cause mortality at one year after randomisation
- Quality adjusted life years (QALY) at one year after randomisation

Tertiary outcome measures:

Tertiary outcomes will quantify harm associated with CPAP (appendix). The following pre-defined adverse events will be measured within 24 hours of the end of surgery:
- Interface intolerance due to excessive air leaks
- Pain
- Cutaneous pressure sore or pressure area
- Claustrophobia
- Oro-nasal dryness
- Hypercapnia
- Haemodynamic instability
- Vomiting
- Other harm assessed as probably or definitely related to CPAP

In addition, we will use the following process measures:
- 30-day re-admission
- Days in critical care
- Duration of hospital stay

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:	2000
Total international sample size (including UK):	4800
Total in European Economic Area:	4800

Further details:

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.*

In order to detect a reduction from 11.7% to 8.8% in the primary outcome measure (relative risk reduction of 25%), with a power of 90%, an overall type I error rate of 5%, a loss to follow up rate of 4%, we would require a total sample size of 4800 patients (2400 per group). This sample size will allow us to detect a 26% relative risk reduction in the secondary outcome measure of mortality at one year after randomisation, with a power of 80% and an overall type I error rate of 5%.

A61. Will participants be allocated to groups at random?

(●) Yes ( ) No

If yes, please give details of the intended method of randomisation:
Participants will be centrally allocated to treatment groups (1:1) by a computer generated dynamic procedure (minimisation) with a random component. Minimisation will be performed by country, surgical procedure category and planned use of epidural anaesthesia. The surgical procedure categories are: resection of colon, rectum or small bowel; resection of liver, pancreas or gall bladder; resection of stomach (non-obesity surgery); obesity surgery; vascular procedure; or other intra-peritoneal procedure. Each participant will be allocated with 80% probability to the group that minimises between group differences in these factors among all participants recruited to the trial to date, and to the alternative group with 20% probability.

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.

Statistical analysis

All analyses will be conducted according to intention-to-treat principles, meaning that all patients with a recorded outcome will be included in the analysis, and will be analysed according to the treatment group to which they were randomised. The primary outcome (pneumonia, endotracheal re-intubation, or death within 30 days of randomisation) will be analysed using a mixed-effect logistic regression model. Centre will be included as a random-intercept, and the model will be adjusted for the minimisation variables (country, planned use of epidural anaesthesia and planned surgical procedure category (resection of colon, rectum or small bowel; resection of liver, pancreas or gall bladder; resection of stomach (non-obesity surgery); obesity surgery; vascular procedure; or other intra-peritoneal procedure) and planned use of epidural anaesthesia), as well as the following pre-specified baseline covariates: age, gender, co-morbid disease (chronic respiratory disease, ischaemic heart disease, diabetes mellitus, heart failure, liver cirrhosis, active cancer, and previous stroke or transient ischaemic attack), smoking status and ASA score. The significance level will be set at 0.05. A full statistical analysis plan will be developed prior to analysis. Clinical outcomes are defined in protocol appendix 1.

Health economic analysis

The health economics analysis will assess whether routine postoperative CPAP is likely to be cost-effective on average. The intervention may have effects that impact on quality and duration of life beyond the trial follow-up period. The cost-effectiveness analysis will therefore take the form of a decision model with one-year mortality as an input in terms of treatment effectiveness. Other stages in the model will relate to subsequent non-fatal events. Effectiveness of the intervention will be defined by any differences in mortality and will be used as a parameter input into the model. Unit costs will be estimated from published literature, NHS and government sources, including NHS Reference costs and Personal Social Services Research Unit Costs of Health and Social Care, to generate a total cost per trial participant for the relevant resource use. Quality adjusted life years (QALYs) over the patients' lifetime will be used as the primary outcome measure of the cost-effectiveness analysis. Trial mortality data will be quality-adjusted on the basis of EQ-5D data and allowing for non-fatal clinical events experienced in the two trial arms. A long-term extrapolation will be undertaken to estimate QALYs over a patient's expected lifetime. This will involve the use of parametric survival modelling together with relevant clinical and epidemiological data on patients' long-term life expectancy given their age, recovery from high-risk an abdominal surgery and whether or not they have experienced non-fatal clinical events following surgery.

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
	Professor	Marco	Ranieri
Post	Professor of Anaesthesia and Intensive Care Medicine,		
Qualifications	MD		
Employer	University of Rome, Italy		
Work Address	Corso Re Umberto 25		
Post Code			
Telephone	00338 6373744		
Fax			
Mobile			
Work Email	marco.ranieri@uniroma1.it		

	Title	Forename/Initials	Surname
	Dr	Andrew	Rhodes
Post	Consultant in Anaesthesia and Intensive Care Medicine		
Qualifications	MBBS MD (Res.) FFICM FRCP FRCA		
Employer	St. Georges Healthcare NHS Trust		
Work Address	Blackshaw Road		
	Tooting		
	London		
Post Code	SW17 0QT		
Telephone	0208 725 5699		
Fax			
Mobile			
Work Email	andrewrhodes@nhs.net		

	Title	Forename/Initials	Surname
	Dr	Tom	Abbott
Post	Clinical Research Fellow in Perioperative Medicine		
Qualifications	BA BM BCh MRCP		
Employer	Barts Health NHS Trust		
Work Address	Adult Critical Care Research Office, Room 14, Central Tower		
	Royal London Hospital		
	Whitechapel		
Post Code	E1 1BB		
Telephone	0203 59 40352		
Fax			
Mobile			
Work Email	tom.abbott@bartshealth.nhs.uk		

	Title	Forename/Initials	Surname
	Mr	Richard	Haslop
Post	Senior Research Manager		

Qualifications	BSc Biochemistry
Employer	Queen Mary University of London
Work Address	Adult Critical Care Research Office, Room 14, Central Tower Royal London Hospital Whitechapel
Post Code	E1 1BB
Telephone	0203 59 40352
Fax	
Mobile	
Work Email	r.haslop@qmul.ac.uk

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	Queen Mary University of London
Given name	Sally
Family name	Burtles
Address	Joint Research Management Office (JRMO), Queen Mary Innovation Centre, LG Floor, 5 Walden St
Town/city	London
Post code	E1 2EF
Country	UNITED KINGDOM
Telephone	020 7882 7250
Fax	020 7882 7276
E-mail	s.burtles@qmul.ac.uk

Is the sponsor based outside the UK?

○ Yes ◉ No

Under the Research Governance Framework for Health and Social Care, a sponsor outside the UK must appoint a legal representative established in the UK. Please consult the guidance notes.

A65. Has external funding for the research been secured?

- [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	NIHR Trainee's co-ordinating centre
Address	Leeds Innovation Centre 103 Clarendon Road Leeds
Post Code	LS2 9DF
Telephone	0113 346 6260
Fax	
Mobile	
Email	

Funding Application Status: ◉ Secured ○ In progress

Amount: £1,300,000.00

Duration
Years: 5
Months: 0

If applicable, please specify the programme/ funding stream:

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

Organisation	National Institute of Academic Anaesthesia and AAGBI
Address	21 Portland Place London
Post Code	WIB 1PY
Telephone	02070921680
Fax	02070921730
Mobile	
Email	secretariat@aagbi.org

Funding Application Status: ◉ Secured ○ In progress

Amount: £48,598.00

Duration
Years: 4
Months: 0

If applicable, please specify the programme/ funding stream:

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

Organisation	Intersurgical Ltd
Address	Crane House Molly Millars Lane Wokingham, Berkshire
Post Code	RG41 2RZ
Telephone	0118 9656 300
Fax	
Mobile	
Email	

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

Amount: £181,000

Duration
Years: 4
Months: 0

If applicable, please specify the programme/ funding stream:

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

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

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	Sally	Burtles

Organisation	Queen Mary University
Address	Queen Mary University London Joint R&D Office

	5 Walden Street, London
Post Code	E1 2EF
Work Email	sponsorsrep@bartshealth.nhs.uk
Telephone	020 7882 7250
Fax	020 7882 7276
Mobile	

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

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

Planned start date: 01/10/2015
Planned end date: 30/09/2019
Total duration:
Years: 3 Months: 11 Days: 30

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 15

Number of sites anticipated in the Community 35

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	12
☑ NHS organisations in Wales	2
☑ NHS organisations in Scotland	1
☐ 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: 15

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?

The Sponsor will have oversight of the trial conduct at each site. The trial team will take day-to-day responsibility for ensuring compliance with the requirements of GCP in terms of quality control and quality assurance of the data collected as well as safety reporting. The PRISM Trial Management Group will communicate closely with individual sites and the Sponsor's representatives to ensure these processes are effective.

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?

A Data Monitoring and Ethics Committee (DMEC) will be appointed. The committee is independent of the trial team and comprises of two clinicians with experience in undertaking clinical trials and a statistician. The DMEC agree conduct and remit, which will include the early termination process. The DMEC will perform a single interim analysis as it sees fit. The trial will be terminated early if there is evidence of harm in the intervention group or if recruitment is futile. The DMEC functions primarily as a check for safety by reviewing adverse events.

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 Trial Steering Committee will decide if the trial should be stopped early. They will review any reccomendations from the Data Monitoring and Ethics Committee and will make any decisionsin continuing or stopping the trial, or modifying the protocol.

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.

- ☐ NHS indemnity scheme will apply (NHS sponsors only)
- ☑ Other insurance or indemnity arrangements will apply (give details below)

Queen Mary University of London Indemnity arrangements will apply.

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)

Queen Mary University of London Indemnity arrangements will apply.

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 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 NHS sites, the host organisation is the Trust or Health Board. Where the research site is a primary care site, e.g. GP practice, please insert the host organisation (PCT or Health Board) in the Institution row and insert the research site (e.g. GP practice) in the Department row.*

Investigator identifier	Research site	Investigator Name
IN1 ☐	◉ NHS site ○ Non-NHS site Country: England Organisation name: BARTS AND THE LONDON NHS TRUST Address: TRUST OFFICES, WHITECHAPEL THE ROYAL LONDON HOSPITAL WHITECHAPEL LONDON GREATER LONDON Post Code: E1 1BB	Forename: Rupert Middle name: Family name: Pearse Email: r.pearse@qmul.ac.uk Qualification (MD...): BSc(Hons) MBBS MD FRCA FFICM 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 abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.

3. 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.

4. 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.

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

6. 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.

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

8. 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 1998.

9. 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.

10. 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 1998.

11. 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.

12. 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 below. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

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

NRES 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 Rupert Pearse on 05/09/2015 12:15.

Job Title/Post:	Professor of Intensive Care Medicine
Organisation:	Queen Mary University of London
Email:	r.pearse@qmul.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 duties of sponsors set out in the Research Governance Framework for Health and Social Care will be undertaken 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 Sally Burtles on 17/11/2015 12:10.

Job Title/Post:	Director of Research Services & Business Development
Organisation:	Barts Health NHS Trust
Email:	sponsorsrep@bartshealth.nhs.uk