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 enter a short title for this project (maximum 70 characters)
EVALUATING THE AGE EXTENSION OF THE NHS BREAST SCREENING PROGRAMME

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 or clinical investigation
( ) 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, other human biological samples and/or 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) Does the study involve the use of any ionising radiation?	(●) Yes	( ) No
b) Will you be taking new human tissue samples (or other human biological samples)?	( ) Yes	(●) No
c) Will you be using existing human tissue samples (or other human biological samples)?	( ) Yes	(●) No

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

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

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

(●) England
( ) Scotland

- ○ Wales
- ○ Northern Ireland
- ○ This study does not involve the NHS

4. Which review bodies are you applying to?

- ☑ NHS/HSC Research and Development offices
- ☐ Social Care Research Ethics Committee
- ☑ Research Ethics Committee
- ☑ National Information Governance Board for Health and Social Care (NIGB)
- ☐ Ministry of Justice (MoJ)

4a. Will you be seeking data from Hospital Episode Statistics (HES) or the Secondary Uses Service (SUS)?

○ Yes ◉ No

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

◉ Yes ○ No

5a. Do you want your application to be processed through the NIHR Coordinated System for gaining NHS Permission?

○ Yes ◉ No

If yes, you must complete and submit the NIHR CSP Application Form immediately after completing this project filter, before proceeding with completing and submitting other applications.

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

○ Yes ◉ No

7. Do you plan to include any participants who are adults unable to consent for themselves through physical or mental incapacity?*The guidance notes explain how an adult is defined for this purpose.*

◉ Yes ○ No

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

○ Yes ◉ No

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

○ Yes ◉ No

10. Is this project financially supported by the United States Department for Health and Human Services?

○ Yes ◉ No

11. Will identifiable patient data be accessed outside the clinical 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 research

National Patient Safety Agency
National Research Ethics Service

Application to NHS/HSC Research Ethics Committee

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.

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
EVALUATING THE AGE EXTENSION OF THE NHS BREAST SCREENING PROGRAMME

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

REC Name:
Ealing and West London Research Ethics Committee

REC Reference Number:
10/H0710/9

Submission date:
08/01/2010

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

EVALUATING THE NET EFFECTS OF EXTENDING THE AGE RANGE FOR BREAST SCREENING IN THE NHS BREAST SCREENING PROGRAMME IN ENGLAND FROM 50-70 YEARS TO 47-73 YEARS

A3. Chief Investigator:

	Title	Forename/Initials	Surname
	Professor	Julietta	Patnick
Post	Director, NHS Cancer Screening Programmes; Visiting Professor, Cancer Epidemiology Unit, Oxford University		
Qualifications	BA (Hons), FFPH, HonMRCR		
Employer	Yorkshire and Humber Strategic Health Authority		
Work Address	Fulwood House Old Fulwood Road Sheffield		
Post Code	S10 3TH		
Work E-mail			
* Personal E-mail	as above		
Work Telephone			

* Personal Telephone/Mobile
Fax

** This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*

A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

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

	Title	Forename/Initials	Surname
	Ms	Kath	Moser
Address	Cancer Epidemiology Unit		
	Richard Doll Building		
	Roosevelt Drive, Oxford		
Post Code	OX3 7LF		
E-mail			
Telephone			
Fax			

A5-1. Research reference numbers. *Please gi study:*

Applicant's/organisation's own reference number, e.g. R & D (if available):
Sponsor's/protocol number:
Protocol Version: 1
Protocol Date: 26/11/2009
Funder's reference number:
International Standard Randomised Controlled Trial Number (ISRCTN):
ClinicalTrials.gov Identifier (NCT number):
European Clinical Trials Database (EudraCT) number: N/A
Project website: http://www.cancerscreening.nhs.uk/breastscreen/

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.
This application follows on from the pilot study.
PILOT STUDY OF THE FEASIBILITY AND ACCEPTABILITY OF RANDOMISING THE PHASING-IN OF THE AGE EXTENSION OF THE NHS BREAST SCREENING PROGRAMME IN ENGLAND
EALING AND WEST LONDON RESEARCH ETHICS COMMITTEE: 09/H0710/2
Submission date: 14/01/2009

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. This summary will be published on the website of the National Research Ethics Service following the ethical review.*

Currently all women aged 50-70 are invited for breast screening every three years. In 2007 the Cancer Reform Strategy announced that from 2012 the NHS Breast Screening Programme (NHSBSP) would cover women aged 47-73. As capacity does not allow for full immediate roll out across the whole of England, this age extension is being phased-in with full coverage intended from 2012 although this may now be delayed due to slower than expected introduction of digital mammography.

To date there is limited evidence on the net benefit of extending (up or down) the age range for breast screening; no trial has looked at the added value of one extra screen within an existing screening programme.

This study proposes randomising the phasing-in of the age extension and collecting information on breast cancer incidence and mortality over the following 10 years. This would provide unbiased evidence on the net effects of extending the age range for breast screening. The findings have the potential to inform future screening policy in the UK and elsewhere. If the study is not carried out, this unique opportunity of establishing the net benefit of adding an extra early and extra late screen to an existing screening programme will be missed.

All Breast Screening Units in England will participate in the study with the exception of a few using a non-standard method to invite women for screening.

The age extension is funded by central government, and will proceed regardless of whether our study goes ahead or not, and therefore regardless of whether the phasing-in is randomised or not. Follow-up of study members for breast cancer incidence and mortality will be funded by the NHSBSP.

A6-2. Summary of main issues. *Please summarise the main ethical and design issues arising from the study and say how you have addressed them.*

Currently all women aged 50-70 are invited for breast screening every three years (as described in Breast Screening: a pocket guide – see attached). The NHS Breast Screening Programme (NHSBSP) is being extended to cover women between the ages of 47 and 73 as announced in the 2007 Cancer Reform Strategy (see attached). This age extension will be phased-in with full coverage intended from 2012 although this may now be delayed due to slower than expected introduction of digital mammography. Extending the age range for screening is not at issue as it is government policy and will proceed regardless of this proposed study. However, by randomising the phasing-in of the age extension and collecting information on subsequent breast cancer incidence and mortality, this proposal provides a unique opportunity to obtain unbiased evidence on the risks and benefits of extending the age range for breast screening. The findings have the potential to inform future screening policy in the UK and elsewhere.

There has been recent criticism of breast screening (KJ Jørgensen & PC Gøtzsche. Overdiagnosis in publicly organised mammography screening programmes: systematic review of incidence trends BMJ 2009;339:b2587) and so-called overdiagnosis and associated harms. We are therefore particularly anxious to evaluate the harms and benefits of screening. By generating information on breast cancer incidence in the groups invited and not invited for screening we will be able to look into this.

The study builds on the pilot study (Pilot study of the feasibility and acceptability of randomising the phasing-in of the age extension of the NHS Breast Screening Programme in England. Ealing and West London REC: 09/H0710/2) which has been investigating the feasibility and acceptability of randomising the phasing-in of the age extension in several pilot sites. The interim report of the pilot is attached. To date 126 screening batches and 26,000 women have been randomised in 5 pilot sites. The batches vary in size with on average 200 study participants per batch. Phone calls have been monitored and workload issues logged. In advance of the pilot, two issues had been of particular concern: 1) that large numbers of women aged 47-49 randomised not to be invited for screening would self-refer, and 2) that workload would increase and be hard to plan for. In fact, very few women aged 47-49 randomised out are self-referring, and, on balance, randomisation is not adding to the workload and sites are managing to keep to their targets. Many useful lessons have been learnt from the pilot which will inform the planning and implementation of the full roll-out of the age extension. As the proposed study is embedded in a service, with lead time needed for planning that service, we need to submit this application on the basis of 5 months pilot data, rather than waiting until the pilot has finished.

The study protocol, including the approach to addressing the main ethical and design issues in the study, developed out of discussions between the investigators, and at meetings at the Department of Health, of the NHSBSP and of the Advisory Committee on Breast Cancer Screening. Lay users and patient representatives are regularly involved in discussions concerning the breast screening programme at the Department of Health and there are lay representatives on the Advisory Committee on Breast Cancer Screening.

The method of randomisation was discussed, in particular how to define the clusters for randomisation. It was decided to randomise by cluster not by individual, where the cluster is the screening invitation batch. The NHAIS Exeter system creates screening invitation batches of on average 1,000 women spanning ages 50 to 70 years. With the age extension, slightly larger batches of women aged 47 to 73 years will be created. Each batch will be randomly allocated to one of two groups, that is, to include either women aged 47-70 or women aged 50-73. Randomisation of the screening invitation batches will be done with equal (50/50) probability and no stratification. Study participants are the women aged 47-49 and 71-73 in these screening batches; on average, there will be of the order of 200 such women in each batch. All Breast Screening Units in England will participate in the study with the exception of a few using a non-standard batch creation system. Sites participating in the pilot study will also be included in this study.

As a result of randomisation half the women aged 47-49 and 71-73 will be invited for screening at this stage, while the rest will not be invited until full implementation of the age extension. The ethics of this are as follows. Firstly, the age extension has to be phased-in as immediate full roll-out is not feasible, so inevitably some women in the extended age groups will be invited before others. We are proposing phasing-in randomly, rather than in the more haphazard way that would happen routinely in the NHS. Secondly, there is limited evidence on the extent to which it is beneficial to extend the age range for breast screening and the extent of the net benefit is unknown. Thirdly, women aged 47-49, who are not invited for screening as part of this study, will be screened on request if they live in an area that has started extending the age range. Any woman over 70 is already able to request screening every three years.

The process by which women are selected into screening invitation batches is fully automated and data transfer for screening purposes uses the secure networks in place and is covered by approval granted to the NHS Cancer Screening Programmes (NHSCSP) under Section 251 of the NHS Act 2006 (originally enacted under Section 60 of the Health and Social Care Act 2001)(Application Number A0044, PIAG 1-08(a)/2003). From the point when women are invited for screening everything will be done in accordance with NHSBSP procedures including the NHSBSP policy on confidentiality of personal data which receives full compliance across the service.

Relevant data items held on local National Breast Screening Systems (NBSS) will be downloaded annually, during 2010-12 as the age extension is phased-in, for all study participants. This download will include the patient identifiable data required for tracing women on the NHS Central Register (NHSCR) and clinical information on screening, assessment procedures, outcomes and treatments. Data will be encrypted and transferred electronically from each screening centre to the Cancer Epidemiology Unit (CEU) at Oxford University where they will be stored securely in accordance with CEU procedures and policies. Study participants will be followed up at NHSCR for breast cancer incidence and mortality and data subsequently transferred to CEU. Although the study will link individual patient records there is no interest in individual identities. Data will be treated with utmost confidentiality, used only for medical research, and anonymised once data linkage has been completed. All data will be analysed only in anonymised form and publications will not identify any individuals.

The NHSBSP uses implied consent. When invited for screening, a woman receives the NHS breast screening information booklet The Facts that describes breast screening [NB. The Facts booklet is in the process of being updated. We attach the current booklet, and the section relevant to the age extension from the draft of the updated version]. This enables her to make an informed choice as to whether to attend or not and if she turns up for her appointment this is taken as implied, valid consent. In this study all women invited for screening, of whatever age, will receive an information leaflet about the study enclosed with their invitation for screening and The Facts booklet. On the basis of this information each woman can decide whether or not to attend her screening appointment; if she attends this is taken as implied consent. Thus, participants invited for screening (i.e. randomised in) and attending their appointment are taken to have given implied consent for screening. The approval held by the NHSCSP under Section 251 of the NHS Act 2006 covers the routine follow-up undertaken by the NHSBSP of screening outcomes to women invited for screening regardless of whether they attend or not.

However, there are several ways in which this study goes beyond the routine permissions in place. 1) Patient identifiable data will be downloaded from the NBSS systems for all participants (i.e. those randomised in and those randomised out) in order that their records can be flagged at NHSCR. 2) Clinical screening follow-up data will be seen by persons outside the immediate healthcare team for participants randomised in. 3) All participants will be followed-up at NHSCR for cancer incidence and mortality. 4) Participants randomised out will not know that they are part of the study. 5) Data will be held at the CEU, although as soon as data linkage has been completed the data will be anonymised. We will not be obtaining consent from participants to cover these activities. Application is being made to the National Information Governance Board for Health and Social Care for Section 251 approval for the use of patient identifiable data without consent and access to medical records by those outside the direct healthcare team.

We will not be informing General Practitioners (GPs) that specific patients of theirs are taking part in the study, but screening units will inform local GPs that the study is taking place in their area. The NHSBSP always informs GPs when their patients have been invited for screening and what the outcome was (even if they did not attend). The participants invited for screening (i.e. randomised in) in this study will be treated in exactly the same way. We attach examples of the reports sent to GPs. However GPs will be unaware of which patients of theirs have been randomised not to be invited for screening unless their practice is covered by a single screening batch in which case they will know

about all their women.

The NHSBSP routinely includes women with learning difficulties in invitations for screening and has protocols for dealing with this situation. Until a woman is invited, the Programme has no way of identifying such women. With any problem that arises, radiologists deal with whoever (e.g. carer) is most appropriate to determine the woman's best interests, but if she does not consent to be screened she will not be screened.

Currently there is limited evidence on the risks and benefits of extending the age range for breast screening; that is why we are proposing this study. There may be a benefit to those study participants randomised for screening invitation of having an extra screen. Similarly there may be risks and burdens although none of these are particular to the randomisation that is central to our study. They apply to all routine breast screening carried out by the NHSBSP and will be experienced by women in the extended age groups whether or not our study goes ahead since the age range of the NHSBSP is being extended regardless of our study. Risks are minimised as all activity is carried out to NHSBSP standards including rigorous quality control. Participants randomised not to be invited for screening, and who do not request screening, have the potential risk of not having an extra mammogram. However we do not know if that is a risk or not; that is exactly what this study is intended to evaluate.

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

To evaluate the net effect of extending the age range for breast screening in the NHS Breast Screening Programme in England from 50-70 years to 47-73 years.

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

None.

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

The NHS Breast Screening Programme (NHSBSP) is being extended to cover women between the ages of 47 and 73. As capacity does not allow for full immediate roll out across the whole of England, this age extension is being phased-in with full coverage intended from 2012 although this may now be delayed due to slower than expected introduction of digital mammography. This proposal is to randomise the phasing-in of the age extension and collect information on subsequent breast cancer incidence and mortality. Randomising the phasing-in will provide unbiased evidence on the risks and benefits of extending the age range for breast screening. To date there is limited evidence on this as no trial worldwide has looked at the added value of one extra screen within an existing screening programme. The findings therefore have the potential to inform screening policy in the UK and elsewhere.

A13. Please give a full summary of 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 NHS Breast Screening Programme (NHSBSP) is being extended to cover women between the ages of 47 and 73. This age extension will be phased-in with full coverage intended from 2012 although this may now be delayed due to slower than expected introduction of digital mammography. However, by randomising the phasing-in and collecting information on subsequent breast cancer incidence and mortality, this study will be able to provide evidence on the risks and benefits of extending the age range for breast screening. The study builds on the pilot study which to date has demonstrated no significant problems of feasibility or acceptability in randomising the phasing-in of the age extension in 5 sites. This has paved the way for randomised phasing-in of the age extension across the whole of England.

As part of the routine breast screening process, the NHAIS Exeter system creates screening invitation batches of on average 1,000 women spanning ages 50 to 70 years. Invitations to attend for breast screening are sent out at the same time to all the women in such a batch. In this study slightly larger batches will be created of women aged 47-73 which will be randomly allocated to one of two groups, that is, to include ages 47-70 years or ages 50-73 years, instead of, as now, 50-70 years. The randomisation will be done with equal (50/50) probability and no stratification.

Study participants are the women aged 47-49 and 71-73 in these screening batches; on average, there will be of the order of 200 such women in each batch. Women aged 50-70 are not study participants as they will be unaffected by the randomisation process; they are in the age group already eligible for routine screening, and their invitations for screening will continue as normal regardless of whether the pilot study is being undertaken. All Breast Screening Units in England will participate in the study with the exception of a few using a non-standard batch creation system. Sites

participating in the pilot study will also be included in this study.

All women invited for screening in the study areas, of whatever age, will receive an information leaflet about the study enclosed with their invitation for screening and the standard NHS breast screening information booklet "The Facts" (attached). On the basis of this information each woman can decide whether or not to attend her screening appointment. If she attends this is taken as implied consent for screening. Every aspect of screening will be carried out according to the standard procedures in place for breast screening. The only aspect that differs in this study is the randomisation of screening batches.

Women aged 47-49 who are not invited for screening can request to be screened if they live in an area where the age extension has started. Any woman over 70 is already able to request screening every three years.

Data will be downloaded annually from local National Breast Screening Systems (NBSS) and transferred to the Cancer Epidemiology Unit (CEU) at Oxford University where the study is being conducted. These data on the study population and screening outcomes will be analysed on an ongoing basis.

Study participants will be flagged at the NHS Central Registry (NHSCR) and followed-up for ten years for breast cancer incidence and mortality. Data on these events will be transferred to CEU and analysed at the end of the follow-up.

Before proceeding, ethical approval is required. Also, Section 251 support is needed for the use of patient identifiable data without consent, and access to medical records by those outside the direct healthcare team.

Timetable:
Prepare patient information leaflet, August/Sept 2009
Submit applications for ethical and Section 251 approvals, autumn 2009
Confirm study areas, early 2010
Start study (i.e. randomisation of screening batches) in each area, early 2010 onwards
Establish mechanism for data download from local NBSS systems to CEU, early 2010
Annual data downloads of study participants from local NBSS systems to CEU, during 2010-12
Flagging of study participants at NHSCR, ongoing from 2010
Analysis and interpretation of NBSS data on study population and screening data, ongoing 2010 -12 with each annual data download
Analysis and interpretation of NHSCR data on breast cancer incidence and mortality to study participants, after 10 years follow-up, 2020 onwards

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
- [ ] Management of the research
- [ ] Undertaking the research
- [ ] Analysis of results
- [ ] Dissemination of findings
- [ ] None of the above

Give details of involvement, or if none please justify the absence of involvement.
Lay users are already regularly involved in discussions concerning the breast screening programme at the Department of Health. There are lay representatives on the Advisory Committee on Breast Cancer Screening.

4. RISKS AND ETHICAL ISSUES

RESEARCH PARTICIPANTS

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

Female, aged 47-49 or 71-73 years, and in a Breast Screening Unit participating in the study. All Breast Screening Units in England will participate in the study with the exception of a few that use a non-standard batch creation system.

Women satisfying these criteria in the sites included in the pilot study (see A5-2) will also be included.

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

Anyone not satisfying the above inclusion criteria.

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
None.				

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
2 view mammography	1	1	30 minutes	Radiographer conducts mammogram. Mammogram is done at the breast screening centre nearest to where the woman is registered with the NHS.
If the mammogram is not normal, subsequent procedures may be required such as recall for repeat mammogram; biopsy; surgery.				

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?

Each participant will enter the study from the date when the screening batch they are in is randomised such that either the 47-70 age group or the 50-73 age group is invited for screening. From this date, participants will be followed up at the National Health Service Central Register for approximately 10 years for breast cancer incidence and mortality. However no contact will be made with participants by the research team at any stage of the study.

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.

The following risks and burdens are not particular to the randomisation that is central to our study. They apply to all routine breast screening carried out by the NHSBSP. They therefore will be experienced by the women in our study population whether or not our study goes ahead since the age range of the NHSBSP is being extended anyway regardless of our study. These risks/burdens are minimised as all activity is carried out to NHSBSP standards including rigorous quality control.

1. Time and discomfort of having a mammogram.
2. Risk of radiation especially to younger women.
3. Anxiety about the results.
4. Possibility of being recalled for repeat mammogram.
5. False positives.
6. Subsequent investigations/treatment if indicated by the results.

The participants randomised not to be invited for screening have the potential risk of not having an extra mammogram. However we do not know if that is a risk or not; that is what this study is intended to evaluate.

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?

Women who have cancer detected as a result of the extra screen have the potential benefit of it being picked up earlier than it would have been otherwise. This leads to greater treatment options.

To date there is limited evidence on the risks and benefits of extending the age range for breast screening. However there may be an overall benefit to participants in our study of having an extra early or late screen. This is what this study is designed to evaluate.

However this potential benefit does not depend on the randomisation that is central to our study. It will be experienced by the women in our study population whether or not our study goes ahead since the age range of the NHSBSP is being extended anyway regardless of our study.

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.*

Regardless of this study, the age range for breast screening in the NHS Breast Screening Programme is being extended from ages 50-70 to ages 47-73. This age extension is being phased-in so that there is full implementation intended from 2012 although this may now be delayed due to slower than expected introduction of digital mammography. This will proceed irrespective of this study.

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

No obvious risk.

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).

As part of the routine breast screening process, the NHAIS Exeter system creates screening invitation batches of on average 1,000 women spanning ages 50 to 70 years. This process is fully automated. Invitations to attend for breast screening are sent out at the same time to all the women in such a batch.

In this study slightly larger batches will be created of women aged 47 to 73 years. Each batch will be randomly allocated to one of two groups, that is, to include ages 47 to 70 years or ages 50 to 73 years, instead of, as now, 50 to 70 years. Randomisation will be done with equal (50/50) probability and no stratification.

The study participants are the women aged 47-49 and 71-73 in these screening batches. In other words, both the women randomised for screening invitation and those randomised not to get a screening invitation form the study population. On average, there will be of the order of on average 200 such women in each batch.

Women aged 50 to 70 are not study participants as they will be unaffected by the randomisation process; they are in the age group already eligible for routine screening, and their invitations for screening will continue as normal regardless of the age extension.

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:
Date of birth will be used to identify women in the appropriate age ranges. Postcode and GP practice may also be used in the selection of screening batches depending on local procedures. However this process will all be done automatically by the computer systems and is covered by the Section 251 support (reference A0044, PIAG 1-08 (a)/2003) held by the NHS Cancer Screening Programmes for contacting NHAIS data subjects for Cancer Screening Programmes in England.

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

◉ Yes ○ No

A27-5. Has prior consent been obtained or will it be obtained for access to identifiable personal information?

○ Yes ◉ No

If No, and your application involves identifiable patient information, application should be made to the National Information Governance Board for Health and Social Care (NIGB) to process identifiable information of patients in England and Wales without consent – see guidance notes.

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?

Participants randomised in (i.e. to be invited for screening) will receive a standard letter from the NHS Breast Screening Programme inviting them for screening. Enclosed with their invitation they will receive the standard NHS breast screening information booklet The Facts and an additional information sheet about this study (all attached).

Participants randomised out (i.e. not to be invited for screening) will not know that they are part of the study and therefore will not be approached.

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

○ Yes ◉ No

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

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

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

It is essential to include all study participants in this study; 100% coverage is essential for the scientific validity of the study, and excluding participants for whom we cannot get consent could seriously bias the results particularly as they are unlikely to be randomly spread throughout the population. Women randomised to be invited for screening are informed in the information leaflet of the fact that the phasing-in of the age extension is randomised in order that the net benefit of extending the age range for breast screening can be scientifically evaluated, and that researchers will be analysing the results on behalf of the NHS Breast Screening Programme (NHSBSP). Consent is implied for those who attend for screening because of the standard procedures of the NHSBSP which uses implied consent, and the information leaflet. It is not possible to ask consent of women randomised not to be invited for screening, without whom the study would be meaningless; however, information about the study will be sent to all women invited for screening in a community and therefore widely known.

We are applying to the National Information Governance Board for Health and Social Care for Section 251 support to process patient identifiable information without consent.

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

If No, how will it be recorded?

It is essential to include all study participants in this study; 100% coverage is essential for the scientific validity of the study, and excluding participants for whom we cannot get consent could seriously bias the results particularly as they are unlikely to be randomly spread throughout the population. Women randomised to be invited for screening are informed in the information leaflet of the fact that the phasing-in of the age extension is randomised in order that the net benefit of extending the age range for breast screening can be scientifically evaluated, and that researchers will be analysing the results on behalf of the NHS Breast Screening Programme (NHSBSP). Consent is implied for those who attend for screening because of the standard procedures of the NHSBSP which uses implied consent and the information leaflet. It is not possible to ask consent of women randomised not to be invited for screening, without whom the study would be meaningless but information about the study will be sent to all women invited for screening in a community and therefore widely known.

We are applying to the National Information Governance Board for Health and Social Care for Section 251 support to process patient identifiable information without consent.

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

The letter inviting women for screening will include an appointment date and time approximately 2 weeks ahead. The woman will need to keep that appointment or ring to change it to a more suitable date. Should she not attend she can change her mind and request a new appointment at any time.

This is the standard process used in the NHS Breast Screening Programme.

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?

There are currently no other NHS Breast Screening Programme trials affecting the age groups of the participants in this study. However as this study includes a large number of women it is possible that some of them are, or have recently been, involved in other research of some sort. The older women may have been involved in earlier trials (e.g. the One vs. Two view trial) or studies (e.g. the Million Women Study).

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)*

Different language versions and a large print version will be available on the NHS Breast Screening Programme website.

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?

Continued participation is not an issue in this study as women only participate once when they are invited for screening.

We will disseminate the results of the study in peer reviewed journals, conference presentations, and publication on the website. However we will not inform study participants of the findings directly.

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
- [x] Electronic transfer by magnetic or optical media, email or computer networks
- [x] Sharing of personal data with other organisations
- [ ] Export of personal data outside the EEA
- [x] Use of personal addresses, postcodes, faxes, emails or telephone numbers
- [ ] Publication of direct quotations from respondents
- [ ] Publication of data that might allow identification of individuals
- [ ] Use of audio/visual recording devices
- [x] Storage of personal data on any of the following:
  - [x] Manual files including X−rays
  - [x] NHS computers
  - [ ] Home or other personal computers
  - [x] University computers
  - [ ] Private company computers
  - [ ] Laptop computers

Further details:
Relevant data items held on local National Breast Screening Systems (NBSS) will be downloaded annually, during 2010-12 as the age extension is phased-in, for all study participants. Data items will include the patient identifiable data required for tracing women on the NHS Central Register (NHSCR) and clinical information on recall following screening, assessment procedures, outcomes and treatments. These data will be encrypted and transferred electronically from each screening centre to the Cancer Epidemiology Unit (CEU) at Oxford University where they will be

stored securely in accordance with CEU procedures and policies. Any patient identifiable data held on paper will similarly be stored securely in accordance with CEU procedures. Please see enclosed CEU documents (Data Access and Data Handling Policy; IT Security Policy; Confidentiality Form) for further details.

Study participants will be traced and flagged at the NHSCR and data on breast cancer incidence and mortality subsequently transferred to CEU over the duration of the study. This transfer will proceed according to NHSCR protocols for data transfer. CEU will link NHSCR data to the study population.

Although the study will link individual patient records there is no interest in individual identities. The study will be conducted in accordance with relevant aspects of the Data Protection Act. The data will be treated with utmost confidentiality and used only for medical research. The data will be anonymised once data linkage has been completed. All data will be analysed only in anonymised form and publications will not identify any individual women.

Application is being made for Section 251 approval for the use of patient identifiable data and access to medical records by those outside the direct healthcare team.

Data transfer, and access to medical records by people outside the immediate healthcare team for QA and evaluation purposes, that occurs as part of the routine NHS Breast Screening Programme activities is covered by the Section 251 approval granted to the NHS Cancer Screening Programmes.

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.*

Identifiable patient information will be held within the Cancer Epidemiology Unit (CEU) at Oxford University which is where the study will take place. The CEU has longstanding experience of holding and working with patient identifiable data, specifically the Million Women Study, and the EPIC study of nutrition and health.

The CEU and its staff comply with all relevant guidelines and best practice within the medical research sector. In addition to the University of Oxford Policy on Data Protection, the CEU has a 'Data Access and Data Handling' policy. Both of these documents are attached. All staff are required to sign a confidentiality form (attached) on employment in the CEU. A breach of confidence would be regarded as a serious offence and treated as gross misconduct.

All Unit staff are made aware of their responsibilities regarding data handling on joining the CEU. The Acceptable Use Policy (attached) is signed by all staff upon the start of their employment. It indicates to staff what their responsibilities are with respect to use of computing and network systems, and to matters of data protection and confidentiality. All staff are obliged to comply with the Unit's Data Access and Data Handling policy (attached). Advice on the collection and processing of personal data is available from the University of Oxford Data Protection Officer.

The proposed use of patient identifiable information satisfies the requirements of the Data Protection Act and other legislation.

The data will be anonymised as soon as data linkage has been completed. All data will be analysed only in anonymised form and publications will not identify any individual women.

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.*

Named researchers at the Cancer Epidemiology Unit at Oxford University will have access to participants' personal data. Personnel at the NHS Central Register (NHSCR) will have access to the personal data items required in order to identify women on the NHSCR.

Consent is not being sought. However Section 251 approval is being sought.

Patient identifiable data is only required in order to link datasets. Once this has been done the data will be anonymised. The research has no interest in individual identities, and only aggregate data will be presented.

Storage and use of data after the end of the study

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:
Once follow-up has finished some additional time will need to be allowed to ensure that all relevant cancer and death notifications have been received by NHSCR and passed on to the research team at the Cancer Epidemiology Unit (CEU). The data will be anonymised following the completion of all record linkage. All patient identifiable information will then be destroyed in accordance with procedures in place in the CEU.

INCENTIVES AND PAYMENTS

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

○ Yes ◉ No

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

○ Yes ◉ No

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

○ Yes ◉ No

NOTIFICATION OF OTHER PROFESSIONALS

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

○ Yes ◉ No

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

PUBLICATION AND DISSEMINATION

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

◉ Yes ○ No

Please give details, or justify if not registering the research.
The study will be registered on the ISRCTN register and the ClinicalTrials.gov register

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

- ☑ Peer reviewed scientific journals
- ☐ Internal report

- [x] Conference presentation
- [x] 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)

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.
We will disseminate the results of the research in peer reviewed scientific journals, conference presentations, and on the website, but we will not inform individual participants of the findings.

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
- [x] Review within a multi−centre research group
- [x] Review within the Chief Investigator's institution or host organisation
- [x] 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 plan has been discussed at meetings in the Department of Health and of providers of screening services. We attach notes of the meeting held at the Department of Health in February 2008 to discuss the age extension of the NHSBSP, issues arising, implementation and research plan. This was a multidisciplinary group with patient representation.

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
- [x] Review by a statistician within the Chief Investigator's institution
- [x] 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
	Professor Sir	Richard	Peto FRS
Department	Professor of Medical Statistics, Co-director, Clinical Trial Service Unit (CTSU)		
Institution	University of Oxford		
Work Address	CTSU, Richard Doll Building		
	Old Road Campus		
	Oxford		
Post Code	OX3 7LF		
Telephone			
Fax			
Mobile			
E-mail			

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

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

(1) Mortality from breast cancer by age 60, comparing women invited to have an additional early screen (before age 50) versus those not and (2) mortality from breast cancer by age 80 comparing women invited to have an additional late screen (after age 70) versus those not.

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

Breast cancer registrations in the screened and unscreened groups.

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: 1100000
Total international sample size (including UK): 1100000
Total in European Economic Area:

Further details:
1.1 million study participants in total. Half will be randomly allocated for an extra screening invitation, half will not.

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.*

All women in England aged 47-49 or 71-73 at the time their area is invited for screening, unless their Breast Screening Unit is one of the few that use a non-standard batch creation system.

A61. Will participants be allocated to groups at random?

(●) Yes ( ) No

If yes, please give details of the intended method of randomisation:
As part of the routine breast screening process, screening invitation batches are created of on average 1,000 women spanning ages 50 to 70 years, all living in the same small geographical locality. In this study slightly larger batches will be created of all women aged 47 to 73 years. These batches will be randomly allocated to one of two groups, that is, to include either ages 47-70 years or ages 50-73 years. Randomisation will be by cluster not by individual, where the cluster is the screening invitation batch. The randomisation will be done with equal (50/50) probability and no stratification. The study participants will be the women aged 47-49 and 71-73 in the screening invitation batches; this will amount to on average about 200 women in each batch. (The women aged 50-70 are not study participants as they

will all be invited for screening as normal.)

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.

The main outcome will be mortality from breast cancer by age 60 for women allocated for invitation for an additional early screen and by age 80 for those allocated for invitation for an additional later screen. All comparisons will be on an intention to treat basis (i.e. invitation for screening) with the screening batch as the unit of comparison. For each age group, women in batches where that age group was randomised in (i.e. invited for screening) will be compared with women of that age group in batches where randomisation for screening invitation was offered to the alternative age group. In order to minimise the dilution of any effect by pre-existent breast cancer, women with prior breast cancer will be omitted from analyses of breast cancer mortality.

Similarly, we will compare breast cancer incidence in the screened and unscreened groups.

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 Dame	Valerie	Beral
Post	Director, Cancer Epidemiology Unit & Chair, Advisory Committee on Breast Cancer Screening		
Qualifications	FRS MBBS FRCP		
Employer	University of Oxford		
Work Address	Richard Doll Building		
	Roosevelt Drive		
	Oxford		
Post Code	OX3 7LF		
Telephone			
Fax			
Mobile			
Work Email			

	Title	Forename/Initials	Surname
	Professor Sir	Richard	Peto
Post	Professor of Medical Statistics & Co-director, Clinical Trial Service Unit (CTSU)		
Qualifications	FRS MSc(Statistics)		
Employer	University of Oxford		
Work Address	CTSU, Richard Doll Building		
	Roosevelt Drive		
	Oxford		
Post Code	OX3 7LF		
Telephone			
Fax			
Mobile			
Work Email			

	Title	Forename/Initials	Surname
	Professor Sir	Mike	Richards

Post	National Cancer Director; Sainsbury Professor of Palliative Medicine, Guy's and St Thomas' Hospital
Qualifications	CBE MD FRCP DSc(Hon)
Employer	Department of Health
Work Address	c/o Dept of Palliative Medicine St Thomas' Hospital Lambeth Palace Road, London
Post Code	SE1 7EH
Telephone	
Fax	
Mobile	
Work Email	

Title	Forename/Initials	Surname
Ms	Kath	Moser

Post	Senior researcher, Cancer Epidemiology Unit
Qualifications	BA MSc(Medical Demography)
Employer	University of Oxford
Work Address	Cancer Epidemiology Unit Richard Doll Building Roosevelt Drive, Oxford
Post Code	OX3 7LF
Telephone	
Fax	
Mobile	
Work Email	

A64. Details of research sponsor(s)

A64-1. Sponsor

Lead Sponsor

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

Commercial status: Non-Commercial

If Other, please specify:

Contact person

Name of organisation	Oxford University
Given name	Heather
Family name	House
Address	Clinical Trials & Research Governance
Town/city	Manor House, John Radcliffe Hospital, Oxford

Post code	OX3 9DU
Country	UNITED KINGDOM
Telephone	
Fax	
E-mail	

Is the sponsor based outside the UK?

◯ Yes ◉ No

Where the lead sponsor is not established within the UK, a legal representative in the UK may need to be appointed. Please consult the guidance notes.

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

	Title	Forename/Initials	Surname
	Ms	Heather	House
Organisation	Clinical Trials & Reserach Governance		
Address	Manor House		
	John Radcliffe Hospital		
	Oxford		
Post Code	OX3 9DU		
Work Email			
Telephone			
Fax			
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: 01/01/2010
Planned end date: 31/12/2022
Total duration:
Years: 13 Months: 0 Days: 0

A71-1. Is this study?

◯ Single centre
◉ Multicentre

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

- [x] England
- [ ] Scotland
- [ ] Wales
- [ ] Northern Ireland
- [ ] Other countries in European Economic Area

Total UK sites in study 72

Does this trial involve countries outside the EU?

○ Yes ◉ No

A72. What host organisations (NHS or other) in the UK will be responsible for the research sites? *Please indicate the type of organisation by ticking the box and give approximate numbers of planned research sites:*

[x] NHS organisations in England	72
[ ] NHS organisations in Wales	
[ ] NHS organisations in Scotland	
[ ] HSC organisations in Northern Ireland	
[ ] GP practices in England	
[ ] GP practices in Wales	
[ ] GP practices in Scotland	
[ ] GP practices in Northern Ireland	
[ ] Social care organisations	
[ ] Phase 1 trial units	
[ ] Prison establishments	
[ ] Probation areas	
[ ] Independent hospitals	
[ ] Educational establishments	
[ ] Independent research units	
[ ] Other (give details)	
Total UK sites in study:	72

A75-1. Will a data monitoring committee (DMC) be convened?

◉ Yes ○ No

If Yes, please forward details of the membership of the DMC, its standard operating procedures and summary reports of interim analyses to the Research Ethics Committee which gives a favourable opinion of the study (or to GTAC if applicable).

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

The randomisation only lasts for the first 3 years of the study. It therefore comes to an end long before information is available on the main outcomes of the study i.e. breast cancer registrations and deaths which will be available after 10 years of follow-up.

It is already government policy to extend the age range for breast screening. The risks of routine screening are well documented. They are minimsed as all activity is carried out to NHS Breast Screening Programme standards including rigorous quality control and we do not anticipate anything untoward.

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)

The University has arrangements in place to provide for harm arising from participation in the study for which the University is the Research Sponsor. NHS indemnity operates in respect of the clinical treatment which is provided.

Please enclose a copy of relevant documents.

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

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

- ☐ NHS indemnity scheme will apply (protocol authors with NHS contracts only)
- ☑ Other insurance or indemnity arrangements will apply (give details below)

The University has arrangements in place to provide for harm arising from participation in the study for which the University is the Research Sponsor. NHS indemnity operates in respect of the clinical treatment which is provided.

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.

PART B: Section 3 – Exposure to ionising radiation

Complete sub-sections A and/or B as applicable with input from relevant experts. It is advisable to discuss the proposed research at an early stage with (a) a Medical Physics Expert and (b) a Clinical Radiation Expert, who will carry out the required assessments for sub-sections C and D. The lead MPE can also facilitate the completion of sub-sections A and/or B if necessary.

1. Does the study involve exposure to radioactive materials?

○ Yes ◉ No

2. Does the study involve other diagnostic or therapeutic ionising radiation?

◉ Yes ○ No

A. Radioactive materials

Details of radioactive materials

B. Other ionising radiation

B1. Details of other ionising radiation

Give details by completing the table below:

Procedure	No of procedures	Estimated procedure dose *(use national Diagnostic Reference Levels where available)*
2 view mammography	1	7 mGy mean glandular dose

C. Dose and risk assessment

C1. What is the total research protocol dose from the exposures in A1 and/or B1, and what component of this is the additional dose over and above standard practice? What are the risks associated with these two doses (total and additional)?

The dose and risk assessment should be set out below. This should be prepared by a Medical Physics Expert (MPE) who is a registered health care professional and has expertise relevant to the planned exposures. Where the study involves different types of exposure (for example, both radioactive materials and other ionising radiation, or more than one imaging method), advice may need to be sought from other MPEs with relevant expertise. The lead MPE should produce a combined assessment for the ethics committee, giving the names of any other MPEs who have contributed to the assessment. Further guidance is available by clicking on the information button or in the document "Approval of research involving ionising radiation", available here: http://www.nres.npsa.nhs.uk/applicants/guidance/

The recommended dose constraint is the national diagnostic reference level for mammography which is a mean glandular dose of 3.5 mGy for an oblique view (MLO) mammogram for breasts of average size. A second CC view is normally also taken of both breasts as part of the screening examination and the dose for these views is normally slightly less than for the MLO views. Thus the maximum dose for a 2-view examination is 7 mGy for women of average size.

Although the imaging procedure proposed is standard an extra round of imaging is proposed for some women in the age range of 47 to 49 and for other women aged 71 to 73.The dose for the younger women is additional. For the older women they could already request a screening mammogram and the change is that in this proposal they will be invited.

The radiation dose involved in mammography examinations by the NHS Breast Screening programme are routinely monitored and have been analysed and published periodically.(1,2) The additional lifetime risk of inducing a breast cancer due to an extra screening round is estimated to be approximately 1 in 10,000 at the maximum dose level at

age 47-49 and 1 in 100,000 at age 71-73. (Calculated assuming an induction rate of 15 per million per mGy at age 47-49 and 2 per million per mGy at age 71-73.)` The implications of induced cancers due to screening at different ages have been previously considered and it has been concluded that the benefits of earlier cancer detection substantially exceed the risks of cancer induction at these age ranges and at the dose levels specified here.(3,4)

Thus on the basis of currently available evidence extending screening in the higher and lower age groups results in a benefit that substantially exceeds the risk.

1. Radiation doses in the United Kingdom trial of breast screening in women aged 40-48 years. Young KC. British Journal of Radiology 75; 362-370 (2002)
2. Radiation doses received in the UK breast screening programme in 2001 and 2002. Young KC, Burch A. Oduko JM. British Journal of Radiology 78; 207-218 (2005).
3. Risk factors for induction of breast cancer by x-rays and their implications for breast screening. Law, J., K. Faulkner, and K. C. Young. British Journal of Radiology 80; 261-266 (2007).
4. Review of radiation risk in breast screening. Young KC, Faulkner K, Wall B, Muirhead C. NHSBSP Publication No 54 February 2003.

Special attention must be paid to pregnant/potentially pregnant women or those who are breast feeding, or other potentially vulnerable groups.

C2. Declaration by lead Medical Physics Expert

I am satisfied that the information in sub-sections A and/or B and the assessment in sub-section C provide a reasonable estimate of the ionising radiation exposure planned in this research and the associated risks.

This section was signed electronically by Professor Kenneth Young on 04/01/2010 04:35.

Job Title/Post:	Consultant Physicist
Organisation:	Royal Surrey County Hospital
Email:	

C3. Details of person acting as lead Medical Physics Expert

	Title	Forename/Initials	Surname
	Professor	Kenneth C	Young
Post	National QA Physicist for the NHS Breast Screening Programme		
Details of professional registration	Clinical Scientist CS002538		
Organisation	National Coordinating Centre for the Physics of Mammography, Royal Surrey County Hospital		
Address	Egerton Road Guildford		
Post Code	GU2 7XX		
Telephone			
Fax			
Mobile			
Email			

D. Clinical assessment

This sub-section should be completed by a Clinical Radiation Expert (CRE) who is a registered health professional with clinical expertise relevant to the planned exposures. The assessment should cover potential exposure at all research sites, taking account of possible variation in normal clinical practice. Where the study involves different types of exposure (for

example, both radiotherapy and other ionising radiation), advice may need to be sought from other CREs with relevant expertise. The lead CRE should produce a combined assessment for the ethics committee, giving the names of any other CREs who have contributed to the assessment. The guidance notes give advice to Chief Investigators on who can act as lead Clinical Radiation Expert (CRE) and advice for the CRE on the assessment of exposures having regard to IRMER.

Special attention must be paid to pregnant/potentially pregnant women or those who are breast feeding, or other potentially vulnerable groups.

D1. Will the exposure exceed the exposure that might be received as part of normal care at any proposed research site?

○ Yes ◉ No

D3. Declaration by lead Clinical Radiation Expert

I am satisfied that the exposure to ionising radiation planned in this research study (as defined in A1 and/or B1) is reasonable and that the risks are adequately described in the participant information sheet for the study.

Signature:…….. Date:

D4. Details of lead Clinical Radiation Expert

	Title	Forename/Initials	Surname
	Dr	Michael	Michell
Post	Consultant radiologist		
Details of professional registration	General Medical Council registration number 2434085		
Organisation	SE London Breast Screening Programme & National Training Centre		
Address	Breast Radiology Dept		
	King's College Hospital		
	Denmark Hill, London		
Post Code	SE5 9RS		
Telephone			
Fax			
Mobile			
Email			

Employers responsible for radiation facilities at research sites must have written procedures to meet the requirements of the Ionising Radiation (Medical Exposure) Regulations 2000 (IRMER). R & D offices for NHS sites will seek confirmation from local radiation experts that local IRMER authorisation procedures have been followed. Where the local Medical Physics Expert or IRMER Practitioner disagrees with the assessments made in this Section and/or the care organisation is unable to adhere to the protocol, this should be discussed with the Chief Investigator and the lead experts for the study. Any necessary variation in the protocol or participant information sheet at particular sites should be notified to the main REC as a substantial amendment and an ethical opinion sought.

B. All research other than CTIMPs

In this sub-section, an adult means a person aged 16 or over.

B1. What impairing condition(s) will the participants have?

The study must be connected to this condition or its treatment.

The participants are drawn from all women aged 47-49 and 71-73 in the population. They will therefore have a similar range of conditions to those found in these age groups in the general population.

B2. Justify the inclusion of adults unable to consent for themselves. It should be clear why the research could not be carried out as effectively if confined to adults capable of giving consent.

The NHS Breast Screening Programme (NHSBSP) routinely includes women with learning difficulties in invitations for screening. There are protocols in place for dealing with this situation and specialised literature. If a woman does not consent to be screened she will not be screened. Radiologists are trained to deal with this situation and routinely meet it. With any problem that arises they deal with whoever (e.g. carer, spouse, parent) is most appropriate to determine the woman's best interests. In summary, the ways this will be dealt with in the age ranges 47-49 and 71-73 years will be identical to the ways it is already being (and will continue to be) dealt with throughout the NHSBSP.

EQUAL ACCESS TO BREAST AND CERVICAL SCREENING FOR DISABLED WOMEN. NHS Breast Screening Programme, Cancer Screening Series No 2. NHS Cancer Screening Programmes: Sheffield, 2006.

B3. Who in the research team will decide whether or not the participants have the capacity to give consent? What training/experience will they have to enable them to reach this decision?

Standard procedure, see B2 above

B4. Does the research have the potential to benefit participants who are unable to consent for themselves?

(●) Yes ( ) No

If Yes, please indicate the nature of this benefit. You may refer back to your answer to Question A24.

Women who have cancer detected as a result of the extra screen have the potential benefit of it being picked up earlier than it would have been otherwise. This leads to greater treatment options.

However this potential benefit is not particular to the randomisation that is central to our study. It will be experienced by the women in our study population whether or not our study goes ahead since the age range of the NHSBSP is being extended anyway regardless of our study.

B5. Will the research contribute to knowledge of the causes or the treatment or care of persons with the same impairing condition (or a similar condition)?

( ) Yes (●) No

B6. Will the research involve any foreseeable risk or burden for these participants, or interfere in any way with their freedom of action or privacy?

(●) Yes ( ) No

If Yes, please give an assessment below. Highlight any risk, burden or discomfort specific to these participants and say what will be done to minimise it. You may refer back to your answers to Questions A22 and A23.

There are no risks and burdens specific to participants unable to consent for themselves.

There are, however, risks and burdens (as outlined in A22) that apply to all routine breast screening carried out by the NHSBSP. They are not particular to the randomisation that is central to our study and will therefore be experienced by the study population whether or not our study goes ahead since the age range of the NHSBSP is

being extended anyway regardless of our study. These risks/burdens are minimised as all activity is carried out to NHSBSP standards including rigorous quality control.

B7. What arrangements will be made to identify and consult persons able to advise on the presumed wishes and feelings of participants unable to consent for themselves and on their inclusion in the research?

Standard procedure, see B2 above

Please enclose a copy of the written information to be provided to consultees. This should describe their role under section 32 of the Mental Capacity Act and provide information about the research similar to that which might be given to participants able to consent for themselves.

B8. Is it possible that a participant might need to be treated urgently as part of the research before it is possible to identify and consult a person under B7?

○ Yes ◉ No

B9. What arrangements will be made to continue to consult such persons during the course of the research where necessary?

N/A

B10. What steps will you take, if appropriate, to provide participants who are unable to consent for themselves with information about the research, and to consider their wishes and feelings?

Standard procedure, see B2 above

B11. Is it possible that the capacity of participants could fluctuate during the research? How would this be handled?

N/A

B12. What will be the criteria for withdrawal of participants?

N/A

B13. Describe what steps will be taken to ensure that nothing is done to which participants appear to object (unless it is to protect them from harm or minimise pain or discomfort).

Standard procedure, see B2 above

B14. Describe what steps will be taken to ensure that nothing is done which is contrary to any advance decision or statement by the participant?

Standard procedure, see B2 above

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.*

Research site		Investigator/ Collaborator/ Contact	
Institution name	University Hospitals Bristol NHS Foundation Trust	Title	Dr
Department name	R&D Education Centre, Univ Hospitals Bristol	First name/ Initials	Monica
Street address	Level 3, Upper Maudlin St	Surname	Lamont
Town/city	Bristol		
Post Code	BS2 8AE		
Institution name	Buckinghamshire Hospitals NHS Trust	Title	Dr
Department name	R&D Stoke Mandeville Hospital	First name/ Initials	C
Street address	Mandeville Road	Surname	Record
Town/city	Aylesbury		
Post Code	HP21 8AL		
Institution name	Barking, Havering, Redbridge & University Hospitals NHS Trust	Title	Dr
Department name	R&D Room G10451, Green Zone	First name/ Initials	M J
Street address	Queens Hospital	Surname	Alsewan
Town/city	Romford		
Post Code	RM7 0AG		
Institution name	Barnsley Hospital NHS Foundation Trust	Title	Dr
Department name	R&D Barnsley District General Hospital	First name/ Initials	S
Street address	Block 14, Gawber Road	Surname	Gelep
Town/city	Barnsley		
Post Code	S75 2EP		
Institution name	Luton & Dunstable NHS Trust	Title	Dr
Department name	Research and Development Department	First name/ Initials	Simon
Street address	Lewsley Road	Surname	Allen
Town/city	Luton		
Post Code	LU4 0DZ		
Institution name	Royal Bolton NHS Foundation Trust	Title	Dr
Department name	R&D Royal Bolton Hospital	First name/ Initials	A J
Street address	N Block, Minerva Road	Surname	Maxwell
Town/city	Bolton		
Post Code	BL4 0JR		

Institution name	Countess Of Chester Hospital NHS Foundation Trust	Title	Dr
Department name	R&D Clinical Governance Support Unit, T Block	First name/ Initials	G
Street address	Liverpool Road	Surname	Doyle
Town/city	Chester		
Post Code	CH2 1UL		

Institution name	Barts And The London NHS Trust	Title	Dr
Department name	R&D	First name/ Initials	S
Street address	24-26 Walden Street, Whitechapel	Surname	Vinnicombe
Town/city	London		
Post Code	E1 2AN		

Institution name	Chesterfield Royal Hospital NHS Foundation Trust	Title	Dr
Department name	R&D, Education Centre	First name/ Initials	P W
Street address	Calow	Surname	Sheppard
Town/city	Chesterfield		
Post Code	S44 5BL		

Institution name	Sandwell & West Birmingham Hospital NHS Trust	Title	Dr
Department name	R&D Arden House, City Hospital	First name/ Initials	Ramesh
Street address	Dudley Road	Surname	Bhatt
Town/city	Birmingham		
Post Code	B18 7QH		

Institution name	Royal Cornwall Hospitals NHS Trust	Title	Dr
Department name	R&D Office	First name/ Initials	Donna
Street address	The Knowledge Spa	Surname	Christensen
Town/city	Truro		
Post Code	TR1 3HD		

Institution name	The Mid Cheshire Hospitals NHS Trust	Title	Dr
Department name	R&D Leighton Hospital	First name/ Initials	J
Street address	Middlewich Road	Surname	Scally
Town/city	Crewe		
Post Code	CW1 4QJ		

Institution name	Derby Hospitals NHS Foundation Trust	Title	Dr
Department name	R&D University of Nottingham Medical School at Derby	First name/ Initials	A
Street address	Derby City General Hospital, Uttoxe	Surname	Turnball
Town/city	Derby		
Post Code	DE22 3DT		

Institution name	Doncaster And Bassetlaw Hospitals NHS Foundation Trust	Title	Dr
Department name	Department of Clinical Audit, Research & Effectiveness C Block	First name/ Initials	D A
Street address	Doncaster Royal Infirmary Armthorpe	Surname	Ward
Town/city	Doncaster		

Post Code	DN2 5LT		
Institution name	Poole Hospital NHS Foundation Trust	Title	Dr
Department name	Research Governance Department Cornelia House	First name/ Initials	M
Street address	Poole Hospital NHS Trust Longfleet		
Town/city	Poole	Surname	Creagh-Barry
Post Code	BH15 2JB		
Institution name	Dudley Group Of Hospitals NHS Trust	Title	Dr
Department name	Research & Development Clinical Trials Unit	First name/ Initials	Elizabeth
Street address	1st Floor, North Wing Russells Hall		
Town/city	Dudley	Surname	Allan
Post Code	DY1 2HQ		
Institution name	Heatherwood And Wexham Park Hospitals NHS Trust	Title	Dr
Department name	Research & Development Office Postgraduate Medical Centre	First name/ Initials	Richard
Street address	Wexham Park Hospital		
Town/city	Wexham, Slough	Surname	Ashford
Post Code	SL2 4HL		
Institution name	Lancashire Teaching Hospitals Foundation NHS Trust	Title	Dr
Department name	Research & Development, Royal Preston Hospital	First name/ Initials	Richard
Street address	Sharoe Green Lane, Fulwood		
Town/city	Preston	Surname	Dobrashian
Post Code	PR2 9HT		
Institution name	Brighton And Sussex University Hospitals NHS Trust	Title	Dr
Department name	R&D Royal Sussex County Hospital	First name/ Initials	Graham
Street address	Eastern Road		
Town/city	Brighton	Surname	Evans
Post Code	BN2 5BE		
Institution name	The Princess Alexandra Hospital NHS Trust	Title	Dr
Department name	Research & Development, Parndon Hall	First name/ Initials	A
Street address	Hamstel Road		
Town/city	Harlow	Surname	Aylwin
Post Code	CM20 1QX		
Institution name	Gloucestershire Hospitals NHS Foundation Trust	Title	Prof
Department name	Gloucestershire RDSU Leadon House	First name/ Initials	I D
Street address	Gloucestershire Royal Hospital Grea		
Town/city	Gloucester	Surname	Lyburn
Post Code	GL1 3NN		
Institution name	Worcestershire PCT	Title	Dr

Department name	West Midlands (South) Comprehensive Local Research Network Fourth Floor Rotunda (ADA40017)	First name/ Initials	F
Street address	University Hospital, Clifford Bridg	Surname	Jenkins
Town/city	Coventry		
Post Code	CV2 2DX		

Institution name	Hull And East Yorkshire Hospitals NHS Trust	Title	Dr
Department name	Office 6 R & D 2nd floor Daisy Building	First name/ Initials	Anne
Street address	Castle Hill Hospital, Castle Road	Surname	Hubbard
Town/city	Cottingham		
Post Code	HU16 5JQ		

Institution name	Surrey PCT	Title	Dr
Department name	Research Department, Worthing & Southlands Hospitals NHS Trust	First name/ Initials	Julie
Street address	Lyndhurst Road	Surname	Cook
Town/city	Worthing		
Post Code	BN11 2DH		

Institution name	East Kent Hospitals NHS University Foundation Trust	Title	Dr
Department name	Research & Development	First name/ Initials	Susan
Street address	Buckland Hospital Coombe Valley Roa	Surname	Lowe
Town/city	Dover		
Post Code	CT17 0HB		

Institution name	Maidstone And Tunbridge Wells NHS Trust	Title	Dr
Department name	Research Management and Governance Centre	First name/ Initials	P
Street address	Main House, Preston Hall Hospital	Surname	Mills
Town/city	Aylesford		
Post Code	ME20 7NJ		

Institution name	Kettering General Hospital NHS Trust	Title	Dr
Department name	Research and Development (c/o Linda Lavelle)	First name/ Initials	Caroline
Street address	Rothwell Road	Surname	Clark
Town/city	Northamptonshire		
Post Code	NN16 8UZ		

Institution name	Leeds Teaching Hospitals NHS Trust	Title	Dr
Department name	Research & Development Department	First name/ Initials	Nisha
Street address	34 Hyde Terrace	Surname	Sharma
Town/city	Leeds		
Post Code	LS2 9LN		

Institution name	University Hospitals Leicester NHS Trust	Title	Dr
Department name	Research Office Leicester General Hospital	First name/ Initials	Elizabeth
Street address	Gwendolen Road	Surname	Denton
Town/city	Leicester		

Post Code	LE5 4PW		
Institution name	United Lincolnshire Hospitals NHS Trust	Title	Dr
Department name	Department of Research & Development	First name/ Initials	Gerald
Street address	Lincoln County Hospital Greetwell R	Surname	Thorpe
Town/city	Lincoln		
Post Code	LN2 5QY		
Institution name	United Lincolnshire Hospitals NHS Trust	Title	Dr
Department name	Department of Research & Development	First name/ Initials	R
Street address	Lincoln County Hospital Greetwell R	Surname	Jones
Town/city	Lincoln		
Post Code	LN2 5QY		
Institution name	Royal Liverpool And Broadgreen University Hospitals NHS Trust	Title	Dr
Department name	Research & Development 4th Floor, Linda McCartney Centre	First name/ Initials	Cath
Street address	Royal Liverpool University Hospital	Surname	Beattie
Town/city	Liverpool		
Post Code	L7 8XP		
Institution name	East Cheshire NHS Trust	Title	Dr
Department name	Clinical Effectiveness, Research & Development Dept., Education & Training Centre	First name/ Initials	M
Street address	Victoria Road	Surname	Crotch-Harvey
Town/city	Macclesfield		
Post Code	SK10 3BL		
Institution name	University Hospital of South Manchester NHS Foundation Trust	Title	Dr
Department name	R&D Directorate, Education and Research Centre	First name/ Initials	M
Street address	Wythenshawe Hospital Southmoor Road	Surname	Wilson
Town/city	Manchester		
Post Code	M23 9LT		
Institution name	Milton Keynes Hospital NHS Foundation Trust	Title	Dr
Department name	R&D Department Postgraduate Education Centre	First name/ Initials	Amanda
Street address	Standing Way, Eaglestone	Surname	Harvard
Town/city	Milton Keynes		
Post Code	MK6 5LD		
Institution name	University Hospitals of Morecambe Bay NHS Trust	Title	Dr
Department name	Research & Development	First name/ Initials	Janet
Street address	Royal Lancaster Infirmary, Ashton R	Surname	Lavelle
Town/city	Lancaster		
Post Code	LA1 4RP		
Institution name	Newcastle Upon Tyne Hospitals NHS Foundation Trust	Title	Dr

Department name	Joint Research Office 4th Floor Leazes Wing	First name/ Initials	Brenda
Street address	Royal Victoria Infirmary Queen Vict	Surname	Kaye
Town/city	Newcastle upon Tyne		
Post Code	NE1 4LP		

Institution name	Royal Devon And Exeter NHS Foundation Trust	Title	Dr
Department name	R&D Office Noy Scott House	First name/ Initials	Russell
Street address	Royal Devon & Exeter Hospital Wonfo	Surname	Davies
Town/city	Exeter		
Post Code	EX2 5DW		

Institution name	Winchester And Eastleigh Healthcare NHS Trust	Title	Dr
Department name	Research & Development Office (MP 80)	First name/ Initials	J
Street address	Royal Hampshire County Hospital Rom	Surname	Hogg
Town/city	Winchester		
Post Code	SO22 5DG		

Institution name	North Cumbria University Hospitals NHS Trust	Title	Dr
Department name	Research & Development, Education Centre	First name/ Initials	Geoff
Street address	Cumberland Infirmary	Surname	Athey
Town/city	Carlisle		
Post Code	CA2 7HY		

Institution name	North West London Hospitals NHS Trust	Title	Dr
Department name	R&D Office, Northwick Park Hospital	First name/ Initials	W
Street address	Watford Road	Surname	Teh
Town/city	Harrow		
Post Code	HA1 3UJ		

Institution name	University Hospital Of North Staffordshire NHS Trust	Title	Dr
Department name	North Staffordshire R&D Consortium Medical Research Unit	First name/ Initials	Saba
Street address	Thornburrow Drive, Hartshill	Surname	Bajwa
Town/city	Stoke on Trent		
Post Code	ST4 7QB		

Institution name	North Tees and Hartlepool NHS Foundation Trust	Title	Dr
Department name	Research & Development	First name/ Initials	W D
Street address	Hardwick Road	Surname	Thompson
Town/city	Stockton-on-Tees		
Post Code	TS19 8PE		

Institution name	York Hospitals NHS Trust	Title	Dr
Department name	North Yorkshire Alliance R&D Unit	First name/ Initials	A
Street address	Learning and Research Centre York H	Surname	Murphy
Town/city	York		
Post Code	YO31 8HE		

Institution name	Northampton General Hospital NHS Trust	Title	Dr
Department name	Research & Development	First name/ Initials	C
Street address	Cliftonville	Surname	Pal
Town/city	Northampton		
Post Code	NN1 5BD		

Institution name	Sherwood Forest Hospitals NHS Trust	Title	Dr
Department name	Research & Development	First name/ Initials	T
Street address	King's Mill Hospital Mansfield Road	Surname	Rasheed
Town/city	Sutton in Ashfield		
Post Code	NG17 4JL		

Institution name	Oxford Radcliffe Hospitals NHS Trust	Title	Dr
Department name	R&D Manor House	First name/ Initials	R
Street address	The John Radcliffe	Surname	English
Town/city	Oxford		
Post Code	OX3 9DZ		

Institution name	Bradford Teaching Hospitals NHS Foundation Trust	Title	Dr
Department name	Bradford Institute for Health Research	First name/ Initials	Peter
Street address	Temple Bank House, Bradford Royal I	Surname	James
Town/city	Bradford		
Post Code	BD9 6RJ		

Institution name	Portsmouth Hospitals NHS Trust	Title	Dr
Department name	R&D Office	First name/ Initials	Linda
Street address	1st Floor, Gloucester House, Queen	Surname	Campbell
Town/city	Cosham		
Post Code	PO6 3LY		

Institution name	The Rotherham NHS Foundation Trust	Title	Dr
Department name	Research & Development	First name/ Initials	S
Street address	Moorgate Road, Oakwood	Surname	Varkey
Town/city	Rotherham		
Post Code	S60 2UD		

Institution name	South London Healthcare NHS Trust	Title	Dr
Department name	Research & Development	First name/ Initials	Jane
Street address	Global House 10 Station Approach	Surname	Goligher
Town/city	Hayes, Kent		
Post Code	BR2 7EH		

Institution name	Sheffield Teaching Hospitals NHS Foundation Trust	Title	Dr
Department name	Research & Development, 3rd Floor Pegasus House	First name/ Initials	C
Street address	463a Glossop Road		

Town/city	Sheffield	Surname	Ingram
Post Code	S10 2QD		

Institution name	Shrewsbury and Telford Hospital NHS Trust	Title	Dr
Department name	Trials Office	First name/ Initials	J A
Street address	Royal Shrewsbury Hospital Mytton Oa	Surname	Fielding
Town/city	Shrewsbury		
Post Code	SY3 8XQ		

Institution name	Taunton and Somerset NHS Foundation Trust	Title	Dr
Department name	The Research Office	First name/ Initials	S
Street address	Musgrove Park Hospital	Surname	Wilson
Town/city	Taunton, Somerset		
Post Code	TA1 5DA		

Institution name	University Hospital Birmingham NHS Foundation Trust	Title	Dr
Department name	R&D Office 4th Floor Nuffield House	First name/ Initials	Sally
Street address	Queen Elizabeth Hospital, Edgbaston	Surname	Bradley
Town/city	Birmingham		
Post Code	B15 2TH		

Institution name	South Devon Healthcare NHS FoundationTrust	Title	
Department name	R&D Dept, Horizon Centre	First name/ Initials	Rebecca
Street address	Torbay Hospital, Lowes Bridge	Surname	Green
Town/city	Torquay		
Post Code	TQ2 7AA		

Institution name	King's College Hospital NHS Foundation Trust	Title	Dr
Department name	R&D Department	First name/ Initials	M
Street address	1st Floor, Jennie Lee House 34 Love	Surname	Michell
Town/city	London		
Post Code	SE5 8AD		

Institution name	Southend University Hospital NHS Foundation Trust	Title	Mr
Department name	Service Reliability & Safety Department Education Centre	First name/ Initials	N
Street address	Prittlewell Chase	Surname	Rothnie
Town/city	Westcliff on Sea		
Post Code	SS0 0RY		

Institution name	Mid Staffordshire General Hospitals NHS Trust	Title	Dr
Department name	Research & Development Department	First name/ Initials	Manjit
Street address	Staffordshire General Hospital West	Surname	Obhrai
Town/city	Stafford		
Post Code	ST16 3SA		

Institution name	St George's Healthcare NHS Trust	Title	Dr
Department name	St George's Joint Research Office, Ground Floor, Hunter Wing	First name/ Initials	Louise
Street address	St. George's University of London C	Surname	Wilkinson
Town/city	London		
Post Code	SW17 0RE		

Institution name	Southampton University Hospitals NHS Trust	Title	Dr
Department name	Research & Development Duthie (Trust), Ground Floor	First name/ Initials	C
Street address	Mailpoint 138, Southampton General	Surname	Rubin
Town/city	Southampton		
Post Code	SO16 6YD		

Institution name	Colchester Hospital University NHS Foundation Trust	Title	Dr
Department name	Research and Development, Colchester General Hospital	First name/ Initials	R
Street address	Postgraduate Medical Centre Turner	Surname	Whitney
Town/city	Colchester		
Post Code	CO4 5JL		

Institution name	Warrington & Halton Hospitals NHS Foundation Trust	Title	Dr
Department name	Research and Development, Warrington Hospital	First name/ Initials	A
Street address	Lovely Lane	Surname	Sheridan
Town/city	Warrington		
Post Code	WA5 1QG		

Institution name	University Hospitals Coventry And Warwickshire NHS Trust	Title	Dr
Department name	R&D Department First Floor Rotunda (opposite Cardiac)	First name/ Initials	Alison
Street address	University Hospital, Clifford Bridg	Surname	Duncan
Town/city	Coventry		
Post Code	CV2 2DX		

Institution name	Royal Berkshire NHS Foundation Trust	Title	Dr
Department name	Research and Development Level 3, Main Entrance Building	First name/ Initials	Marjon
Street address	Royal Berkshire Hospital, London Ro	Surname	Bell
Town/city	Reading		
Post Code	RG1 5AN		

Institution name	Plymouth Hospitals NHS Trust	Title	Dr
Department name	R&D Office, Room N17 ITTC Building	First name/ Initials	J
Street address	Tamar Science Park, Derriford	Surname	Steel
Town/city	Plymouth		
Post Code	PL6 8BX		

Institution name	Imperial College Healthcare NHS Trust (Hammersmith Hospital, Charing Queen Charlotte & Chelsea)	Title	Dr
Department name	R&D Office 1st floor, Hammersmith House	First name/ Initials	N K
Street address	150 Du Cane Road	Surname	Barrett
Town/city	London		

Post Code	W12 0HS		

Institution name	Western Sussex Hospitals NHS Trust	Title	Dr
Department name	Research Department Worthing Hospital	First name/ Initials	Olga
Street address	Lyndhurst Road	Surname	Strukowska
Town/city	Worthing		
Post Code	BN11 2DH		

Institution name	Whipps Cross University Hospital NHS Trust	Title	Dr
Department name	Joint R&D Office	First name/ Initials	Indra
Street address	24-26 Walden Street, Whitechapel	Surname	Mootasamy
Town/city	London		
Post Code	E1 2AN		

Institution name	Wrightington, Wigan and Leigh NHS Foundation Trust	Title	Mr
Department name	R&D Unit, Junction 2	First name/ Initials	R
Street address	Whipps Cross Road	Surname	Harland
Town/city	Leytonstone, London		
Post Code	E11 1NR		

Institution name	Great Western Hospitals NHS Foundation Trust	Title	Dr
Department name	Research & Development	First name/ Initials	S
Street address	Great Western Hospital Marlborough	Surname	Taylor
Town/city	Swindon		
Post Code	SN3 6BB		

Institution name	Wirral University Teaching Hospital NHS Foundation Trust	Title	Dr
Department name	R&D Department, Arrowe Park Hospital	First name/ Initials	Simon
Street address	Upton	Surname	Lea
Town/city	Wirral		
Post Code	CH49 5PE		

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 main REC or the GTAC (as 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 main REC, 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.
    - 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.

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 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 Julietta Patnick on 04/01/2010 03:30.

Job Title/Post:	Director
Organisation:	NHS Cancer Screening Programmes
Email:	
Signature:	.....
Print Name:	
Date:	*(dd/mm/yyyy)*

D2. Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the coû 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.

7. 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.

Signature: .....

Print Name:

Post:

Organisation:

Date: *(dd/mm/yyyy)*