ETHICS, IRAS & DATA PROTECTION

Clinical Research Methods Course

14th March 2017

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Definitions

CI: Chief Investigator

CTIMP: Clinical Trial of an Investigational Medicinal Product

IRAS: Integrated Research Applications system

MHRA: Medicines and Healthcare products Regulatory Agency

HRA: Health Research Authority

REC: Research Ethics Committee

CRN: Clinical Research Network
Who are the main organisations?

- HRA/REC
- MHRA
- Sponsor
- Sites
- CRN
- CI
- Patients
Clinical trial pathway

http://www.ct-toolkit.ac.uk/routemap/
Where do I start?

Trial Documents
- Protocol
- IRAS
- Patient Information Sheet
- Informed Consent
- GP letter
- Funding
- Contracts

Collaborators
- Statistician
- CI
- QA Manager
- Database Manager
- Trial Manager/Coordinator
- Sponsor
Is Your Study Ethical?

Ethical Framework

- Beneficence
  - Do good
- Autonomy
  - Patients rights
- Justice
  - For society
- Non-maleficence
  - Do no harm

Study protocol

Consent Form(s)

Patient Information Sheet
Ethics application – Part 1

Peer reports/ Risk assessments

Local Peer Review

Sponsor

Trial team

Trial documents
Integrated Research Application System (IRAS)

Standardised platform for Permissions & Approvals for UK Health Research

- Register for an IRAS account ([https://www.myresearchproject.org.uk](https://www.myresearchproject.org.uk))
- Create a new project
  - Transcribe study protocol into Project document
  - Provide further clarification around study procedures & ethical considerations
- Single system for approvals for research in the UK
- Depending on the type of study, uses filters to ensure the appropriate information is collected
- Add participating sites and the principal investigators
IRAS - Registration

Welcome to the Integrated Research Application System (IRAS)

April 2013 - From April 2013, Primary Care Trusts (PCTs) no longer exist in England. Arrangements to support primary care research will continue throughout England. Although PCTs no longer exist, IRAS will continue to include reference to historic PCT names and allow applications to be made with the historic PCT site name. This is in recognition of the importance of providing continuity to applicants using well-known geographical boundaries. Guidance on applications for primary care in England is available here.

25 March 2013 - IRAS has been updated to v3.5
An update to electronic authorisations functionality has been implemented that will affect authorisations obtained prior to this version update. IRAS v3.5 also includes significant updates to applications to ARSAC and NHS SSI question 23 as well as withdrawal of the Ministry of Justice form and addition of a new question for Phase 1 CTIMP studies. Additionally, all applications for NHS permission through NIHR CSP are now electronically submitted. All projects in IRAS have been automatically updated to IRAS v3.5 therefore it is strongly recommended that users refer to the Updates page for more information.

The Integrated Research Application System (IRAS)

- Is a single system for applying for the permissions and approvals for health and social care / community care research in the UK
- Enables you to enter the information about your project once instead of duplicating information in separate application forms
- Uses filters to ensure that the data collected and collated is appropriate to the type of study, and consequently the permissions and approvals required
- Helps you to meet regulatory and governance requirements
- Retains familiar aspects of the NRES form system

IRAS captures the information needed for the relevant approvals from the following review bodies:

- Administration of Radioactive Substances Advisory Committee (ARSAC)
- Gene Therapy Advisory Committee (GTAC)
- Medicines and Healthcare products Regulatory Agency (MHRA)
- NHS / HSC R&D offices
- NRES/ NHS / HSC Research Ethics Committees
- National Information Governance Board (NIGB)
- National Offender Management Service (NOMS)
- Social Care Research Ethics Committee

Please help us to improve IRAS by sending your feedback to iras.queries@nhs.net. Your comments and suggestions will be included in the next review of the system.

https://www.myresearchproject.org.uk
### IRAS – Create New Project

![IRAS Project Creation Screen](https://www.myresearchproject.org.uk)

<table>
<thead>
<tr>
<th>Project Title</th>
<th>IRAS Project ID</th>
<th>Created On</th>
<th>Status</th>
<th>Last Opened</th>
</tr>
</thead>
</table>
| OPTIMISE II   | 209688          | 29/05/2016 | Project Status: Active  
NHS SSI - 328501 [Dr Tamas Szakmany (ANEURIN BEVAN LOCAL HEALTH BOA...] Transferred Out  
NHS SSI - 328502 [Dr Mortimer Kelleher (NHS LOTHIAN)] Transferred Out | 08/03/2017 |
| SPACE         | 207629          | 27/04/2016 | Project Status: Transferred In  
NIHR CRN Portfolio Application Form: Transferred In  
IRAS Form: Transferred In  
MHRA Medicines (EudraCT application form): Transferred In | 07/03/2017 |

https://www.myresearchproject.org.uk
IRAS – Core Study Questions

<table>
<thead>
<tr>
<th>SECTION</th>
<th>QUESTION RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part A: Core study information</td>
<td></td>
</tr>
<tr>
<td>Administrative details</td>
<td>Proj. Title-A1 A2 A3 A4-A5</td>
</tr>
<tr>
<td>Overview of the research</td>
<td>A6</td>
</tr>
<tr>
<td>Purpose and design of the research</td>
<td>A7 A8-A9 A10-A13 A14 14</td>
</tr>
<tr>
<td>Risks and ethical issues</td>
<td>A15 A16 A17</td>
</tr>
<tr>
<td>Research procedures, risks and benefits</td>
<td>A18 A19 A20-A22 A23-A26</td>
</tr>
<tr>
<td>Recruitment and informed consent</td>
<td>A27 A28-A30 A31-A35</td>
</tr>
<tr>
<td>Confidentiality</td>
<td>A36-A38 A39 A40-A42 A43-A45 A46-A49</td>
</tr>
<tr>
<td>Part A</td>
<td></td>
</tr>
<tr>
<td>Publication and dissemination</td>
<td>A50-A53</td>
</tr>
<tr>
<td>Scientific and Statistical Review</td>
<td>A54 A55 A56-A57 A58-A62</td>
</tr>
<tr>
<td>Management of the research</td>
<td>A63-A64 A65-A69 A70 A71-A72 A73-A75 A76-A79</td>
</tr>
<tr>
<td>Part B: Additional information</td>
<td>A80</td>
</tr>
</tbody>
</table>
IRAS – Project filter questions non-CTIMP

Please enter a short title for this project (maximum 70 characters)

OPTIMISE II

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
IRAS – Project filter questions CTIMP

Please enter a short title for this project (maximum 70 characters)

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
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   - Research database

If your work does not fit any of these categories, select the option below:
   - Other study
• CTIMPS need to be registered on EudraCT (ISRCTN for non-CTIMPS)

• Clinical Trial Application Form needs to be completed

  Provide further information on the - Investigational Medicinal Products (IMPs)

  - Placebos if required

IRAS – Project filter questions CTIMP

<table>
<thead>
<tr>
<th>SUB-SECTION</th>
<th>QUESTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: Trial identification</td>
<td>A1-A7 A8</td>
</tr>
<tr>
<td>B: Sponsor</td>
<td>B1</td>
</tr>
<tr>
<td>C: Application</td>
<td>C1</td>
</tr>
<tr>
<td>D: Information on the IMPs</td>
<td>D</td>
</tr>
<tr>
<td>Medicinal Products</td>
<td></td>
</tr>
<tr>
<td>IMP - PR1</td>
<td>D1-D2 D3 D3 D4-D5 D6 D7</td>
</tr>
<tr>
<td>IMP - PR3</td>
<td>D1-D2 D3 D3 D3 D4-D5 D6 D7</td>
</tr>
<tr>
<td>D8: Information on the Placebos</td>
<td>D8</td>
</tr>
<tr>
<td>D9: Site(s) where the qualified person certifies batch release</td>
<td>D9</td>
</tr>
<tr>
<td>E: General information on the trial</td>
<td>E1 E2 E3-E5 E6-E7 E8</td>
</tr>
<tr>
<td>F: Population of Trial Subjects</td>
<td>F1-F3 F4-F5</td>
</tr>
<tr>
<td>G: Clinical Trial Sites/Investigators in the Member State</td>
<td>G1-G2 G3 G4-G5</td>
</tr>
<tr>
<td>H: Ethics Committee/National Competent Authority</td>
<td>H1-H2</td>
</tr>
<tr>
<td>I: Signature of the applicant in the member state</td>
<td>I1-I2</td>
</tr>
<tr>
<td>J: Checklist of Information</td>
<td>EudraCT Checklist</td>
</tr>
</tbody>
</table>
## IRAS – Check List

<table>
<thead>
<tr>
<th>Document</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Project Information:</strong></td>
</tr>
<tr>
<td>(All documents must be dated and/or have version numbers)</td>
</tr>
<tr>
<td>Covering letter on headed paper</td>
</tr>
<tr>
<td>Research protocol or project proposal</td>
</tr>
<tr>
<td>Summary CV for Chief Investigator (CI)</td>
</tr>
<tr>
<td>Participant information sheet (PIS)</td>
</tr>
<tr>
<td>Participant consent form</td>
</tr>
<tr>
<td>Letters of invitation to participant</td>
</tr>
<tr>
<td>GP/consultant information sheets or letters</td>
</tr>
<tr>
<td>Sample diary card/patient card</td>
</tr>
<tr>
<td>Interview schedules or topic guides for participants</td>
</tr>
<tr>
<td>Validated questionnaire</td>
</tr>
<tr>
<td>Non-validated questionnaire</td>
</tr>
<tr>
<td>Referee’s report or other scientific critique report</td>
</tr>
<tr>
<td>Summary, synopsis or diagram (flowchart) of protocol in non-technical language</td>
</tr>
<tr>
<td>Copies of advertisement materials for research participants</td>
</tr>
<tr>
<td><strong>Finance Agreements:</strong></td>
</tr>
<tr>
<td>Letter from sponsor</td>
</tr>
<tr>
<td>Letter from funder</td>
</tr>
<tr>
<td>Letter from statistician</td>
</tr>
<tr>
<td>Costing template (commercial projects)</td>
</tr>
<tr>
<td>Contract/Study Agreement</td>
</tr>
<tr>
<td>Evidence of Sponsor insurance or indemnity (non-NHS Sponsors only)</td>
</tr>
</tbody>
</table>

### CTIMPS only

Documents required prior to Approval being issued:
(in England, HRA will work with MHRA and CAG (formerly NIGB) and other regulators to receive these documents but may be in contact with researcher should there be queries)

- MHRA "Notice of No Objection" Letter (Medical Devices) and relevant correspondence
- Confirmation of any other regulatory approvals (e.g. CAG) and all correspondence
- Laboratory Manual
- Instructions for use of medical device

### Other documents

- Other (please specify)
- Other (please specify)
Provisional Sponsorship

1. Essential Documents; all studies

- Costings
  - For Barts Health Studies (Sponsors or a ‘site’) contact Juan-Carlos Rodriguez Prados
  - For QMUL Studies (Sponsors or a ‘site’) contact Garry Collins or Richard Ottaway

- Funding letter (this should detail who the funder is, the amount and that it has been secured)

- IRAS R&D Form (Signed by Sponsor and CI for hosted projects)

- Insurance documents (for hosted projects which are not NHS Sponsored)

- Signed and dated CV of Chief Investigator and local Principal Investigator

- IRAS SSI form

2. REC & HRA

- REC Approval letter (for hosted projects)

All documents to be submitted to REC & HRA including:

- HRA Schedule of Events

- HRA Statement of Activities

- Covering letter to REC on headed paper

- Research Protocol

- Participant information sheet (PIS) (On BH/QM headed paper with local details)

- Participant consent form (On BH/QM headed paper with local details)

- Letters (or emails) of invitation to participant

- GP/consultant information sheets or letters

- Letter from statistician

- Referee’s report or other scientific critique report

SOP 11 Additional Document 1 - JRMO Submission checklist V6.4 16/3/16

Document check list

Provisional Sponsorship and Indemnity

http://bartshealth.nhs.uk/research/strategy-and-policy/standard-operating-procedures/
IRAS – Electronic Authorisations

Please click here for downloadable step-by-step instructions on electronic authorisations. You must obtain electronic authorisations before you print the form for submission.

The following electronic authorisations are available for this form type:

<table>
<thead>
<tr>
<th>Authorisation Type</th>
<th>Status</th>
<th>Signing User</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor’s representative</td>
<td>Invalid</td>
<td>Dr Sally Burtles</td>
<td>Request</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sign</td>
</tr>
<tr>
<td>Chief Investigator</td>
<td>Invalid</td>
<td>Dr Rupert Pearse</td>
<td>Request</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sign</td>
</tr>
</tbody>
</table>

Enter e-mail address of authoriser and press "Send" to request an electronic authorisation from another user in the system.

Send Request >>  Cancel

- Book meeting with the REC
- Submission can be made only after electronic authorisations
- If you change any information after authorisations, signatures will need to be requested again
• Studies funded as a result of open competition in England with high quality peer review

• Research that is of clear value to the NHS

• Studies that take appropriate account of the priorities, needs and realities of the NHS
REC/HRA Approvals Pathway

Application received

REC validation → Initial Assessment

REC review ↔ HRA assessment

REC Favourable Opinion → Collate approvals

HRA Approval
Capacity and Capability

1. Identify
   - Site identification
     - Starts before or after HRA application
     - Network support if needed

2. Assess
   - Assess capacity & capability
     - Send final protocol to research team and R&D/ LCRN support
     - Official site selection

3. Arrange
   - Practical arranging
     - Send local information pack to research team and R&D/ LCRN support (includes HRA Initial Assessment Letter)

4. Confirm
   - Exchange contracts
     - Send contract for signature
     - Site should be ready to recruit to agreed plan

5. Site Initiation
   - Sponsor initiates site
     - Send IMP
     - Undertake site initiation visit

HRA submission

- HRA initial Assessment letter issued
- HRA Approval letter issued
- Site ready to recruit

This presentation is designed to provide general information only. Our website Terms and Conditions apply www.hra.nhs.uk

2 February 2016
Approvals Checklist

- REC Favourable opinion
- Letter of HRA approval
- NIHR Portfolio adoption
- Confirmation of Capacity and Capability
- Full Sponsorship
IRAS - Amendments

Substantial amendments:

A substantial amendment is defined as a change to the terms of the REC application, the protocol or any other document submitted with the application, which significantly affects one of the following: The safety or physical or mental integrity of study participants

- The conduct or management of the study
- The scientific value of the study
- The quality or safety of any investigational medicinal product used in the study

For studies other than clinical trials of investigational medicinal products, addition of new research sites or changes to the local Principal Investigators listed in Part C of IRAS do not qualify as substantial amendments.

Please use the NRES Notice of Substantial Amendment form available in IRAS.

The completed Notice of Substantial Amendment form should be either signed in ink by the Chief Investigator or authorised using electronic authorisation in IRAS.

Please submit a single hard copy of the form to the REC, together with all relevant enclosures. All substantial amendments should be approved in principle by the sponsor(s) before submission.
Data Protection Act 1998

Data must:

1. Be obtained and used fairly and lawfully
2. Only be used for intended purpose
3. Be relevant and adequate (not excessive)
4. Be accurate and kept up to date
5. Not be kept for longer than necessary
6. Not violate rights of individuals
7. Be suitably safeguarded
8. Not be transferred out of the country unless DP safeguards in place
Importance of Consent in Data Collection

UK PATIENT CONSENT FORM

I confirm that I have read and understand the information sheet dated DD/MM/YYYY (version N N) for the OPTIMISE II trial. I have had the opportunity to consider the information, ask questions and have these answered satisfactorily.

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason, or my medical care or legal rights being affected.

I understand that sections of my medical notes and data collected during the trial may be looked at by the research team, the national or international co-ordinating centre, the sponsor and its representatives, the regulatory authorities, or the NHS Trust/Health Board where it is relevant to this research. I give permission for these individuals and bodies to have access to my records.

I agree for the research team to contact my primary care practitioner (GP) in order to gather basic information about my health and to inform them of my involvement in this study.

I understand that information collected about me including my name, DOB and NHS number will be shared with NHS Digital and other central NHS bodies to provide information about my health status for this research.

I understand that data collected about me for this trial will be used for study analysis. I agree for my data to be securely stored and archived by Queen Mary University of London.

I agree for my anonymised data to be shared with other researchers for further research and research publications on this topic.

I agree to take part in the OPTIMISE II trial.

Print name of participant: ____________________________ Date: ____________________________ Signature: ____________________________

Print name of person taking consent (designated responsible person): ____________________________ Date: ____________________________ Signature: ____________________________

Print name of researcher: ____________________________ Date: ____________________________ Signature: ____________________________

I understand that information collected about me including my name, DOB and NHS number will be shared with NHS Digital and other central NHS bodies to provide information about my health status for this research.

When completed, give one copy to the patient, file the original in the Investigator Site File, and place one copy in the medical notes.
Sharing of Study Materials

- Study Protocol
- Data
- PIS & Consent Forms
- Consent logs
- CRF
- Local Stores
- Centralised Repositories
- Future Network Projects?

Your Project

Study Patient → Data → Tissue → Local Stores → Centralised Repositories

Diagram showing the flow of study materials from study patient to data, tissue, local stores, and centralised repositories.
Summary

YOU NEED CONSENT AND ETHICAL APPROVAL FOR YOUR MATERIALS

• Partner the Sponsor when seeking ethical approvals for your studies

• Use DEIDENTIFIED MATERIALS wherever possible

• Create application PDFs using IRAS:
  • New projects
  • One system to apply for all the required approvals
  • Changing the study (Substantial Amendments)

• Implement robust documents to protect your study materials:
  • Standardised SOPs (Study protocol, Database, Biobank)
  • Data Usage Agreements (DUA) / Materials Transfer Agreements (MTA)
QUESTIONS?