Once completed, this protocol should not include any highlighted text.

Yellow highlighted text – instructions / guidance for investigators. These should all be deleted before finalising the document. All sample text is in ‘basic text’ style. This text of course will be altered or deleted as required while you produce the draft.

Blue highlighted text - Advisory text for deletion/rearrangement. If not relevant, sections may be deleted entirely. There may also be instances where rearrangement of the subsections within section 8 is appropriate, in order to match with the order of study processes.

**Information on Clinical Research Study Protocol Template – please read before starting**

This protocol template has been designed for clinical research studies that do not fall within the scope of the Medicines for Human use (Clinical Trials) Regulations 2004.

An algorithm is available to help you decide whether or not your study is a Clinical Trial under the regulations. This is usually, but not always, sufficiently helpful, especially regarding studies involving Healthy Volunteers. See <http://www.mhra.gov.uk/home/groups/l-unit1/documents/websiteresources/con009394.pdf>.

The template must be used by all investigators who are carrying out clinical research studies sponsored by LJMU – because the template directs investigators to include information required for LJMU to decide whether to sponsor the research.

Repetition of information throughout the protocol is not necessary; it may be useful to cross-reference other sections of the protocol to avoid repetition.

# Full/long title of the study:

Aim: To identify the study to enable retrieval from literature or internet searches. It should be immediately evident what the study is investigating and on whom to allow rapid judgment of relevance.

# Short study title/acronym

Aim: To provide a summary of the long title. It is usually the title used on information sheets and consent forms for research participants or others giving consent or assent on their behalf.

The short title should be:

* Sufficiently detailed to make clear to participants what the research is about in simple English
* If acronyms are used the full title should explain them. The proposed acronym should not drive the long title

# Date and version No:

Insert

Aim: To track changes to the document for study conduct, review, and oversight so it is clear which is the most recent document.

Version control (entered into the Footer):

• All draft versions should be numbered 0.1, 0.2 etc.

• The final version for submission should be numbered 1.0

• The changes made relative to the previous protocol version should be listed after submission

# Research reference numbers

|  |  |
| --- | --- |
| **IRAS Number** |  |
| **Sponsor reference number** |  |
| **ISRCTN number** |  |
| **REC reference number** |  |

This protocol has regard for the HRA guidance

# Signature page

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to adhere to the signed LJMU’s Sponsorship CI declaration.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

Chief Investigator:

Signature: .................................................................................................. Date: ......../……...../…….....

Name: (please print):......................................................................................................

# Sponsor statement:

Where LJMU takes on the sponsor role for protocol development oversight, the signing of the IRAS form by the sponsor will serve as confirmation of approval of this protocol.

# Confidentiality statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, HRA, host organisation, and members of the Research Ethics Committee, unless authorised to do so.

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# Key study contacts

|  |  |
| --- | --- |
| **Chief Investigator:** | Insert name and contact details, including institutional affiliation |
| **Investigators:** | Insert names of key collaborators, including institutional affiliations |
| **Sponsor:** | Liverpool John Moores University |
| **Funder:** | Insert details of organisation providing funding |
| **Chief Investigator Signature:** | The approved protocol should be signed by author(s) and/or person(s) authorised to sign the protocol |

Please declare any/no potential conflicts of interest.

# Training / CPD

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Name of investigator (add new row if required)** | **Date completed LJMU REC training** | **Date completed LJMU research integrity training** | **Date completed research governance training** | **Date completed HTA training (or NA)** | **Date completed other training (add new column if required)** |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

# Study summary

Include a brief synopsis of the study for quick reference. Complete information and, if required, add additional rows.

|  |  |  |
| --- | --- | --- |
| **Study Title** |  | |
| **Internal ref. no. / short title** |  | |
| **Proposed start date** |  | |
| **Proposed end date** |  | |
| **Countries in which the study will take place** |  | |
| **Lead NHS trust & R&D contact** |  | |
| **Study Design** |  | |
| **Study Participants** |  | |
| **Planned Sample Size** |  | |
| **Planned Study Period** |  | |
|  | **Objectives** | **Outcome Measures** |
| **Primary** |  |  |
| **Secondary** |  |  |

# Funding and support in kind

Please provide details of how the study is being funded, both internally and externally.

|  |  |
| --- | --- |
| **FUNDER(S)**  (Names and contact details of ALL organisations providing funding and/or support in kind for this study) | **FINANCIAL AND NON FINANCIALSUPPORT GIVEN** |
|  |  |
|  |  |

# Role of study sponsor and funder

Aim: To clarify the potential influence of sponsor and funders over the study

The sponsor can be defined as the company, institution, or organisation assuming overall responsibility for the initiation and management of the study, and is not necessarily the main funder. Identification of the study sponsor provides transparency and accountability.

The protocol should explicitly outline the roles and responsibilities of the sponsor(s) and any funder(s) in study design, conduct, data analysis and interpretation, manuscript writing, and dissemination of results. It is also important to state whether the sponsor(s) or funder(s) controls the final decision regarding any of these aspects of the study.

# Roles and responsibilities of study management committees/groups and individuals

Aim: To outline any committees or groups involved in study coordination and conduct.

For each committee/group the protocol should state their roles and responsibilities and degree of independence from Sponsor and Investigators. If not included in the document the protocol should state where the information on the committee/group can be found.

Patient & Public Involvement Group:

Public involvement plays an important role in study design and planning and can help reduce delays in approvals. Public involvement in study design and study documentation can help with the acceptability of a study to the public which in turn can assist with study set-up and recruitment. Ongoing involvement of the public can help understand blockages to recruitment and the acceptability and relevance of study findings.

For guidance on Patient & Public Involvement follow this link: <http://www.invo.org.uk/find-out-more/information-for-researchers/>

# Protocol contributors

Aim: To describe all the contributors to the protocol.

The protocol should:

* Explicitly outline the roles and responsibilities of the sponsor and any funders in study design, conduct, data analysis and interpretation, manuscript writing, and dissemination of results.
* It is also important to state whether the sponsor or funder controls the final decision regarding any of these aspects of the study.
* Describe in what aspects of the protocol design have patients, service users, and/or their carers, or members of the public been involved.

KEY WORDS: Insert relevant key words to describe the study; no more than 6 phrases. This may be useful for future use when searching for relevant publications e.g. Medical Subject Headings.

# Study flow chart

Aim: To give readers a schematic overview of the study

A flow diagram should be included.

Careful consideration must be given by the protocol authors to ensure that the protocol is sensibly structured and ordered to allow users of the document to follow the patient and study pathway accurately and with ease. Flow diagrams are helpful tools to guide users of the protocol through the patient and study pathway. A schedule of events can be included as an appendix to the protocol.

For study designs using less complex methods a Gantt chart or timeline of activity outlining the timing of study management is helpful.

# Abbreviations

Define all unusual or ‘technical’ terms related to the project. Add or delete as appropriate to your study. Maintain alphabetical order for ease of reference.

|  |  |
| --- | --- |
| CI | Chief Investigator |
| GCP | Good Clinical Practice |
| GP | General Practitioner |
| HRA | Health Research Authority |
| ICF | Informed Consent Form |
| LJMU REG | LJMU Research Ethics and Governance |
| NHS | National Health Service |
| NRES | National Research Ethics Service |
| PI | Principal Investigator |
| PIS | Participant/ Patient Information Sheet |
| R&D | NHS Trust R&D Department |
| REC | Research Ethics Committee |
| SOP | Standard Operating Procedure |

# Background

Aim: To place the study in the context of available evidence.

The background should be supported by appropriate references to published literature on the area of interest:

* A thorough literature review of relevant studies and analysis, new research should build on formal review of prior evidence.
* A brief description of the proposed study.
* A description of the population to be studied.

It should be written so it is easy to read and understand by someone with a basic sense of the topic who may not necessarily be an expert in the area. Some explanation of terms and concepts is likely to be beneficial

# Rationale

Aim: To explain why the research questions/aim(s) being addressed are important and why closely related questions are not being covered.

This should include:

* A clear explanation of the research question/aim(s) and the justification of the study i.e. why the question is worth asking and, through consultation with public and patient groups, why this is worthwhile to participants or wider service delivery.
* A contextual framing of the research question/aim(s) in relation to relevant policy and historical and/or literature bases.

# Research Question

Clearly worded as a question and appropriately linked to the research objectives, aims and outcomes

# Objectives and outcome measures

Quantitative research:

In quantitative research there is usually only one primary objective, the rest are secondary objectives.

The wording of the objectives should be clear, unambiguous and as specific as possible – the study will be judged on how, and how well, the objectives were satisfied.

Complete table below with all relevant information. The objectives may be phrased using neutral wording (e.g. “to explore renal patients’ perceptions of their first dialysis session”) rather than in terms of a particular direction of effect.

Please ensure these match with those stated in the synopsis and on the IRAS form.

|  |  |  |
| --- | --- | --- |
| **Objectives** | **Outcome Measures** | **Timepoint(s) of evaluation of this outcome measure (if applicable)** |
| **Primary Objective** Example: To compare the effect of treatment A versus treatment B on the levels of protein X in the blood | Describe the outcome measures and how/when they will be measured during the study.  Outcome measures should reflect the objectives. It is important that only one outcome measure is selected as it will be used to decide the overall results or ‘success’ of the study. The primary outcome measure should be measurable, clinically relevant to participants and widely accepted by the scientific and medical community.  Example: Concentration of protein X in blood samples from participants on each treatment | Example: Blood sampling at day 0 and day 28 post-treatment |
| **Secondary Objectives** Example: To assess the safety of treatment A in <insert condition/population> | As above |  |
| **Tertiary Objectives** Please add if applicable, otherwise delete this row | As Above |  |

Qualitative research

Qualitative work is usually organised according to its aims (overall purpose and research question) and objectives (questions or tasks to reach that aim). The following is taken from <http://www.erm.ecs.soton.ac.uk/theme4/aims_and_objectives.html>. The wording of the aim and objectives should be clear, unambiguous and as specific as possible – the study will be judged on how, and how well, the objectives were satisfied. Complete table below with all relevant information.

|  |  |
| --- | --- |
| **Aim/Research Questions** | **Objectives** |
| **Primary** Example:  To critically assess the relationship between the patient’s care within the NHS (by their care team) and outside the NHS (through mobile apps, online group support, voluntary sector services, etc). In other words, how do patients "transition" between different "modes" of service delivery? | Example:  Gather information about services used by patients Categorise and critically evaluate current points of connection or disjunction between services from view point of services and patients |
| **Secondary**  Example:  To explore how these "transitions" affect the work of the patients' care team | Example:  Survey/Interview care team workers about experiences of patient transitions. |

# Study design and methods of data collection and data analysis

A suitable design should be chosen to reflect the aim(s) of the study and the chosen theoretical framework. A suitable design might include ethnography, interviews, focus groups, documents, and so on. Data collection methods (including identifying source documents) should be described in detail.

* Observation- What will be observed? What resources or equipment will be used if recording observation? Who will be observing?
* In-Depth Interviews- How will the prompt guide or interview schedule be developed? Who is conducting the interviews? By telephone or in person? How are the interviews being recorded?
* Focus Groups-Who is leading the focus group? How are the focus groups being recorded?

Data analysis methods may include content analysis, the constant comparative method, framework analysis, interpretative phenomenological analysis, and so on. The methodology for analysis linked to outcome measures should be described.

The protocol should clearly describe how and by whom data will be (for example)

* Transcribed.
* Coded.
* De-identified.
* Stored/Transferred.
* Accessed.
* Archived.

Any software to be used in assisting the analysis should be specified.

The process for human tissue collection, storage, processing and analysis (to include destruction/storage after use) should be detailed, where applicable.

### Randomisation and blinding

If applicable, describe how randomisation and blinding are going to be carried out, and when (otherwise delete this section).

Describe the method of generating the allocation sequence (e.g., computer-generated random numbers), and list any factors for stratification.

Describe the mechanism of implementing the allocation sequence (e.g., telephone, sealed envelopes, automated alerts), describing any steps to conceal the sequence until interventions are assigned.

Describe who will generate the allocation sequence, who will enrol the participants and assign them to the intervention/study arm.

### Baseline assessments

Specify and describe all baseline assessments. They must reflect the objectives and outcome measures.

If there will only be one study visit, this section should be renamed ‘Study Visit’ and full details of this visit be included. The next section ‘Subsequent Visits’ can then be deleted.

### Interventions (if applicable)

Describe any intervention(s), including the name(s) of procedure/device, schedule(s), treatment period(s), if applicable.

N.B - Interventions are procedures that affect physiology or psychology and include, for example, administration of a drug, surgical procedures, or psychological therapy. Blood tests and biopsies are ‘invasive’ but are not considered interventions.

If there are no interventions, then delete this section.

### Subsequent visits

Specify when participants will be followed up and what assessments will be conducted. Specify if they are clinic visits, telephone assessments, or home visits by the study staff. Add visit numbers and window periods if applicable. Clearly number these visits.

For each visit, list appropriate assessment, and consider inclusion of the following, where appropriate. Refer to the study schedule (appendix):

* eligibility check
* assessment of outcome measures
* assessments of safety including general (e.g. physical examination), specific safety assessments (e.g. specific laboratory tests according to the applicable product information and/or population) and adverse event collection
* recording of concomitant medications

Include a flowchart for the project (here, or as an appendix), if appropriate.

### Devices (if applicable)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **4.6.1** | If this application is for a Clinical Investigation of a Medical Device please define the type of study; | | | | | | |
| a. |  | Clinical study of a non-CE marked device where commercialisation of the product is intended | | | | |
| b. |  | Clinical study of a non-CE marked device for use within the institution, where commercialisation is not intended | | | | |
| c. |  | Clinical study of one or more CE marked devices for an off-label indication | | | | |
| d. |  | Clinical study of one or more CE marked devices for a labelled indication, involving a change to standard care or randomisation between groups | | | | |
| e. |  | Clinical study of one or more CE marked devices for a labelled indication, involving no change to standard care or randomisation between groups | | | | |
| f. |  | Pre-clinical device development or performance testing | | | | |
| **4.6.2** | Please give details of device and supplier | | |  | | | |
| **4.6.3** | Has this device been approved by the Lead NHS Trust devices committee? | | | | Yes  **Please provide evidence** | | No |
| **4.6.4** | Is the Device CE marked? | | | | Yes  **Please provide evidence** | | No |
| **4.6.5** | Please provide details of who will indemnify the device; | | | | | | |
| Against harm to the patient | | |  | | | |
| Against theft or loss of the device | | |  | | | |
| **4.6.6** | Is there a maintenance contract in place? | | | | Yes  Please go to E**7** | No | |
| **4.6.7** | Please provide details of who this contract is with | | |  | | | |

### Study setting

Aim: To state where the data will be collected, explain what activities will take place in that site, and justify the choice of site and any special requirements.

The protocol should address:

* Where and how you are accessing your participants?
* How the research setting is appropriate to address the research question/aim(s)?
* If it is a multicentre or single centre study.
* If there are any site specific requirements to run the study.

Outline if there are different ‘types’ of activity being undertaken at each site (e.g. identifying or recruiting) and what the specific requirements are for each.

### Statistics and analysis

If applicable, describe the statistical methods to be employed, including timing of any planned interim analysis(es).

State the approximate number of participants required to complete (commence). Justify choice of sample size, including reflections on (or calculations of) the power of the study and clinical justification. It is the primary outcome that determines the sample size needed. Take into account any potential withdrawals.

Describe analysis of primary and secondary outcome measures. Include details as to which participant data will be used (e.g. all participants, including/excluding those that withdrew consent, or have been unblinded).

Describe method of analysis for objectives (e.g. content analysis, constant comparative method, framework analysis, interpretive phenomenological analysis) and how this is most appropriate for kind of data collected.

Include details as to what participant data will be used and any software proposed.

# Participant recruitment

### Study participants

Give an overall description of the study participants.

Qualitative research

It may not always be possible to estimate the size of a sample e.g. if you continue sampling until you reach saturation. In this case, describe how your sampling strategy will allow you to address your aim/research question.

### Inclusion criteria

Inclusion criteria should define the population the study is aiming to include. Example criteria only (amend as appropriate):

* Participant is willing and able to give informed consent for participation in the study.
* Male or Female, aged 18 years or above.
* Clinical condition: Diagnosed with required disease/severity/symptoms, any specific assessment criteria for these, or, if healthy volunteer study: be in good health.
* location
* Additional study specific criteria as required.

### Exclusion criteria

Example criteria only (amend as appropriate):

The participant may not enter the study if ANY of the following apply:

* Specify any diseases/disorders/ conditions that would preclude entry into the study.
* Additional study specific criteria as required.
* Contraindications

### Recruitment technique

Aim: To describe the selection of participants.

This section should detail the methods of selection used for example:

* At random, snowball, convenience sampling, purposive sampling?
* Where has the recruitment technique been derived from?
* What is the rationale for this recruitment strategy? The rationale should reflect the methodological and theoretical framework for the study.

### Participant identification

The following should be described in the protocol (as applicable):

* Who will identify the participants and what method will be used?
* Who will identify participants?
* What resources will be used?
* The proposed NHS and non-NHS recruitment sites
* Will any participants be recruited through Patient Identification Centres (PICs)?
* Will any participants be recruited by publicity; posters, leaflets, adverts or websites?
* Will CRNs be involved, and will it be registered on the NIHR portfolio?
* Details of the sources of identifiable personal information that will be used to identify potential participant. In the case of healthcare research on patients usually only a member of the patient’s existing clinical care team should have access to patient records without explicit consent in order to identify potential participants, check whether they meet the inclusion criteria or make the initial approach to patients. If the research proposes to use someone outside the clinical team to identify suitable participants or as first contact with the participant, the reason for this should be explained.
* The arrangements for referral if the participants are to be identified by a separate research team.
* If patient or disease registers are used to identify potential participants a brief description of the consent and confidentiality arrangements of the register should be included.

The protocol should also detail all intended payments to participants e.g. reasonable travel expenses for any visits additional to normal care.

For guidance on payments to participants please follow this link: <http://www.hra.nhs.uk/documents/2014/05/hra-guidance-payments-incentives-research-v1-0-final-2014-05-21.pdf>

### Screening and eligibility assessment

Specify the maximum duration allowed between screening and recruitment (if applicable).

Describe the screening procedures in detail, such as demographics, medical history, concomitant medication, physical examination, ECG, laboratory tests, biopsies and samples, scans.

If any screening procedures (such as blood sampling) require prior informed consent, then this section should be moved to between ‘Informed Consent’ and ‘Randomisation’.

### Informed consent

You need to specify who will take informed consent, how and when it will be taken. Informed Consent must be obtained prior to any study related procedures being undertaken.

The protocol should fully describe the process of gaining informed consent which could involve:

* discussion between the potential participant or his/her legally acceptable representative and an individual knowledgeable about the research, about the nature and objectives of the study and possible risks associated with their participation
* the presentation of written material (e.g., information leaflet and consent documents) which must be approved by the REC, local regulatory requirements and legal requirements
* the opportunity for potential participants to ask questions
* assessment of capacity. For consent to be ethical and valid in law, participants must be capable of giving consent for themselves, unless defined by law. A capable person will:
* understand the purpose and nature of the research
* understand what the research involves, its benefits (or lack of benefits), risks and burdens
* understand the alternatives to taking part
* be able to retain the information long enough to make an effective decision.
* be able to make a free choice
* be capable of making this particular decision at the time it needs to be made (though their capacity may fluctuate, and they may be capable of making some decisions but not others depending on their complexity)
* where participants are capable of consenting for themselves but are particularly susceptible to coercion, it is important to explain how their interests will be protected

For a very limited range of activities – such as some ethnographic observations – individuals in a research setting may not be deemed to be research “participants” and it may not be possible to gain consent from each individual observed. In such instances, a full explanation should be given of how the rights and privacy will be protected for those observed or otherwise involved in some way in a research activity for which it is not proposed to gain individual consent.

For further details on the ethical considerations of informed consent for research see the guidance notes available on the HRA website: <http://www.hra.nhs.uk/resources/before-you-apply/consent-and-participation/consent-and-participant-information/>

The process for withdrawal, including the subsequent impact on data and sample storage should be detailed.

Example:

The \*participant must personally sign and date the latest approved version of the Informed Consent form before any study specific procedures are performed.

Written and verbal versions of the Participant Information and Informed Consent will be presented to the participants detailing no less than: the exact nature of the study; what it will involve for the participant; the implications and constraints of the protocol; the known side effects and any risks involved in taking part. It will be clearly stated that the participant is free to withdraw from the study at any time for any reason without prejudice to future care, without affecting their legal rights, and with no obligation to give the reason for withdrawal.

The participant will be allowed as much time as wished to consider the information, and the opportunity to question the Investigator, their GP or other independent parties to decide whether they will participate in the study. Written Informed Consent will then be obtained by means of participant dated signature and dated signature of the person who presented and obtained the Informed Consent. The person who obtained the consent must be suitably qualified and experienced, and have been authorised to do so by the Chief/Principal Investigator. A copy of the signed Informed Consent will be given to the participant. The original signed form will be retained at the study site.

\*can be substituted parent/guardian or legally authorised representative, as appropriate, make sure that the term is consistent throughout the document.

### Discontinuation/withdrawal of participants from study

Example:

Each participant has the right to withdraw from the study at any time. In addition, the Investigator may discontinue a participant from the study at any time if the Investigator considers it necessary for any reason including:

delete/add as appropriate

* Pregnancy
* Ineligibility (either arising during the study or retrospectively having been overlooked at screening)
* Significant protocol deviation
* Significant non-compliance with treatment regimen or study requirements
* Withdrawal of Consent
* Loss to follow up

Specify any procedures and observations that will continue to be required until the end of the study even if the treatment has been withdrawn. Why will this be necessary?

State whether withdrawal from the study will result in exclusion of the data for that participant from analysis. In particular, consideration to audio recordings must be made. If an audio recording has already been transcribed and anonymised, would you be able to exclude their data? Where participants were part of a focus group, consider whether  an individual’s data impinges on/is directly related to that of other participants.

State whether or not withdrawn participants will be replaced.

The reason for withdrawal by researcher (and by participant, if this information is volunteered) will be recorded in a study file.

# Data management

### Access to data

Direct access will be granted to the research team, authorised representatives from the Sponsor and host institution for monitoring and/or audit of the study to ensure compliance with regulations.

### Data recording and record keeping

Describe method(s) of data collection, entry and management, including details of data management tools. Describe where, and for how long, data will be retained. Ensure compliance with the relevant Sponsor organisation’s policy.

### Sample handling

If not mentioned previously, describe the samples that will be taken from each participant (e.g. blood, urine, tissue), the volume of sample, and the frequency of sampling. Give brief details as to how the sample will be processed and stored once taken, who will have access (i.e. Study team only for this project, or will it be stored long-term for use in future ethically approved studies), and duration of storage. Provide an overview of the laboratory analyses that will be performed.

If no samples will be taken, please delete this section entirely.

# Safety reporting

Aim: To explain how Adverse Events, Adverse Reactions and Serious Adverse Events will be recorded and reported. The protocol should define and clarify what safety reporting will be undertaken and how this will be recorded

# Quality assurance procedures

Provide details of how data monitoring and other quality control measures will be performed.

Example:

The study may be monitored, or audited in accordance with the current approved protocol, GCP, relevant regulations and standard operating procedures.

# Ethical and regulatory considerations

### Declaration of Helsinki

The Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki and relevant regulations

NB. The 2013 Declaration of Helsinki provides detail on what must be included in a protocol: funding, sponsorship, affiliations and potential conflicts of interest, incentives to participate and compensation for harm.

### Assessment and management of risk

Aim: To describe a risk analysis plus risk management if the researcher were to come into information which had safeguarding implications.

* A clear explanation of any potential hazards/risks of the study.
* A clear explanation of how the hazards/risks will be minimised.
* A risk management plan for dealing with any potential risk/harm to the participant. For example whilst undertaking an interview the researchers obtain information that the participant is suicidal. What mechanisms for safeguarding the participant would be put in place? Who should the information be shared with to mitigate harm to the participant?
* A management plan for dealing with safeguarding issues for potential harm to others. For example if the participant discloses information about intention to harm others. What mechanisms for safeguarding others outside of the research would be put in place? Who should the information be shared with to mitigate harm to others?

### Participant confidentiality

The protocol should state that all investigators and study site staff must comply with the requirements of data protection legislation with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act’s core principles.

The protocol should describe the means whereby personal information is collected, kept secure, and maintained. In general, this involves:

* Data to be anonymised as soon as it is practical to do so.
* The creation of coded, depersonalised data where the participant’s identifying information is replaced by an unrelated sequence of characters.
* Secure maintenance of the data and the linking code in separate locations using encrypted digital files within password protected folders and storage media.
* Limiting access to the minimum number of individuals necessary for quality control, audit, and analysis.
* How the confidentiality of data will be preserved when the data are transmitted to sponsors and co-investigators
* How long the data will be stored for.
* Identifying the data custodian.

### Expenses and benefits

Detail all intended payments to participants and any other benefits (Declaration of Helsinki requirement).

Example:

Reasonable travel expenses for any visits additional to normal care will be reimbursed on production of receipts, or a mileage allowance provided as appropriate.

### Other ethical considerations

Include any other general and study-specific ethical considerations, e.g. involvement of vulnerable participants, or participants who are unable to consent for themselves.

For studies that could identifying abnormal or clinically significant findings consider adding something like:

In the unlikely event of finding any abnormalities or anything of clinical significance, the findings will be checked by a clinical specialist. If the specialist feels that the abnormality was medically important, they will discuss the implications with the participant and arrange for further investigations as necessary. Participants will not be informed unless the doctor considers the finding has clear implications for their current or future health. It is important to note that data collected are not carried out for diagnostic purposes, and therefore the data are not a substitute for a clinical appointment. Rather, the data are intended for research purposes only.

### Research Ethics Committee (REC) and other regulatory review & reports

Aim: to demonstrate that the study will receive ethical review and approval from the necessary regulatory bodies

The protocol should state that:

* Before the start of the study, a favourable opinion will be sought from a REC for the study protocol, informed consent forms and other relevant documents e.g. advertisements. [researchers should check if they are required to gain a favourable opinion from the UK Health Departments Research Ethics Service NHS REC or other REC approval]
* Approval will be obtained from LJMU REG (and Co-Sponsors) for any amendments to, or changes of status in the study **prior to** submission to the REC that ethically approved the study and any other regulatory authorities
* All correspondence will be retained.
* If required The protocol, informed consent form, participant information sheet and any proposed advertising material will be submitted to the HRA for written approval.

STUDIES APPROVED by NHS REC & HRA

* Annual Progress Reports will be submitted to the NHS REC which gave the favourable opinion, the HRA ([hra.approval@nhs.net](mailto:hra.approval@nhs.net)) and the Sponsor ([Sponsor@ljmu.ac.uk](mailto:Sponsor@ljmu.ac.uk)) on the anniversary of NHS REC Favourable Opinion, and annually thereafter until the End of Study Declaration has been submitted to the NHS REC which gave the favourable opinion, the HRA and the Sponsor
* Upon the completion of the study (in most cases, the date of the last visit of the last participant or the completion of any follow-up monitoring and data collection described in the protocol) an End of Study Declaration (within 90 days of the end of the study) and End of Study Report (within 12 months of the end of the study) will be submitted to the NHS REC which gave the favourable opinion and LJMU REG ([sponsor@ljmu.ac.uk](mailto:sponsor@ljmu.ac.uk))

STUDIES APPROVED by NHS REC only

* Annual Progress Reports will be submitted to the NHS REC which gave the favourable opinion and the Sponsor ([Sponsor@ljmu.ac.uk](mailto:Sponsor@ljmu.ac.uk)) on the anniversary of HRA approval, and annually thereafter until the End of Study Declaration has been submitted to the NHS REC which gave the favourable opinion and the Sponsor.
* Upon the completion of the study (in most cases, the date of the last visit of the last participant or the completion of any follow-up monitoring and data collection described in the protocol) an End of Study Declaration (within 90 days of the end of the study) and End of Study Report (within 12 months of the end of the study) will be submitted to the NHS REC which gave the favourable opinion and LJMU REG ([sponsor@ljmu.ac.uk](mailto:sponsor@ljmu.ac.uk))

STUDIES APPROVED by HRA, but not approved by a NHS REC

* Annual Progress Reports will be submitted to the HRA ([hra.approval@nhs.net](mailto:hra.approval@nhs.net)) and the Sponsor ([Sponsor@ljmu.ac.uk](mailto:Sponsor@ljmu.ac.uk)) on the anniversary of the HRA Approval, and annually thereafter until the End of Study Declaration has been submitted to the HRA and the Sponsor;
* The HRA ([hra.approval@nhs.net](mailto:hra.approval@nhs.net)) and LJMU REG ([sponsor@ljmu.ac.uk](mailto:sponsor@ljmu.ac.uk)) will be notified that the research has ended.
* Early termination or suspension of the research will be reported to all relevant review bodies and the Sponsor ([sponsor@ljmu.ac.uk](mailto:sponsor@ljmu.ac.uk)) within 15 days.

# Scientific review

Aim: to describe the scientific review process for the study

The protocol should provide details on who reviewed this study protocol e.g. the funder or an internal Trust department/committee, but not include individual names unless the person in question gives their express permission.

The National Institute Health Research (NIHR) Clinical Research Network (CRN) provide the following standard for peer review for studies:

High quality peer review - Peer review must be independent, expert, and proportionate:

a) Independent: At least two individual experts should have reviewed the study. The definition of independent used here is that the reviewers must be external to the investigators’ host institution and not involved in the study in any way. Reviewers do not need to be anonymous.

b) Expert: Reviewers should have knowledge of the relevant discipline to consider the clinical and/or service based aspects of the protocol, and/or have the expertise to assess the methodological qualitative aspects of the study.

c) Proportionate: Peer review should be commensurate with the size and complexity of the study. Large multicentre studies should have higher level (more reviewers with broader expertise and often independent review committee or board), and potentially international peer review.

Peer review may be commensurate with the minimum requirements dependent on the study type and relative risk. The Chief Investigator is responsible for satisfying themselves that the research proposal has been submitted for appropriate peer review and revised in light of that review. The below table which details the minimum requirements for peer review for different study types can be used as a guide by researchers. The Sponsor and the NHS REC may and in certain circumstances request further appropriate independent expert peer review. If research is funded by an external funder (i.e. Medical Research Council, Government department or Charitable Organisation) which has their own peer review system the minimum requirements below may not be appropriate.

|  |  |  |  |
| --- | --- | --- | --- |
| **Level 1 No Peer Review Required** – minimal risk (no patient contact) | **Level 2 Review by project supervisor** (student projects with either no or minor patient/participant involvement) | **Level 3 Review by departmental colleague** (Low-risk projects with minimal patient involvement) | **Level 4 External, independent peer review** |
| Short questionnaire studies for use among hospital staff or GPs. | Human tissue samples [anonymous to investigator] | Human tissue samples [anonymous to investigator] | Clinical trial of an investigational medicinal product |
| Questionnaires asking patients about the quality of hospital services. | Study administering questionnaires | Study administering questionnaires | Clinical trial of a medical device |
| Use of data from medical notes by clinician looking after patient. | Qualitative study | Qualitative study | Performance Evaluation of an in vitro diagnostic device |
|  | Study limited to working with data | Study limited to working with data | Other clinical trial or clinical investigation |
|  |  | Non-intimate examination techniques, e.g. blood pressure measurement. | Research Tissue Bank |
|  |  |  | Human tissue (tissue samples and data) [newly obtained, identifiable or obtained from surplus] |

# Patient & public involvement

Aim: to describe the involvement of the Public in the research

This section of the protocol should detail which aspects of the research process have actively involved, or will involve, patients, service users, and/or their carers, or members of the public in particular;

* The acceptability of the research
* Design of the research
* Management of the research
* Undertaking the research
* Analysis of results
* Dissemination of findings

Guidance on involving the public in research can be found on the INVOLVE website. <http://www.invo.org.uk/>

# Protocol compliance

Aim: to demonstrate how protocol compliance will be managed

Protocol deviations, non-compliances, or breaches are departures from the approved protocol. The protocol should state that:

Accidental protocol deviations can happen at any time. They will be adequately documented on the relevant forms and reported to the Chief Investigator and Sponsor immediately.

Deviations from the protocol which are found to frequently recur are not acceptable, will require immediate action and could potentially be classified as a serious breach.

The protocol should detail how the quality of the study will be assured, and what monitoring will take place (as applicable).

The process for reporting suspected Serious Breaches must be detailed.

# Insurance

Table 11.1

|  |  |
| --- | --- |
| **The research study includes the following:** | **Please state YES or NO to at least one.** |
| treating or preventing disease or diagnosing disease |  |
| ascertaining the existence degree of or extent of a physiological condition |  |
| assisting with or altering in any way the process of conception |  |
| investigating or participating in methods of contraception |  |
| inducing anaesthesia |  |
| otherwise preventing or interfering with the normal operation of a physiological function |  |
| None of the above |  |

If you stated ‘YES’ to ‘none of the above’ in Table 11.1, please state:

LJMU has Public Liability insurance to cover the legal liability of the University as Research Sponsor in the eventuality of harm to a research participant arising from management and design of the research by the University and the activities here are included within that coverage.

LJMU’s Public Liability and Professional Indemnity insurance policies provide an indemnity to our employees and students for their potential liability for harm to participants during the conduct of the research and the activities here are included within that coverage.

If you stated ‘No’ to ‘none of the above’ in Table 11.1, please complete Table 11.2

Table 11.2

|  |  |
| --- | --- |
| **The study is limited to the following activities and will be undertaken in the UK.** | **Please state YES or NO** |
| Questionnaires, interviews, psychological activity including CBT |  |
| Venepuncture (withdrawal of blood) |  |
| Muscle biopsy |  |
| Measurements of physiological processes including scanning |  |
| Collections of body secretions by non-invasive methods |  |
| Intake of foods or nutrients or variation of diet (other than administration of drugs). |  |

If you stated ‘YES’ in Table 11.2 - that the study is limited to the activities listed in Table 11.2, please state

LJMU has Clinical Trials insurance to cover the legal liability of the University as Research Sponsor in the eventuality of harm to a research participant arising from management and design of the research by the University and the activities here are included within that coverage.

LJMU’s Clinical Trials insurance policies provide an indemnity to our employees and students for their potential liability for harm to participants during the conduct of the research and the activities here are included within that coverage.

If you stated ‘NO’ in Table 11.2 - that the study is NOT limited to the activities listed in Table 11.2, please email the completed clinical trials insurance questionnaire, the study protocol and any other relevant material to the LJMU Insurance Officer so that cover can be arranged. Once you have received a letter confirming extension to the clinical trials insurance, please state:

LJMU has Clinical Trials insurance to cover the legal liability of the University as Research Sponsor in the eventuality of harm to a research participant arising from management and design of the research by the University and the activities here are included within that coverage.

LJMU’s Clinical Trials insurance policies provide an indemnity to our employees and students for their potential liability for harm to participants during the conduct of the research and the activities here are included within that coverage.

Please append the letter confirming extension to the clinical trials insurance to the protocol

# Financing

Include a full costing breakdown. Stipulate NHS and University costs, consumables and other non-staff pay. You need to determine what are research, NHS support and excess treatment costs. Please refer to Attributing the costs of health and social care Research & Development (AcoRD) guidance found at

([*http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\_133882*](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_133882)) Briefly these three categories are defined as;

* **Research Costs** - the costs of the R&D itself that end when the research ends. They relate to activities that are being undertaken to answer the research questions. (e.g. cost associated with screening/assessment, data collection, participant recruitment, participant follow-up, imaging, research staff, equipment, travel, etc.)
* **NHS Treatment Costs** - the patient care costs, which would continue to be incurred if the patient care service in question continued to be provided after the R&D study had stopped.
* **NHS Support Costs** - the additional patient care costs associated with the research, which would end once the R&D study in question had stopped, even if the patient care involved continued to be provided.

Please confirm whether financial approval has been sought or received from the R&I/R&D Finance Manager

|  |  |  |  |
| --- | --- | --- | --- |
| **Service (please also list other research costs for any that are not showing)** | **Grant/Cost Code** | **Total Amount to be paid to the NHS** | **Confirmation attached from the service provider** |
| Screening/assessment |  |  |  |
| Data collection |  |  |  |
| Participant recruitment |  |  |  |
| Participant follow-up |  |  |  |
| Imaging |  |  |  |
| Research Staff |  |  |  |
| Equipment |  |  |  |
| Travel |  |  |  |
| Other (please list details) |  |  |  |
| If the study is multi-site, please list sites names |  |  |  |
| Financial approval received from the R&I/R&D Finance Manager | | | Yes/No |

# Contracts and agreements

Please provide details of agreed contracts/agreements or contracts/agreements in negotiation (e.g. co-sponsorship agreements, Research site agreements (e.g. statement of activities, standard Non-Commercial Model Agreement (mNCA)), collaboration agreement, material transfer agreement, data transfer agreement, confidentiality agreements, third party agreements etc..

NHS site agreements - Clinical trials, medical device studies, research using patient data only and research using human tissue should use a Statement of Activities or a standard Non-Commercial Model Agreement (mNCA). Non-intervention studies should use a HRA statement of activity.

Please state whether there is a requirement for a human resources arrangement or research passport (honorary research contract or letter of access) for investigators who need to undertake the research within the NHS.

# Definition of end of study

The definition of end of study must be provided. In most cases the end of study will be the date of the last visit of the last participant.

Example:

The end of study is the date of the last visit / telephone follow up / home visit of the last participant.

# End of study and archiving

Clarify the definition of the end of the study and archiving arrangements, including timelines for archiving

# Access to the final study dataset

Aim: to describe who will have access to the final dataset

The protocol should:

* Identify the individuals involved in the study who will have access to the full dataset. For student research, this must include the students supervisors.
* Explicitly describe any restrictions in access for study investigators e.g. for some multicentre studies, only the steering group has access to the full study dataset in order to ensure that the overall results are not disclosed by an individual study site prior to the main publication. For student research, supervisors must not have restricted access.
* State if the study will allow site investigators to access the full dataset if a formal request describing their plans is approved by the steering group.
* If it is envisaged that that dataset will be used for secondary analysis this can only be undertaken with the consent of the participants. All patient documentation should reflect the future use of these data in research.

# Dissemination policy

Aim: to describe the dissemination policy for the study

The protocol should state:

* Who owns the data arising from the study.
* That on completion of the study, the data will be analysed and tabulated and a Final Study Report prepared.
* Where the full study report can be accessed.
* If any of the participating investigators will have rights to publish any of the study data.
* If there are any time limits or review requirements on the publications.
* Whether any funding or supporting body needs to be acknowledged within the publications and whether they have reviewed and publication rights of the data from the study.
* Whether there are any plans to notify the participants of the outcome of the study, either by provision of the publication, or via a specifically designed newsletter, presentation etc.
* If it is possible for the participant to specifically request results from their PI and when would this information be provided e.g. after the Final Study Report had been compiled or after the results had been published.
* Whether the study protocol, full study report, anonymised participant level dataset, and statistical code for generating the results will be made publicly available; and if so, describe where, the timeframe and any other conditions for access.

# Authorship eligibility guidelines and any intended use of professional writers

The publication policy should cover authorship, acknowledgements, and review procedures for scientific publications. If there is a department or institution policy, or agreement, the protocol can refer to it. Ensure that the publication policy stated here is consistent with any contract applicable to the study. Consider describing how study results may be disseminated to study participants.

Example:

The Investigators will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authors will acknowledge that the study was funded by < >. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged.

(The International Committee of Medical Journal Editors has defined authorship criteria for manuscripts submitted for publication, known as the Vancouver Protocol)

# References

Insert references used in text (in alphabetical order).

# Appendices

### Appendix 1- required documentation

List here all the local documentation you require prior to initiating a participating site (e.g. CVs of the research team, Patient Information Sheet (PIS) on headed paper etc.).

### Appendix 2 – schedule of procedures

*Optional* Alter as required, delete if not wanted

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Procedures** | **Visits (insert visit numbers as appropriate)** | | | | |
| **Visit timing**  **e.g. Day 0** | **e.g. Day 7** |  |  |  |
| **Screening** | **Baseline** |  |  |  |
| Informed consent |  |  |  |  |  |
| Demographics |  |  |  |  |  |
| Medical history |  |  |  |  |  |
| Physical examination |  |  |  |  |  |
| ECG |  |  |  |  |  |
| Laboratory tests |  |  |  |  |  |
| Eligibility assessment |  |  |  |  |  |
| Randomisation |  |  |  |  |  |
| Assessment 1 (*describe*) |  |  |  |  |  |
| Assessment 2 (*describe*) |  |  |  |  |  |
| Assessment 3 (*describe*) |  |  |  |  |  |
| Assessment 4 (*describe*) |  |  |  |  |  |
| Adverse event assessments |  |  |  |  |  |

### Appendix 3 – amendment history

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Amendment No.** | **Protocol Version No.** | **Date issued** | **Author(s) of changes** | **Details of Changes made** |
|  |  |  |  |  |

List details of all protocol amendments here whenever a new version of the protocol is produced. This is not necessary prior to initial REC submission.