Welcome to the Integrated Research Application System

IRAS Project Filter

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

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

Please enter a short title for this project (maximum 70 characters)
The 'Big Baby Trial'

1. Is your project research?

(●) Yes ( ) No

2. Select one category from the list below:

( ) Clinical trial of an investigational medicinal product

( ) Clinical investigation or other study of a medical device

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

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

( ) Basic science study involving procedures with human participants

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

( ) Study involving qualitative methods only

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

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

( ) Research tissue bank

( ) Research database

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

( ) Other study

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

( ) Yes (●) No

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

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

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

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

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

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

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

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

4. Which applications do you require?

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

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

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

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

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

(•) Yes ( ) No

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

Please see information button for further details.

( ) Yes (•) No

Please see information button for further details.

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

Please see information button for further details.

(•) Yes ( ) No

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

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

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

◉ Yes ○ No

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

○ Yes ◉ No

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

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

○ Yes ◉ No

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

○ Yes ◉ No

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

○ Yes ◉ No

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

○ Yes ◉ No

NOTICE OF SUBSTANTIAL AMENDMENT

Please use this form to notify the main REC of substantial amendments to all research other than clinical trials of investigational medicinal products (CTIMPs).
The form should be completed by the Chief Investigator using language comprehensible to a lay person.

Details of Chief Investigator:

	Title	Forename/Initials	Surname
	Professor	Siobhan	Quenby
Work Address	Clifford Bridge Road, Coventry		
PostCode	CV2 2DX		
Email	s.quenby@warwick.ac.uk		
Telephone	07873416716		
Fax			

For guidance on this section of the form refer to the guidance

Full title of study:	Induction of labour for predicted macrosomia
Lead sponsor:	University Hospitals Coventry and Warwickshire NHS Trust
Name of REC:	South West-Exeter Research Ethics Committee
REC reference number:	18/SW/0039

International Standard Randomised Controlled Trial Number (ISRCTN):	ISRCTN18229892
ClinicalTrials.gov Identifier (NCT number):	

Additional reference number(s):

Ref.Number Description	Reference Number

Name of lead R&D office:	University Hospitals Coventry & Warwickshire
Date study commenced:	1st January 2018
Protocol reference (if applicable), current version and date:	HTA16-77 Big Baby Protocol V1.1 12th Feb 18
Amendment number and date:	AM01 17th April 2018

Type of amendment

(a) Amendment to information previously given in IRAS

(●) Yes ( ) No

If yes, please refer to relevant sections of IRAS in the "summary of changes" below.

(b) Amendment to the protocol

(●) Yes ( ) No

If yes, please submit either the revised protocol with a new version number and date, highlighting changes in bold, or a document listing the changes and giving both the previous and revised text.

(c) Amendment to the information sheet(s) and consent form(s) for participants, or to any other supporting documentation for the study

(●) Yes ( ) No

If yes, please submit all revised documents with new version numbers and dates, highlighting new text in bold.

Is this a modified version of an amendment previously notified and not approved?

( ) Yes (●) No

Summary of changes

Briefly summarise the main changes proposed in this amendment. Explain the purpose of the changes and their significance for the study.
If this is a modified amendment, please explain how the modifications address the concerns raised previously by the ethics committee.
If the amendment significantly alters the research design or methodology, or could otherwise affect the scientific value of the study, supporting scientific information should be given (or enclosed separately). Indicate whether or not additional scientific critique has been obtained.

Please find below a summary of changes categorised for your convenience.

Baseline questionnaire
Baseline questionnaire: Has been submitted for approval as this was not submitted in the initial application.
Follow up questionnaires
Two month follow up questionnaire A: Has been submitted for approval as this was not submitted in the initial application. This two month follow up questionnaire will be sent to the mothers of the babies who have not died.
Six month follow up questionnaire A: Has been submitted for approval as this was not submitted in the initial application. This six month follow up questionnaire will be sent to the mothers of the babies who have not died.
Two month follow up questionnaire B: Has been submitted for approval as this was not submitted in the initial application. This two month follow up questionnaire will be sent to the mother's who's babies have died with all questions relating to the baby removed. This will be sent alongside the letter to bereaved mother which was approved in the initial submission.
Six month follow up questionnaire B: Has been submitted for approval as this was not submitted in the initial application. This six month follow up questionnaire will be sent to the mother's who's babies have died with all questions relating to the baby removed. This will be sent alongside the letter to bereaved mother which was approved in the initial submission.

Protocol

1. Protocol Section 2.1. It has been clarified that women with a current psychiatric disorder requiring antipsychotic medications will be excluded from the trial. This has been changed so it aligns with section 2.8.2. Exclusion Criteria.
2. Protocol Sections 2.1, 2.8.2 and flowchart (Figure1). Amendment to information previously given in IRAS (A17-2): Intrauterine fetal death has been added to the list of exclusion criteria as it would not be appropriate to include these woman in the trial.
3. Protocol Sections 2.1 and 2.82: Previous neonatal death time-frame has been defined as ≤28 days to add more clarity to the definition.

4. Protocol Sections 2.1, 2.8.2 and figure 1 flow chart. Amendment to information previously given in IRAS (A17-2). The text has been amended to clarify that women taking medications and/or insulin therapy for diabetes or gestational diabetes are excluded from the trial. The word or has been added to provide clarification that women may only take medication or only take insulin.
5. Protocol Section 2.4 (2.1, 2.14 & 2.15): The wording of the intervention has been amended to clarify that the intervention is the booking of induction of labour at 38+0 to 38+4 weeks gestational age. This will ensure that the protocol is aligned to current obstetric practice and reflects the intention to treat.
6. Protocol Section 2.9.2.2: Fever has been re- defined as >38.0 degrees Celsius. This is to align to protocol with the hospital policy at University Hospital Coventry and Warwickshire and the NICE guidelines on intrapartum care.
7. Protocol Section 2.9.2.2: Primary postpartum haemorrhage has been re-defined as ≥500ml as this is the standard definition.
8. Protocol: Section 2.9.2.3. Longer term outcomes. It has been clarified that QoL EQ-5D-5L, Edinburgh Post-natal depression scale, urinary incontinence ICIQ-UI short form and sexual function will be collected at baseline. This was missing on initial submission of the protocol.
9. Protocol: Section 2.9.2.3. Faecal incontinence assessment will be collected at baseline, 2 and 6 months post-partum. This was not specified in the initial submission of the protocol.
10. Protocol: Section 2.9.2.3. It has been clarified that maternal report of infant health will be collected at 2 months and 6 months post-partum. This was not specified in the initial submission of the protocol.
11. Protocol: Section 2.9.2.3. It has been clarified participant health resource used for economic analysis for mother and baby will be collected at 2 and 6 months. This was not specified in the initial submission of the protocol.
12. Protocol: Section 2.9.2.3. Antibiotic prescription at 2 months has been removed and replaced with 'participant health resource used for health economic analysis baby and mother at 2 and 6 months'. This is because antibiotic use now incorporated within the health economic analysis.
13. Protocol: Section 2.9.2.3. It has been clarified that 'Post-partum bonding' and 'Six Simple Questions' will now only be collected at 2 months. 6 months is too far away from birth to be valid for post-partum bonding. Six simple questions is not required at 6 months as it is only required to be collected once.
14. Protocol Section 2.13. Amendment to information previously given in IRAS (A13): Qualitative Interviews. The text has been amended to state that participant interviews will under taken at three pilot sites rather than two and that it will involve 10 women from each group; control, intervention and cohort. Additionally the text has been amended to state that six to nine partners will be approached for interview.
15. Protocol Section 2.14: Recruitment process. Text has been added to define who is responsible for agreeing that the woman is medically suitable to enter the trial and who is responsible for signing trial eligibility. This was not specified in the initial submission of the protocol.
16. Protocol Section 2.15: Informed consent. It has been clarified that the participant information sheet and participant consent form only have obtained a crystal mark from the Plain English Campaign. The other documents previously listed is incorrect as they have not been reviewed the Plain English Campaign.
17. Protocol Section 2.16: Clarification that randomisation will initially be provided by WCTU using a telephone service as the online randomisation system will not be ready in time for the start of recruitment.
18. Protocol Section 4: Adverse event management. Text and tables have been amended to provide greater clarity on the management of Adverse Events (AEs) and Serious Adverse Events (SAEs). Amendments include: clarification of the reporting period (from randomisation until 6 month follow-up); provision of examples of common Adverse Events (AEs); clarification of those Serious Adverse Events (SAEs) that do not require immediate reporting because they are outcomes of the study; and provision of further detail on the process for assessing SAE causality and expectedness.
19. Protocol Section 5.1: The text has been amended to state that participant contact details will also be used to send reminders, ask for clarifications, invite to the interview study and contact the woman or child in the future. It has also been clarified that participants contact details will be held separately within the main database rather than completely separately as originally stated.
20. Protocol throughout: The addition of ISRCTN registration number.
21. Protocol throughout: 'Participant' has replaced 'Patient' where appropriate throughout the document.

Participant Information Sheet

22. Participant Information Sheet: We have included infographics in the section; 'What is the trial about?' to supplement the text for those participants who prefer information to be displayed as diagrams.
23. Participant Information Sheet: In the section 'What will happen if I agree to take part?' we have further explained that although an appointment for a planned induction has been made this may not happen and if they become unhappy with their allocation they can discuss their care with their obstetrician or midwife. This has been added to inform women that won't necessarily receive the intervention they are allocated to.
24. Participant Information Sheet: The wording has been amended in the 'expenses and payments' section to clarify to patients that no extra visits to hospital will be needed to participate in the trial and that there is no payment for participation or reimbursement of travel expenses. This has been changed to align with information provided in the IRAS application A46 where we have stated that no payments or reimbursements of expenses will be paid for taking part in the research.
25. Participant Information Sheet: An explanation has been added to inform women that the ultrasound scan is

inaccurate in 8% of cases of large for gestational age fetuses. This was not specified in the initial submission of the participant information sheet and we feel woman need to be provided with this information in order to make an informed decision as to whether to participate in the trial.
26. Participant Information Sheet: In the section 'Will information about me and my baby be kept confidential?' – A statement has been added that contact details will be collected by the trial team and that research and contact information will be stored separately in the database. A statement has been added explaining that disclosure of personal information or confidentiality broken if there is a concern about risk of harm to mother or child. This was missing from the participant information sheet on initial submission and has therefore been added.
27. Participant Information Sheet: In section 'what will happen to the results of this trial' the text has been amended to state that the results of the trial will be published on the trial website rather than a summary sent. This has been amended to align with the protocol as it will not be practicable to send out a summary of the finding to all participants.
28. Participant Information Sheet: Text has been added to define that the 'trial team' constitutes the trial personnel at Warwick Clinical Trials Unit-WCTU and Perinatal Institute to make it clearer for the women who is involved in the trial.

Site Investigator information sheet

29. Site Investigator information sheet: The section outlining the process for dealing with a concern regarding significant harm to the woman, baby or others has been removed as this was added in error on the initial submission and is not applicable.

Consent form RCT

30. Consent form RCT: Item 1. The text has been amended to allow the trial team to enter the version and date of the participant information sheet provided to allow the Participant information sheet to be updated without needing to update the consent form.
31. Consent form RCT: Item 4. The text has been amended to clarify that the hospital research team will have access to the participant's hospital records to make it clearer to the potential participant.
32. Consent form RCT: Item 5. The text has been amendment to clarify that the hospital research team rather than the trial team will have access to the child's hospital records to make it clearer to the potential participant.
33. Consent form RCT: Items 6 and 7. The wording has been amended to allow permission for the monitoring team to access trial records as the original text did now allow for this. Additionally the text has been amended in item 6 to clarify that the 'trial team' used throughout the consent form is defined as members of the Big Baby trial team located at Warwick Clinical Trials Unit-WCTU and the Perinatal Institute in order to make it clearer to women.
34. Consent form RCT: Item 8. The text has been amended to clarify that it will be the hospital research team rather than the trial team that will contact the relevant hospital trust to obtain medical details should the participant deliver at a different hospital trust
35. Consent form RCT: Items 9 and 10.The text has been amended to clarify that it will be the hospital research team rather than the trial team that will contact the relevant hospital trust if the woman or baby is transferred.
36. Consent form RCT: Item 11: We have clarified the reasons for holding contact details specifying that this is so that the trial team can send reminder and follow-up questionnaires or contact the participant to seek clarifications about the follow-up questionnaires and ask about their and their baby's health. Additionally the point asking for agreement to be contacted to be invited to participate has been removed and replaced the text in item 18: Optional. This allows the participant the option to agree to be contacted regarding the collection of follow up data, but decline to be contacted regarding the interview study.
37. Consent form RCT: Item 12. We have clarified that it will be the hospital research team rather than the trial team who will access the child's NHS hospital records before sending me reminders or the two- or six-month follow-up questionnaires. We have removed the statement about the interview study, as this is covered in item 18.
38. Consent form RCT: Item 18. The text asking for agreement to be contacted for reminders to complete the follow up questionnaires has been removed as this is covered in item 11. It has been replaced by text seeking agreement to be contacted to be invited to participate in an interview. This has previously been explained in amendment item 30.
39. Consent form RCT: Item 20. We have clarified that it will be the hospital research team rather than the trial team who will inform the GP that the participant is taking part in the trial.

Consent form-Cohort

40. Consent form Cohort: Item 4. The text has been amended to clarify that the hospital research team will have access to the participant's hospital records to make it clearer to the potential participant.
41. Consent form Cohort: Item 5. The text has been amendment to clarify that the hospital research team will have access to the child's hospital records to make it clearer to the potential participant.
42. Consent form Cohort: Items 6 & 7.The wording has been amended to allow permission for the monitoring team to access trial records as the original text did now allow for this. Additionally the text has been amended in item 6 to clarify that the 'trial team' used throughout the consent form is defined as members of the Big Baby trial team located

at Warwick Clinical Trials Unit-WCTU and the Perinatal Institute in order to make it clearer to the potential participant.
43. Consent form Cohort: Item 8. The text has been amended to clarify that it will be the hospital research team that will contact the relevant hospital trust to obtain medical details should the participant deliver at a different hospital trust.
44. Consent from Cohort: Items 9 and 10. The text has been amended to clarify that it will be the hospital research team rather than the trial team that will contact the relevant hospital trust if the woman or baby is transferred. It also ensures that the cohort consent form is consistent with the RCT Consent form.
45. Consent form Cohort: Item 11: We have clarified the reasons for holding contact details specifying that this is so that the trial team can send reminder and follow-up questionnaires or contact the participant to seek clarifications about the follow-up questionnaires and ask about their and their baby's health. Additionally the point asking for agreement to be contacted to be invited to participate has been removed and replaced the text in item 18: Optional. This allows the participant the option to agree to be contacted regarding the collection of follow up data, but decline to be contacted regarding the interview study.
46. Consent form Cohort: Item 12. We have clarified that it will be the hospital research team who will access the child's NHS hospital records before sending me reminders or the two- or six-month follow-up questionnaires. We have removed the statement about the interview study, as this is covered in item 18.
47. Consent form Cohort: Item 13, 14, 15, 16, 17 and 18. It has been clarified that the trial team will perform these activities not the research team.
48. Consent form Cohort: Item 20. It has been clarified that the hospital research team will perform this activity rather than the trial team.

Consent forms-Gapped

49. Consent form – RCT - GAPPED: for languages with no translated materials the consent form will have spaces underneath each item for the translator to write a translated version – were possible.
50. Consent form – COHORT - GAPPED: for languages with no translated materials the consent form will have spaces underneath each item for the translator to write a translated version – were possible.

Participant Interview Information Sheet Pilot

51. Participant Interview Information Sheet Pilot. In the section 'What is the purpose of the trial' the word 'fully' has been removed from the text as although we will ensure the potential participant receives, and understands, the relevant information, this does not equate to being fully informed to all of the facts.

Additionally the words 'whenever possible' have been added to the statement regarding disclosing confidential information should a concern about a significant risk of harm to women or baby arise. This is because although extremely rare, it may be necessary to break confidentiality without being able to inform the research participant.

Participant Interview Information Sheet Main

52. Participant Interview Information Sheet Main. The words 'whenever possible' have been added to the statement regarding disclosing confidential information should a concern about a significant risk of harm to women or baby arise. This is because although extremely rare, it may be necessary to break confidentiality without being able to inform the research participant.

Interview topic guides

53. Interview questions - clinicians: Topics have been added that explore uncertainty regarding scan results and previous practice / advice.
54. Interview questions – clinicians: Topics have been added that explore clinicians impressions on the most important factors influencing women's decisions to participate in the RCT or cohort study
55. Interview questions - RCT: Topics have been added that explore uncertainty regarding scan results. and the mother's feelings if the baby was found not to be LGA at birth
56. Interview questions - RCT: Q3: The instruction to show the participants examples of the PIS have been removed as the interview will take place over the telephone.

Any other relevant information

Applicants may indicate any specific issues relating to the amendment, on which the opinion of a reviewing body is sought.

List of enclosed documents

Document	*Version*	*Date*
Protocol-Tracked	2.0	12/04/2018
Protocol-Clean	2.0	12/04/2018
Participant Information Sheet-Tracked	2.0	12/04/2018
Pariticpant Information Sheet-Clean	2.0	12/04/2018
Consent Form RCT-Tracked	2.0	12/04/2018
Consent Form RCT-Clean	2.0	12/04/2018
Consent Form Cohort-Tracked	2.0	12/04/2018
Consent Form Cohort- Clean	2.0	12/04/2018
Consent Form RCT Gapped	2.0	12/04/2018
Consent Form Cohort Gapped	2.0	12/04/2018
Site Investigator Interviews Information Sheet-Tracked	2.0	12/04/2018
Site Investigator Information Sheet-Clean	2.0	12/04/2018
Participant Interview Information Sheet-Pilot-Tracked	2.0	12/04/2018
Participant Interview Information Sheet-Pilot-Clean	2.0	12/04/2018
Participant Interview Information Sheet-Main-Tracked	2.0	12/04/2018
Participant Interview Information Sheet-Main-Clean	2.0	12/04/2018
Interview topic guide-Interviews with clinicians-Tracked	2.0	12/04/2018
Interview topic guide- RCT Interviews-Clean	2.0	12/04/2018
Interview topic guide- RCT interviews-Tracked	2.0	12/04/2018
Interview topic guide-Interviews with clinicians-Clean	2.0	12/04/2018
Baseline questionnaire-Clean	1.0	12/04/2018
Follow up questionnaire- Two months A-Clean	1.0	12/04/2018
Follow up questionnaire- Six months A-Clean	1.0	12/04/2018
Follow up questionnaire- Two months B-Clean	1.0	12/04/2018
Follow up questionnaire- Six months B-Clean	1.0	12/04/2018
Cover letter to REC		

Declaration by Chief Investigator

1. *I confirm that the information in this form is accurate to the best of my knowledge and I take full responsibility for it.*
2. *I consider that it would be reasonable for the proposed amendment to be implemented.*

This section was signed electronically by Professor Siobhan Quenby on 26/04/2018 07:57.

Job Title/Post:	Prof of Obstetrics
Organisation:	University of Warwick
Email:	s.quenby@warwick.ac.uk

Declaration by the sponsor's representative

I confirm the sponsor's support for this substantial amendment.

This section was signed electronically by Ceri Jones on 25/04/2018 16:09.

Job Title/Post:	Head of R&D
Organisation:	UHCW NHS Trust
Email:	ceri.jones@uhcw.nhs.uk