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)
Idiopathic Pulmonary Fibrosis Job Exposures Study (IPF JES)

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. Please answer the following question(s):

a) Will you be taking new samples primarily for research purposes (i.e. not surplus or existing stored samples), including any removal of organs or tissue from the deceased?	(●) Yes	( ) No
b) Will you be using surplus tissue or existing stored samples identifiable to the researcher?	( ) Yes	(●) No
c) Will you be using only surplus tissue or existing stored samples not identifiable to the researcher?	( ) Yes	(●) No
d) Will you be processing identifiable data at any stage of the research (including in the identification of participants)?	(●) 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 applications do you require?

IMPORTANT: If your project is taking place in the NHS and is led from England select 'IRAS Form'. If your project is led from Northern Ireland, Scotland or Wales select 'NHS/HSC Research and Development Offices' and/or relevant Research Ethics Committee applications, as appropriate.

- [x] IRAS Form
- [ ] Confidentiality Advisory Group (CAG)
- [ ] National Offender Management Service (NOMS) (Prisons & Probation)

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

For participating NHS organisations in England different arrangements apply for the provision of site specific information. Refer to IRAS Help for more information.

Most research projects require review by a REC within the UK Health Departments' Research Ethics Service. Is your study exempt from REC review?

( ) Yes (•) No

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 Biomedical Research Unit, NIHR Collaboration for Leadership in Health Research and Care (CLAHRC), NIHR Patient Safety Translational Research Centre or a Diagnostic Evidence Co-operative 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

Please describe briefly the involvement of the student(s):
The Chief Investigator is enrolled as a PhD student at Imperial College London.

9a. Is the project being undertaken in part fulfilment of a PhD or other doctorate?

(•) 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 Research limited to working with human tissue samples and/or data

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)
Idiopathic Pulmonary Fibrosis Job Exposures Study (IPF JES)

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

REC Name:
East Midlands - Nottingham 1

REC Reference Number:
17/EM/0021

Submission date:
19/12/2016

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

Idiopathic Pulmonary Fibrosis Job Exposures Study (IPF JES)

A2-1. Educational projects

Name and contact details of student(s):

Student 1

	Title	Forename/Initials	Surname
	Dr	Carl	Reynolds
Address	National Heart and Lung Institute		
	Room 39, Emmanual Kaye Building		
	1b Manresa Road, London		
Post Code	SW3 6LR		
E-mail	carl.reynolds@imperial.ac.uk		
Telephone	07737904807		
Fax	02073518336		

Give details of the educational course or degree for which this research is being undertaken:

Name and level of course/ degree:
PhD

Name of educational establishment:
Imperial College London

Name and contact details of academic supervisor(s):

Academic supervisor 1

	Title	Forename/Initials	Surname
	Professor	Paul	Cullinan
Address	Room G47		
	Emmanuel Kaye Building		
	1b Manresa Road		
Post Code	SW3 6LR		
E-mail	p.cullinan@imperial.ac.uk		
Telephone	02075947990		
Fax	02073518336		

Please state which academic supervisor(s) has responsibility for which student(s):
Please click "Save now" before completing this table. This will ensure that all of the student and academic supervisor details are shown correctly.

Student(s)	**Academic supervisor(s)**
Student 1 Dr Carl Reynolds	☐ Professor Paul Cullinan

A copy of a current CV for the student and the academic supervisor (maximum 2 pages of A4) must be submitted with the application.

A2-2. Who will act as Chief Investigator for this study?

- ◉ Student
- ○ Academic supervisor
- ○ Other

A3-1. Chief Investigator:

	Title	Forename/Initials	Surname
	Dr	Carl	Reynolds
Post	Doctor		
Qualifications	BSc MSc DPMSA MBBS MRCP SCE		
Employer	Imperial College London		
Work Address	National Heart and Lung Institute		
	Room G39 Emmanual Kaye Building		
	1b Manresa Road, London		
Post Code	SW3 6LR		
Work E-mail	carl.reynolds@imperial.ac.uk		
* Personal E-mail	drcjar@gmail.com		
Work Telephone			
* Personal Telephone/Mobile	07737904807		

Fax	02073518336

** 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
Miss	Ruth	Nicholson

Address	Room 221
	Medical School Building
	Imperial College London, St Marys Campus, Norfolk Place
Post Code	W2 1PG
E-mail	r.nicholson@imperial.ac.uk
Telephone	02075941862
Fax	

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):	16SM3627
Sponsor's/protocol number:	
Protocol Version:	0.3
Protocol Date:	19/12/2016
Funder's reference number:	
Project website:	www.ipfjes.org

Additional reference number(s):

Ref.Number	Description	Reference Number

Registration of research studies is encouraged wherever possible. You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you have registered your study please give details in the "Additional reference number(s)" section.

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.

Idiopathic pulmonary fibrosis (IPF) is a scarring lung disease. It damages the air sacs that allow oxygen to be transferred into the blood and transported to vital organs. These changes make people with IPF cough and feel short of breath. We don't know what causes the damage. People who get IPF are usually older than 40; it's a very serious illness that cannot be cured and gets worse over time. Statistics show that IPF is becoming more common in the UK but it's not known why. It can be difficult for doctors to tell if someone has IPF or another disease called asbestosis. Asbestosis is like IPF but different because we know that breathing in asbestos dust has caused the lung damage.

Our study will help to find out how much IPF is due to breathing in asbestos at work. This will help us to understand IPF, make sure people get the right treatment and compensation they are entitled to, and make sure that the rules about asbestos dust at work are right so that we protect workers and prevent disease in the future.

We will recruit men with new diagnoses of IPF (cases) from several hospitals across England and Wales. For purposes of comparison a group of men of the same age attending the same hospitals at about the same time for other conditions (controls) will be recruited, in a ratio of 1:1; the total number of participants will be 920. Participants will complete a telephone interview and will be invited to provide a blood sample to investigate how genetics and asbestos exposure interact in IPF.

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.

The main risk of participation in this study is an inadvertent disclosure of participants private identifiable information. To minimize the risk of loss of confidentiality interview response data and blood samples will not be labelled with private identifiable information (samples will be stored in an anonymous linked form).

Interview response information will be kept encrypted on a computer in a locked office. Consent forms will be stored in a locked filing cabinet in a locked office. Blood samples will be stored in a secure facility. Participants will not be identified in any report or publication of this study or its results.

Samples will be tracked by the research team. Access to samples and identifying information will be limited to the research team. We may share access to anonymised samples and data with other academic units and any pharmaceutical collaborators.

Secondarily, there is a small risk of distress arising as a consequence of results obtained from the study. Consent will be obtained from participants to inform their clinical teams of any clinically significant findings. Individual research results will be fed back to research participants. Clinically important information will be passed on to the participants clinical team.

It is possible that the research team will be contacted directly by patients with IPF who wish to participate in the study (patient initiates contact with the research team). Should this happen then we would obtain consent from the patient to contact their lead clinician. Provided inclusion and exclusion criteria are met the patient would be provided with a patient information sheet and given opportunity to discuss and consider participation. If patients wish to participate they will be invited to attend the nearest hospital that is in the research network for formal enrolment, blood to be drawn, and to schedule a telephone interview.

Should any lone-working, for example taking blood at a patients home, be necessary it would only be carried out in full compliance with Imperial College London's Lone Working Policy minimize the risks of this.

If occupational asbestos exposure is shown to be an under-recognized cause of idiopathic pulmonary fibrosis then there are implied ethical duties for policy makers and employers. Policy makers must consider whether current work-place exposure limits for asbestos are adequate and whether compensation and treatment access arrangements for IPF and asbestosis are appropriate. Employers of workers with occupational asbestos exposure must consider exposure control and disease surveillance for IPF. I am well positioned to disseminate any positive findings to the relevant academic and policy communities.

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
- [x] Case control
- [ ] Cohort observation
- [ ] Controlled trial without randomisation
- [ ] Cross-sectional study
- [ ] Database analysis
- [x] Epidemiology
- [ ] Feasibility/ pilot study
- [x] Laboratory study
- [ ] Metanalysis
- [ ] Qualitative research
- [x] 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 study will help to find out how much IPF is due to breathing in asbestos at work in the UK. This will help us to better understand IPF, make sure people get the right treatment and compensation they are entitled to, and make sure that the rules about asbestos dust at work are right so that we protect workers and prevent disease in the future.

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

Secondarily, we will investigate how genetic factors associated with susceptibility to IPF modify the effect of exposure to asbestos. This will help us to understand why the disease happens in some people who work with asbestos but not others.

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

Previous studies have found associations between occupational metal, stone, and wood dust exposures and IPF but have not looked specifically at quantitative asbestos exposure.

The question of whether asbestos exposure is important in causing a proportion of cases of IPF arises because:

• classical asbestosis looks very like IPF
• the trends of IPF and asbestos use in the UK are closely aligned; while this does not prove causation it is consistent with a link
• it would explain, at least in part, why the disease is more common in men from certain parts of the country
• men who have worked with wood or metals would commonly be exposed also to asbestos
• preliminary analysis of occupational data for cases and controls obtained from a recent IPF study shows that the odds ratio associated with ever having had a job where asbestos exposure is likely (using a definition from a large mesothelioma case-control study) is 2.8 (95% CI: 1.42-5.75, p = 0.001)

Knowing whether there is a link between asbestos exposure and some cases of IPF would help to better understand the causes of IPF; would change approaches to its current treatment; would have important implications for compensation; and would help to prevent the disease in parts of the world where asbestos is still used widely.

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 study aims to investigate whether asbestos exposure is an under-recognized cause of IPF using a telephone interview and a blood test.

The study will recruit men with new diagnoses of IPF (cases) from a network of hospitals across England, Scotland, and Wales. For purposes of comparison a group of men of the same age attending the same hospitals at about the same time for other conditions (controls) will be recruited, in a ratio of 1:1; the total number of participants will be 920.

To minimize the need for access to patient identifiable potential cases and controls are initially approached differently.

Potential cases will be randomly sampled from all new cases at centers in the research network. They will be sent a cover letter and a copy of the patient information sheet by their direct care team.

Potential controls will be randomly sampled from all new outpatient department attendances in the research network. They will be invited to participate in person by the direct care team and provided with a copy of patient information sheet.

If potential cases and controls wish to participate they are enrolled in the study at their next clinic appointment. Enrolment includes checking study inclusion and exclusion criteria, assessing patients capacity, and written informed consent.

Cases and controls will be invited to give details, through a telephone interview, of all the jobs they have had since leaving school. These jobs will be scored for the likelihood of their incurring exposure to asbestos; the techniques for doing this are well established. The proportions of so-exposed jobs will be compared between the cases and the controls to investigate whether there is a dose-response relationship for occupational asbestos exposure and IPF.

Participants will also be invited to provide a blood sample to allow us to perform tests, including genetic tests, to investigate whether asbestos is causing IPF.

The telephone interview will occur at a time convenient to the research participant and last less than an hour. The blood test will occur when the participant is next due to have routine blood tests where possible (alleviating the need for an additional needlestick and inconvenience). Where this is not possible (because the participant does not have any other blood tests due for example) and the participant still agrees to have a blood test the test will occur in the participants home or at the hospital and reasonable travel and time expenses will be met.

To check that we have enough people in our study to be able to carry out our planned analysis we have involved a statistician.

For the primary analysis unconditional logistic regression will be used to analyse ‘any’ vs ‘no’ asbestos exposure and categories of cumulative exposure adjusting for age and smoking status. Prior data indicate that the probability of exposure among controls is 0.63. If the true OR for disease in exposed subjects relative to unexposed subjects is 1.5, we will need to recruit 460 case patients and 460 control patients to be able to reject the null hypothesis that this odds ratio equals 1 with $\beta = 0.2$ and $\alpha = 0.05$; our planned sample size includes a margin for model stability and incomplete data.

Secondary analysis will investigate gene-environment interaction. The global minor allele frequency of MUC5B rs35705950 is 0.05. With an estimated prevalence of IPF of 20/100000 and with ORs 1.5 for asbestos exposure and 6.8 for rs35705950, 113 cases would be required to detect a minimum interaction OR of 5.0.

All work will be completed between 10.2016 and 10.2019. 0-8 months: setup, recruitment of staff, final questionnaire development. 9-33 months: recruitment of participants, data collection, data cleaning. 34-36 months: statistical analysis and write paper(s).

The estimated schedule is conservative; it is hoped that setup will take less than 8 months and recruitment of participants can begin and conclude sooner.

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?

☑ 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.
I have kept in touch with an IPF patient with asbestos exposure who has recently had a lung transplant and with a relative of a patient who had his diagnosis changed from IPF to asbestosis. Both people contacted me after I presented my work in Amsterdam at the European Respiratory Society meeting. They have, with a patient volunteer from the Brompton patient group,already been very helpful in forming my research plans. All have reviewed my full research proposal. I plan to have ongoing input and feedback from them when my research starts.

I also plan to continue to organise events such as NHS Hack Day[1], blog[2], tweet[3], and discuss my research with the public. I strongly believe in the value of sharing my work publicly and engaging in dialogue around it as a means to improve it.

My host organisation (the NHLI) has a public engagement programme and I intend to participate in workshops, lectures, and summer school through this.

I will engage with the British Lung Foundation's Breathe Easy patient support groups. Specifically I will explain my research plans and listen and respond to any questions that arise. If groups are interested I will be happy to speak about my work and findings at their meetings.

I will have a patient volunteer in my advisory group, I will also organize two IPF patient focus groups. I will seek input from my advisory and focus groups, and more widely, when developing patient information resources, finalizing elements of my research design, and preparing and disseminating my findings. I will support clear and accurate communication of any significant findings arising from my work to a wider audience through a press release using language that is accessible to a lay audience.

I have some experience of dealing with the media from previous work.[4-7]
I am keen to participate in other public engagement opportunities as they arise and also plan to seek further training to improve my skillset in public engagement.

References
1. http://nhshackday.com/
2. http://openhealthcare.org.uk/blog/2015/04/16/which-retracted-pape r-has-the-most-citations/
3. https://twitter.com/drcjar
4. http://www.economist.com/news/britain/21567980-how-scrutiny-freel y-available-data-might-save-nhs-money-beggar-thy-neighbour
5. http://www.europeanlung.org/en/news-and-events/media-centre/press -releases/idiopathic-pulmonary-fibrosis-(ipf)-cases-linked-with -asbestos-exposure
6. http://www.medscape.com/viewarticle/831713
7. http://www3.imperial.ac.uk/newsandeventspggrp/imperialcollege/new ssummary/news_8-9-2014-16-36-47

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
- [ ] Paediatrics
- [ ] Renal and Urogenital
- [ ] Reproductive Health and Childbirth
- [x] Respiratory
- [ ] Skin
- [ ] Stroke

Gender:	Male participants only
Lower age limit: 18	Years
Upper age limit:	No upper age limit

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

Cases:
Male
New diagnosis of IPF between February 2017 and October 2019

Controls:
Male
New outpatient department attendee between February 2016 and October 2019

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

Cases:
Unable to give informed consent
Ever worked outside of the UK

Controls:
Unable to give informed consent
Ever worked outside of the UK
Diagnosis of IPF

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
Seeking consent	1	0	5 min	Research nurse Research assistant Principle investigator Patients hospital doctor Will take place in hospital outpatient department and/or via letter to patients home.
Telephone interview	1	0	60 min	Principle investigator Research assistant Remotely

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
Blood test	1	75%	5 mins	Hospital phlebotomist (as part of routine hospital blood tests) at the hospital. Principle investigator (where patient is not due routine blood tests) at patients home. It is estimated that 75% of participants will have their research blood test sample taken at the same time as their routine bloods are taken.
Provision of research results	1	0%	5 mins	Research team, via letter/email/telephone call as per patient preference.

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

three years

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.

Telephone interview is potentially inconvenient. Participant preference for interview timing will be accommodated where possible.

Blood tests are potentially painful and uncomfortable. Where possible blood for research will be drawn when the participant next has routine blood tests by a phlebotomist. Where this is not possible blood will be drawn by a phlebotomist at the hospital at a convenient time. As a last resort the central research team may arrange for blood to be drawn by a skilled person at the participant's home.

The main risk of participation in this study is an inadvertent disclosure of participants private identifiable information. To minimize the risk of loss of confidentiality interview response data and blood samples will not be labelled with private identifiable information (samples will be stored in an anonymous linked form).

Interview response information will be kept encrypted on a computer in a locked office. Blood samples will be tracked by the research team and stored in a secure facility. Participants will not be identified in any report or publication of this study or its results.

Access to samples and identifying information will be limited to the research team. We may share access to anonymised samples and data with other academic units and any pharmaceutical collaborators.

Secondarily, there is a small risk of distress arising as a consequence of results obtained from the study. Consent will be obtained from participants to inform their clinical teams of any clinically significant findings. Individual research results will be fed back to research participants. Clinically important information will be passed on to the participants clinical team.

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

Participants may gain satisfaction from knowing that they are contributing to our understanding of what causes a disease that kills over 4000 people a year in the UK.

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).*

Incident IPF cases and controls will be identified and contacted by members of the multidisciplinary teams (doctors and nurses) directly caring for the patient at hospitals in our research network.

Identification and recruitment of participating centres
With support from our local NIHR clinical research network we have already identified several potential collaborating centres and obtained agreements in principle.

Recruitment of cases
Cases will be recruited from male patients with a new diagnosis of IPF made during the study period within the research network.

Centres within the research network will provide the research team with a list of the hospital numbers (chosen because these are not identifiable to individual patients by non-hospital staff) for all patients newly diagnosed with IPF in the preceding month, on a monthly basis.

For each centre the research team will randomly select a sample from the provided list on a monthly basis. The size of the sample N will be calculated as follows
N = total number of patients on list provided * (1/number of months in study period).

The research team will request centres write to these patients inviting them to participate in the study and enclosing the patient information sheet. Patients will be enrolled into the study at their next outpatient department attendance, blood will be drawn, and a telephone interview will be scheduled.

Recruitment of cases from a centre stops when (460/number of centres) cases are recruited.

Recruitment of controls
Controls will be recruited from male patients with a new outpatient department attendance at the same hospital cases originate from. One male control, frequency matched on age, will be recruited for each case.

Centres within the research network will provide the research team with a list of the outpatient clinics that take place each month to include details of who the
lead clinician is for each clinic, average list size, average new to follow up ratio, and when the clinic runs.

The research team will list each clinic alphabetically and serially assign an integer range equal to the expected number of new patients for each clinic per month.

The full integer range will then be randomly shuffled and used to derive a list of clinics from which controls will be recruited sequentially. For example, if a
particular TB clinic appeared first on the list then all new male patients attending this clinic within the target age range would be approached to participate as controls.

If one control could not be found from the TB clinic then the same would be repeated at the next clinic on the list. The research team will write to the lead clinician for selected clinics to obtain permission to recruit patients to the study. Potential controls will be invited to participate in the study and provided with a patient information sheet when they attend the outpatient department. Patients will be enrolled into the study at their next outpatient department attendance, blood will be drawn, and a telephone interview will be scheduled.

Recruitment of controls from a centre stops when recruitment of cases stops and one control for each case have been recruited.

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:
For the identification and initial contact of cases members of the patient's existing clinical care team will make use of personally identifiable patient information contained in the medical record.

While it is known in advance that all cases will be cared for by respiratory care teams (because the case diagnosis is made only by respiratory care teams) this is not the case for controls.

It is not possible for identification of controls to be carried out by the patient's direct care team because of case-control study design decisions taken to minimize bias and essential to the scientific quality of the research. Controls are to be sampled from all incident outpatient department attendances across all specialities; identification of controls through this sampling could not be carried out by the controls direct care teams since we do not know who they will be in advance. Instead, identification and initial contact of controls will be carried out as described above.

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.*

Personal information for the identification of potential controls required is minimal. Whether a patient had a new outpatient appointment at a particular hospital in a given month and their age is all that is needed for the identification

of potential controls.

Screening of potential controls requires further that it is established that the patient can give consent, has never worked abroad, and does not have IPF. Because relatively few potential controls are likely to meet exclusion criteria, screening can be carried out easily at the time of enrolment. This obviates the need for individuals not in the patient's direct care team to access the medical record during the identification.

The need for identification of controls to involve processing of non personally identifiable patient data by persons outside of the direct care team is outlined above.

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?

Potential cases and controls will be approached by the patient's direct care team.

The research team will request that centres write to potential cases inviting them to participate in the study and enclosing the patient information sheet. Patients will be enrolled into the study at their next outpatient department attendance, blood will be drawn, and a telephone interview will be scheduled.

Potential controls will be invited to participate in the study and provided with a patient information sheet by the direct care team when they attend the outpatient department. Patients will be enrolled into the study at their next outpatient department attendance, blood will be drawn, and a telephone interview will be scheduled.

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.

The proposed research will be explained to potential participants in person. They will be provided with a written information sheet and the opportunity to ask questions and to have a period of reflection before deciding whether or not to participate.

It will be explained that participation is entirely voluntary and can be withdrawn at any time. It will be explained the decision to take part and/or withdraw will not impact clinical care received in any way.

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?

Potential participants will be given at least 24 hours to reflect on written information provided and ask any questions they have before deciding whether or not to take part.

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)*

It is anticipated that information given in English will be desirable for the majority of potential participants. Where potential participants express a preference for verbal and written information in a language other than English we will seek to meet this request through the use of interpreters and translation services.

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?

Written information will be translated and made available in both Welsh and English to potential participants in Wales.

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:

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
- [ ] 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

☐ Storage of personal data on any of the following:

- ☐ Manual files (includes paper or film)
- ☐ NHS computers
- ☐ Social Care Service computers
- ☐ Home or other personal computers
- ☑ University computers
- ☐ Private company computers
- ☐ Laptop computers

Further details:
In order to conduct a telephone interview and a blood test with individuals who have consented to be research participants it will be necessary to temporarily store their telephone contact details.

After the telephone interview and blood test are completed it will no longer be necessary to store telephone contact details and they will be destroyed within one week of this.

Personal addresses will be retained until the end of the study (October 2019) in order to write to participants with the results of the study.

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

Personal data of research participants will be stored on a computer with full disk encryption in a locked office. An encrypted backup will be stored on an external usb hard drive in the same room.

Physical consent forms will be stored in a locked filing cabinet in a locked office.

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.*

Confidentiality of personal data will be ensured by following the NHS code of confidentiality, the data protection act, and complying with Imperial College London's data collection and retention policy.

As soon as data collection is complete for a given research participant their data will be pseudoanonymised by assigning it a unique research ID and removing personal identifiable data.

An encrypted database mapping unique research IDs to NHS numbers will be retained to allow research participants to be identified to share personal research results and to inform their clinical teams if there are any clinically significant findings.

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 research team comprising the chief investigator and a research assistant will have access to participants' personal data as necessary to conduct and record a telephone interview, obtain a blood test, and write with the results of the study.

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?

Data will be analysed by the research team. It will not leave the UK.

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

	Title	Forename/Initials	Surname
	Dr	Carl	Reynolds
Post	Clinical Research Fellow		
Qualifications	MBBS BSc MSc DPMSA MRCP SCE		
Work Address	National Heart and Lung Institute		
	Room G39 Emmanual Kaye Building		
	1b Mansesa Road, London		
Post Code	SW3 6LR		
Work Email	carl.reynolds@imperial.ac.uk		
Work Telephone	07737904807		
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

If longer than 12 months, please justify:
An encrypted database containing the mapping of research IDs to NHS numbers which would permit deanonymisation will be securely deleted after 10 years.

If any new developments occur which mean that research results have clinical significance for participants the database would be used to identify the participants clinical team to notify them.

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

Years: 10
Months: 0

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.*

Anonymised research data generated will be published.

The encrypted database containing the mapping of research IDs to NHS numbers which would permit deanonymisation will be securely deleted after 10 years.

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

If Yes, please give details. For monetary payments, indicate how much and on what basis this has been determined.
Reasonable travel expenses incurred, as a result of having a blood test for example, will be reimbursed.

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?

◉ Yes ○ No

Please give details, or justify if not registering the research.
The study will be registered on http://www.clinicaltrials.gov

Registration of research studies is encouraged wherever possible.
You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you are aware of a suitable register or other method of publication, please give details. If not, you may indicate that no suitable register exists. 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?

Identifiable personal data will not be published.

Care will be taken in presenting data that individuals are not potentially identifiable following ONS guidance http://www.ons.gov.uk/ons/guide-method/best-practice/disclosure-c ontrol-of-health-statistics/index.html .

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.
Research participants will be asked if they would like to receive updates on the research study including the publications arising and whether they would prefer to receive updates via post or email.

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 research proposal was reviewed by the Wellcome Trust Public Health and Tropical Medicine Interview Committee (PHATIC) who are funding the research and Imperial College London who are sponsoring the research.

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
	Dr	Cosetta	Minelli
Department	National Heart & Lung Institute		
Institution	Imperial College London		
Work Address	National Heart & Lung Institute		
	Room G 49, Emmanuel Kaye Building		
	1b Mansrea Road		
Post Code	SW3 6LR		
Telephone	02075947758		
Fax			
Mobile			
E-mail	cosetta.minelli1@imperial.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?

Association between asbestos exposure and IPF estimated using unconditional logistic regression for 'any' vs 'no' asbestos exposure and categories of cumulative exposure and adjusting for age and smoking status.

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

gene-environment interaction odds ratio (for MUC5B rs35705950 and asbestos exposure)

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:	920
Total international sample size (including UK):	920
Total in European Economic Area:	920

Further details:
460 cases
460 controls

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.*

For the primary analysis unconditional logistic regression will be used to analyse 'any' vs 'no' asbestos exposure and categories of cumulative exposure adjusting for age and smoking status. Prior data indicate that the probability of exposure among controls is 0.63. If the true OR for disease in exposed subjects relative to unexposed subjects is 1.5, I will need to recruit 430 case patients and 430 control patients to be able to reject the null hypothesis that this odds ratio equals 1 with $\beta = 0.2$ and $\alpha = 0.05$; my planned sample size sample size includes a margin for model stability and incomplete data.

Secondary (exploratory) analysis will investigate gene-environment interaction. The global minor allele frequency of MUC5B rs35705950 is 0.05. With an estimated prevalence of IPF of 20/100000 and with ORs 1.5 for asbestos exposure and 6.8 for rs35705950, 430 cases would be required to detect a minimum interaction OR of 5.0.

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.

As above

Cumulative asbestos exposure will be measured using lifetime occupational histories and together with proportionate occupational mortality ratios for mesothelioma and a validated job process assessment tool.

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	Paul	Cullinan
Post	Professor, Honorary consultant physician (respiratory medicine).		
Qualifications	MB BS, MSc, MD, FRCP, FFOM		
Employer	Occupational and Environmental Medicine, NHLI (Imperial), Royal Brompton Hospital, London. Joint appointment; tenured.		
Work Address	National Heart and Lung Institute		
	Room G47 Emmanual Kaye Building		
	1b Mansrea Road, London		
Post Code	SW3 6LR		
Telephone	02075947989		
Fax			
Mobile			
Work Email	p.cullinan@imperial.ac.uk		

	Title	Forename/Initials	Surname
	Dr	Chris	Barber
Post	Consultant physician (respiratory medicine)		
Qualifications	BM, BS, BMedSci, FRCP, AFOM, MD		
Employer	Northern General Hospital		
Work Address	Brearley Outpatients		
	Herries Road		
	Sheffield		
Post Code	S5 7AU		
Telephone	01142434343		
Fax			
Mobile			
Work Email	Chris.Barber2@sth.nhs.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	Imperial College London
Given name	Ruth
Family name	Nicholson
Address	Room 221, 2nd Floor, Medical School, St Mary's Campus, Praed Street
Town/city	London
Post code	W2 1NY
Country	UNITED KINGDOM
Telephone	02075941862
Fax	
E-mail	r.nicholson@imperial.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?

- ☑ 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	Wellcome Trust
Address	Gibbs Building
	215 Euston Rd
	London
Post Code	NW1 2BE
Telephone	02076118888
Fax	
Mobile	
Email	grantenquiries@wellcome.ac.uk

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

Amount: £317,313

Duration
Years: 3
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
Mrs	Ruth	Nicholson

Organisation	Imperial College London and Imperial College Healthcare NHS Trust
Address	Joint Research Compliance Office
	5th Floor, Laboratory Block
	Charing Cross Hospital
Post Code	W6 8RF
Work Email	jrco@imperial.ac.uk
Telephone	02033110212
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:

North West London

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: 01/02/2017
Planned end date: 01/10/2019
Total duration:
Years: 2 Months: 8 Days: 1

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 visit of the last research participant

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 17

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	13
☑ NHS organisations in Wales	1
☑ NHS organisations in Scotland	3
☐ 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: 17

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 research will form the basis of a PhD and will be subject to mandatory NHLI progress assessment which includes six monthly progress reports with an assigned mentor and an early and late stage review, at 9 and 21 months respectively, with two independent external assessors.

Additionally, I will meet with my main supervisor on a weekly basis, and with my project steering group which will include my supervisor, an assigned co-supervisor, and a patient representative on a six monthly basis to review progress made towards milestones and any other arising issues.

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)

Imperial College Indemnity

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)

Imperial College Indemnity

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)

Imperial College Indemnity

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?

Venous blood will be obtained from participants at the same time as blood is taken for routine blood tests where possible.

Samples will be couriered on ice to the NHLI where they will be stored in a -80 degrees Celsius freezer. DNA extraction will be performed to allow genetic analysis to investigate IPF susceptibility that will include (but not be limited to) using a panel of pre-defined candidate susceptibility SNPs including rs35705950. Genotyping will be undertaken using Q-PCR and Taqman assays. Only non-cellular fractions will be stored.

Consent of research participants for the retention of their blood samples for further research will be requested. Where granted samples will be stored for 10 years in line with Imperial College London policy.

2. Who will collect the samples?

Blood will be collected by either the hospital phlebotomist, a doctor, or a nurse trained in venepuncture.

3. Who will the samples be removed from?

☑ 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

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

If Yes, say who will have access to the code and personal information about the donor.

Access to the code and personal information about the donor will be limited to the research team.

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?

Samples will be genotyped using a panel of pre-defined candidate susceptibility SNPs including rs35705950. Genotyping will be undertaken using Q-PCR and Taqman assays. Further analysis of samples to investigate IPF susceptibility including whole genome sequencing may be performed.

Planning to analyze and store participants personal information, including genetic information, creates an ethical duty to obtain informed consent and to protect participant privacy and confidentiality by processing and storing information appropriately.

Individual research results will be fed back to research participants. We will inform the participants clinical team of any clinically important findings.

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

If No, please justify. If Yes, say what arrangements will be made and give details of the support or counselling service.

Consent will be obtained from participants to inform their clinical teams of any clinically significant findings.

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

Samples will be stored and analyzed in a secure accredited lab facility at Imperial College London.

Samples will be stored in a temperature controlled freezer with a backup power supply.

The research team will track samples and record a log of their movements and their current location.

Access to samples and identifying information will be limited to the research team. We may share access to anonymised samples and data with other academic units and any pharmaceutical collaborators.

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:

DNA extraction will occur within hours to days of sample receipt and the cellular fraction will be destroyed and discarded. Samples will be stored for 10 years after the research.

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		Forename Middle name Family name Email Qualification (MD...) Country	Gareth Walters gaxwalters@hotmail.com BSc MD MB ChB MMEd MAcadMedEd DOccMed FHEA UNITED KINGDOM
	Organisation name	UNIVERSITY HOSPITAL BIRMINGHAM NHS FOUNDATION TRUST		
	Address	TRUST HQ, PO BOX 9551 QUEEN ELIZABETH MEDICAL CENTRE EDGBASTON BIRMINGHAM WEST MIDLANDS		
	Post Code	B15 2TH		
IN2	◉ NHS site ○ Non-NHS site Country: Wales		Forename Middle name Family name Email Qualification (MD...) Country	Kim Harrison Kim.Harrison@wales.nhs.uk MBBS MRCP UNITED KINGDOM
	Institution name	Morriston Hospital		
	Department name	Respiratory		
	Street address	Morriston		
	Town/city	Swansea		
	Post Code	SA6 6NL		
IN3	◉ NHS site ○ Non-NHS site Country: England		Forename Middle name Family name Email Qualification (MD...)	Carl Reynolds carl.reynolds@imperial.nhs.uk MBBS BSc MSc DPMSA MRCP

			Country	UNITED KINGDOM
	Organisation name	IMPERIAL COLLEGE HEALTHCARE NHS TRUST		
	Address	ST. MARYS HOSPITAL PRAED STREET LONDON GREATER LONDON		
	Post Code	W2 1NY		

IN4

(●) NHS site
( ) Non-NHS site

Country: England

Forename	Gisli		
Middle name			
Family name	Jenkins		
Email	Gisli.Jenkins@nottingham.ac.uk		
Qualification (MD...)	FRCP PhD		
Country	UNITED KINGDOM		
Organisation name	NOTTINGHAM UNIVERSITY HOSPITALS NHS TRUST		
Address	TRUST HEADQUARTERS QMC CAMPUS DERBY ROAD NOTTINGHAM NOTTINGHAMSHIRE		
Post Code	NG7 2UH		

IN5

(●) NHS site
( ) Non-NHS site

Country: England

Forename	Sophie		
Middle name			
Family name	Fletcher		
Email	Sophie.Fletcher@uhs.nhs.uk		
Qualification (MD...)	BA BM BCh MRCP PG Cert (Med Ed)		
Country	UNITED KINGDOM		
Organisation name	SOUTHAMPTON UNIVERSITY HOSPITALS NHS TRUST		
Address	MAILPOINT 18 SOUTHAMPTON GENERAL HOSPITAL TREMONA ROAD SOUTHAMPTON HAMPSHIRE		
Post Code	SO16 6YD		

IN6

(●) NHS site
( ) Non-NHS site

Forename	Nazia
Middle name	
Family name	Chaudhuri

Country: England

Email	Nazia.Chaudhuri@uhsm.nhs.uk
Qualification (MD...)	MB ChB BSc, PhD, MRCP
Country	UNITED KINGDOM

Organisation name	UNIVERSITY HOSPITAL OF SOUTH MANCHESTER NHS FOUNDATION TRUST
Address	WYTHENSHAWE HOSPITAL SOUTHMOOR ROAD WYTHENSHAWE MANCHESTER GREATER MANCHESTER
Post Code	M23 9LT

IN7

(●) NHS site
( ) Non-NHS site

Country: England

Forename	Helen
Middle name	
Family name	Parfrey
Email	helen.parfrey@papworth.nhs.uk
Qualification (MD...)	BA BM PhD FRCP
Country	UNITED KINGDOM

Organisation name	PAPWORTH HOSPITAL NHS FOUNDATION TRUST
Address	PAPWORTH EVERARD CAMBRIDGE CAMBRIDGESHIRE
Post Code	CB23 3RE

IN8

(●) NHS site
( ) Non-NHS site

Country: England

Forename	Michael
Middle name	
Family name	Gibbons
Email	michael.gibbons2@nhs.net
Qualification (MD...)	MBBS BSc PhD FRCP
Country	UNITED KINGDOM

Organisation name	ROYAL DEVON AND EXETER NHS FOUNDATION TRUST
Address	ROYAL DEVON & EXETER HOSPITAL BARRACK ROAD EXETER DEVON
Post Code	EX2 5DW

IN9

(●) NHS site
( ) Non-NHS site

Forename	Lisa
Middle name	

Country: England

Family name	Spencer
Email	lisa.spencer@aintree.nhs.uk
Qualification (MD...)	MBBS MRCP
Country	UNITED KINGDOM

Organisation name	AINTREE UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
Address	UNIVERSITY HOSPITAL AINTREE FAZAKERLEY HOSPITAL LOWER LANE LIVERPOOL MERSEYSIDE
Post Code	L9 7AL

IN10

(●) NHS site
( ) Non-NHS site

Country: England

Forename	Huzaifa
Middle name	
Family name	Adamali
Email	Huzaifa.Adamali@nbt.nhs.uk
Qualification (MD...)	MBBS MD FRCP
Country	UNITED KINGDOM

Organisation name	NORTH BRISTOL NHS TRUST
Address	FRENCHAY HOSPITAL BECKSPOOL ROAD FRENCHAY BRISTOL AVON
Post Code	BS16 1JE

IN11

(●) NHS site
( ) Non-NHS site

Country: Scotland

Forename	Owen
Middle name	
Family name	Dempsey
Email	owen.dempsey@nhs.net
Qualification (MD...)	MD FRCP
Country	UNITED KINGDOM

Institution name	Aberdeen Royal Infirmary
Department name	Respiratory
Street address	Foresterhill
Town/city	Aberdeen
Post Code	AB25 2ZN

IN12

(●) NHS site
( ) Non-NHS site

Forename	George
Middle	

Country: Scotland

Institution name	Glasgow Royal Infirmary
Department name	Respiratory Medicine
Street address	84 Castle Street
Town/city	Glasgow
Post Code	G4 0SF

name	
Family name	Chalmers
Email	George.Chalmers@ggc.scot.nhs.uk
Qualification (MD...)	LLB, FRCP, MD
Country	UNITED KINGDOM

IN13

(●) NHS site
( ) Non-NHS site

Country: Scotland

Institution name	Royal Infirmary of Edinburgh
Department name	Respiratory
Street address	51 Little France Crescent
Town/city	Edinburgh
Post Code	EH16 4SA

Forename	Nik
Middle name	
Family name	Hirani
Email	nik.hirani@nhslothian.scot.nhs.uk
Qualification (MD...)	BMedSci, BMBS, PhD, MRCP
Country	UNITED KINGDOM

IN14

(●) NHS site
( ) Non-NHS site

Country: England

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

Forename	John
Middle name	
Family name	Simpson
Email	j.simpson@newcastle.ac.uk
Qualification (MD...)	FRCP(Edin), PhD
Country	UNITED KINGDOM

IN15

(●) NHS site
( ) Non-NHS site

Country: England

Organisation	TAUNTON AND SOMERSET

Forename	Justin
Middle name	
Family name	Pepperell
Email	Justin.pepperell@tst.nhs.uk
Qualification (MD...)	MBBChir MA MD FRCP
Country	UNITED KINGDOM

name	NHS FOUNDATION TRUST
Address	MUSGROVE PARK HOSPITAL
	TAUNTON SOMERSET
Post Code	TA1 5DA

IN16

(●) NHS site
( ) Non-NHS site

Country: England

Forename	Monica
Middle name	
Family name	Nordstrom
Email	Monica.Nordstrom@asph.nhs.uk
Qualification (MD...)	
Country	UNITED KINGDOM

Organisation name	ASHFORD AND ST PETER'S HOSPITALS NHS FOUNDATION TRUST
Address	ST PETERS HOSPITAL
	GUILDFORD ROAD
	CHERTSEY SURREY
Post Code	KT16 0PZ

IN17

(●) NHS site
( ) Non-NHS site

Country: England

Forename	Paul
Middle name	
Family name	Beirne
Email	p.beirne@nhs.net
Qualification (MD...)	MA MSc MRCP PhD
Country	UNITED KINGDOM

Organisation name	LEEDS TEACHING HOSPITALS NHS TRUST
Address	ST. JAMES'S UNIVERSITY HOSPITAL
	BECKETT STREET
	LEEDS WEST YORKSHIRE
Post Code	LS9 7TF

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. 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 Carl Reynolds on 19/12/2016 15:40.

Job Title/Post:	Clinical Research Fellow
Organisation:	Imperial College London
Email:	carl.reynolds@imperial.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 Miss Ruth Nicholson on 20/12/2016 09:04.

Job Title/Post:	Research Governance Manager
Organisation:	Imperial College London
Email:	r.nicholson@imperial.ac.uk

D3. Declaration for student projects by academic supervisor(s)

1. I have read and approved both the research proposal and this application. I am satisfied that the scientific content of the research is satisfactory for an educational qualification at this level.

2. I undertake to fulfil the responsibilities of the supervisor for this study as set out in the Research Governance Framework for Health and Social Care.

3. I take responsibility for ensuring that this study is conducted in accordance with the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research, in conjunction with clinical supervisors as appropriate.

4. I take responsibility for ensuring that the applicant is up to date and complies with the requirements of the law and relevant guidelines relating to security and confidentiality of patient and other personal data, in conjunction with clinical supervisors as appropriate.

Academic supervisor 1

This section was signed electronically by Paul Cullinan on 19/12/2016 19:01.

Job Title/Post:	Professor
Organisation:	NHLI (Imperial)
Email:	p.cullinan@imperial.ac.uk