This protocol template is intended as a suggestion for the protocol layout to be used for non-CTIMP studies that are sponsored or co-sponsored by The University of Edinburgh and/or Lothian Health Board. This is minimum criteria so extra information can be added in as necessary.

Some sections may not be applicable, depending on the nature of the study. Please ensure that you remove any sections which are not relevant to your study.

You should include a header/footer with short study title, version number and date.

**Highlighted** text should be replaced with study-specific details.

Text in **blue** is for guidance only and should be deleted prior to submission.

Non-CTIMP Study Protocol

**Full Title of Study**

|  |  |
| --- | --- |
| Co-Sponsors | The University of Edinburgh and/or Lothian Health Board ACCORD  Usher Building  5-7 Little France Road  Edinburgh Bioquarter-Gate 3  Edinburgh, EH16 4UX |
| Chief Investigator | Insert name and title of CI |
| Sponsor number | ACXXXX |
| REC Number | This will be provided at the time of REC submission |
| Funder |  |
| Funder Ref Number |  |
| Project registration | Studies should be registered on a publicly accessible register where possible. |
| Version Number and Date | Version number and date should be entered here (and should correspond with header). Please refer to SOP QA008 Document Version Control for more details. |

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LIST OF ABBREVIATIONS

This is not an exhaustive list.

Any additional abbreviations used within the protocol must also be added here.

|  |  |
| --- | --- |
| **ACCORD** | Academic and Clinical Central Office for Research & Development - Joint office for The University of Edinburgh and Lothian Health Board |
| **CI** | Chief Investigator |
| **CRF** | Case Report Form |
| **GCP** | Good Clinical Practice |
| **ICH** | International Conference on Harmonisation |
| **PI** | Principal Investigator |
| **QA** | Quality Assurance |
| **REC** | Research Ethics Committee |
| **SOP** | Standard Operating Procedure |

# INTRODUCTION

## BACKGROUND

Should include:

* Reviews of previous studies.
* Disease particulars.
* Disease incidence.
* Current treatment options.
* Risks and benefits.

## RATIONALE FOR STUDY

A clear explanation of the research questions, hypothesis and justification of the study is required here, including.

* An explanation of why the study is appropriate, benefits to participants, health services, relevance to current policies etc.
* Description of the indication, its diagnosis, incidence, current treatments, their limitations etc.
* Description of the treatment/procedure under investigation.
* Statement of what would be a worthwhile improvement in study outcomes and what evidence there is that the treatment/procedure under investigation may achieve this.

# STUDY OBJECTIVES

## OBJECTIVES

### Primary Objective

Detail the primary objective.

### Secondary Objectives

Detail the secondary objectives.

## ENDPOINTS

### Primary Endpoint

* Detail the primary endpoint.

### Secondary Endpoints

* Detail the secondary endpoint.

# STUDY DESIGN

* Type of and length of study.
* consider a schematic diagram of the study design.
* duration of participant involvement.
* study setting.

# STUDY POPULATION

## NUMBER OF PARTICIPANTS

* Consider number of participants, participant population, number of sites involved, length of recruitment period.

## INCLUSION CRITERIA

* Detail participant inclusion criteria.

## EXCLUSION CRITERIA

* Detail participant exclusion criteria.

## CO-ENROLMENT

Please refer to ACCORD Co-enrolment Policy (POL008 Co-enrolment Policy)

Detail the policy towards co-enrolment. If co-enrolment will not be allowed in any circumstances, this should be stated. If co-enrolment will be allowed, details of the nature of studies to which co-enrolment will be permitted will be given. Typical details include: interventional/non-interventional studies; nature of any intervention and; study population. Furthermore, details of how co-enrolment will be managed and recorded will be provided.

In addition, when considering permitting co-enrolment, investigators should be mindful of the potential burden upon participants, their families and research staff.

# PARTICIPANT SELECTION AND ENROLMENT

## IDENTIFYING PARTICIPANTS

Describe how potential participants will be identified. This information must correspond with information provided on the ethics application.

Who will identify potential participants? Typically only a member of the participant’s direct care team can have access to their medical records/data prior to consent being given, to check if they meet inclusion criteria.

* How will first approach be made and by whom? If the study proposes to use individuals outside of the usual clinical care team to identify potential participants or make the first approach, the reason for this should be documented.
* Detail any registries to be used e.g. SHARE database
* Consider where participants will be recruited from, refer to POL011 – promoting diversity and inclusion in health-related research studies
* How will the PIS be given to potential participants e.g. at clinic appointment/post/email

## CONSENTING PARTICIPANTS

* How long will participants be permitted to consider the participant information sheet before participating in the study (i.e. from the time the PIS is provided)?
* Who will take informed consent from the participants. Is e-consent intended to be used, if yes please specify the name of the system and vendor who manages it?

### Withdrawal of Study Participants

Participants are free to withdraw from the study at any point or a participant can be withdrawn by the Investigator. If withdrawal occurs, the primary reason for withdrawal will be documented in the participant’s case report form if possible. The participant will have the option of withdrawal from:

(i) all aspects of the study but continued use of data collected up to that point. To safeguard rights, the minimum personally-identifiable information possible will be collected.

(ii) all aspects of the trial including data collected up to that point where it is possible to delete this data e.g. this data will not be used in the final data analysis. To safeguard rights, the minimum personally identifiable information possible will be retained e.g. consent form.

Detail reasons and procedures for a study participant stopping early i.e. stopping rules and discontinuation criteria.

# STUDY ASSESSMENTS

## STUDY ASSESSMENTS

* Describe all study procedures and assessments. Indicate the time points of all assessments and ensure that they are broken down as per visit number if appropriate for clarity. A table of assessments (like the one below) would be useful here.

| **Assessment** | **Screening** | **Day 1**  **baseline** | **Day 2** | **Day 3** | **30 days** | **90 days** | **1 year** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Assessment of Eligibility Criteria | ☒ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Written informed consent | ☒ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Demographic data, contact details | ☒ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Weight | ☒ | ☒ | ☐ | ☐ | ☒ | ☒ | ☒ |
| Blood sample | ☒ | ☒ | ☒ | ☒ | ☒ | ☒ | ☒ |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |

## LONG TERM FOLLOW UP ASSESSMENTS

* The protocol should describe the long term follow up period including the frequency of follow up visits, duration of follow up period and any assessments that will be carried out.
* Include details of any long term data linkage if applicable

## INCIDENTAL FINDINGS

* If there is a risk of incidental findings then the process for dealing with these should be documented.

## STORAGE AND ANALYSIS OF SAMPLES

This section should describe the procedure for dealing with biological samples, if applicable to the study. The section should include:

* Sample types.
* Volume of samples.
* Arrangements for storage (including location) and analysis (e.g. where are samples going to be analysed).
* Will samples be shipped from site?
* For international study settings: Will samples be shipped from local site to a 3rd party, or to other institution/laboratory/company, or to a UK-based institution?
* Will samples be destroyed at the end of the study?
* Will consent be sought for long term storage of samples?
* Whether the sample analysis is critical to the conduct of the study, i.e. is necessary to determine eligibility and/or relates to primary/secondary endpoint data and objectives (e.g. specific mutations associated with eligibility assessments).
* Whether the sample analysis is not critical to the conduct of the study, i.e. relates to tertiary/exploratory endpoint data and objectives.

This information must also be detailed within the PIS/Consent form.

DNA/genome/exome wide analysis must be explicitly consented for by participants.

# DATA COLLECTION

The UK General Data Protection Regulation (GDPR) requires appropriate technical and organisational measures to be in place to implement the data protection principles effectively and safeguard individual rights. This is ‘data protection by design and by default’. In essence, this means you have to integrate or ‘bake in’ data protection into your processing activities and business practices, from the design stage right through the lifecycle.

Detail data to be collected, including:

* Time points for collection (e.g. baseline, during treatment, follow up).
* Who will collect the data.
* Details of any standardised tools to be used (e.g. pain score, questionnaires).
* Describe any methods to maximise completeness of data (e.g. telephoning participants who have not returned questionnaires).
* How will data be recorded? eCRF/pCRF?
* Describe any audio / video recordings and where these will be stored
* If using online methods of collecting data e.g. online survey, what platform will be used
* Describe the use of any transcription services.

## SOURCE DATA DOCUMENTATION

Source data is defined as all information in original records and certified copies of original records or clinical findings, observations, or other activities in a clinical study necessary for the reconstruction and evaluation of the study. Source data are contained in source documents.

Source documents are original documents, data and records where source data are recorded for the first time.

* The source must be detailed here e.g. questionnaire, medical notes, electronic data collection procedures.
* Where the case report form is a source document, source data captured in the CRF must be detailed within this section.
* Where external data is supplied by a third-party, and the third-party stipulate conditions for the security and management of data on the infrastructure to be used, confirmation of the infrastructure to be used and how it meets the third-party conditions should be detailed here and detailed in a contract as appropriate.

## CASE REPORT FORMS

This section should provide information regarding the case report forms to be used, including the type of case report forms (i.e. paper and/or electronic). If electronic case report forms are to be used with personal data, this section must show how the eCRF will provide data protection by design and default, including encryption of data while it is being stored (at rest) and encryption while it is being entered or transferred into the eCRF.

# DATA MANAGEMENT

## PERSONAL DATA

Describe how the data will meet the ‘data protection by design and default’ principles of the UK GDPR legislation at every stage of the Data Information Flow. This may require explanation of the infrastructure and systems that will be used to manage the data, and how they are secured at each stage of the flow.

The following personal data will be collected as part of the research:

Here you should detail what personal identifiable data (e.g. name, CHI number, other unique numeric identifiers, location data, online identifiers (including IP address, cookies), one or more specific identifiers relating to the physical, physiological, genetic, biometric, mental, economic, cultural or social identity of a participant.

## DATA INFORMATION FLOW

Describe the collection, use and deletion of personal data here. It could be useful to provide a list of the IT to be used, how data is secured and insert a flow diagram here.

## DATA STORAGE

Describe where the data will be stored e.g. paper/electronic (if electronic, name organisation and country where data will be hosted). You should distinguish between personal identifiable data and pseudonymised data.

Refer to [guidance](https://www.ed.ac.uk/information-services/research-support/research-data-service/guidance) from the UoE Research Data Service, in particular [Quick Guide 3: Data Storage](https://libraryblogs.is.ed.ac.uk/datablog/files/2019/10/Quick-Guide-3-DATA-STORAGE-OPTIONS-v1.4.pdf) and the [flowchart](https://www.ed.ac.uk/files/atoms/files/rds_flowchart_-_20170608_-_dmd_-_v7.pdf) for data management before, during and after your research.

Personal identifiable data will be digitally stored by the research team using detail location (organisation, country) of all systems involved in the collection, transfer and storage of personal data, and who will have access to it for which purposes.

Personal data (pseudanonymised) will be physically stored by the research team at detail location, organisation, country of data storage, who will have access to personal data and where the code break/key will be kept

Anonymised data will be physically stored by the research team at detail location.

## DATA RETENTION

This section should describe the duration for which paper and electronic trial records will be retained following the end of the trial.

All study documentation will be kept for a minimum of 3 years from the protocol defined end of study point. When the minimum retention period has elapsed, study documentation will be destroyed with permission from the Sponsor.

Refer to [guidance](https://www.ed.ac.uk/information-services/research-support/research-data-service/guidance) from the UoE Research Data Service and the [flowchart](https://www.ed.ac.uk/files/atoms/files/rds_flowchart_-_20170608_-_dmd_-_v7.pdf) for data management before, during and after your research:

Typically, personal data should be stored in a suitable repository e.g. DataStore/[DataVault](https://www.ed.ac.uk/information-services/research-support/research-data-service/after/datavault/why-use-datavault).

Personal identifiable data will be stored for detail duration of personal data retention.

Personal data (pseudonymised will be stored for detail duration of personal data retention.

Anonymous data will be stored for detail duration of personal data retention

## DISPOSAL OF DATA

* How will the data be deleted or made anonymous once the retention period is over?
* Refer to [guidance](https://www.ed.ac.uk/information-services/research-support/research-data-service/guidance) from the UoE Research Data Service.

## EXTERNAL TRANSFER OF DATA

Please detail here if there is an intention for any personal identifiable data to be transferred/stored out with NHS Lothian, e.g. for transcription services, eCRF/database. An NHS Lothian IT security risk assessment for securely transferring personal identifiable data outside of NHS Lothian will be required by NHS Lothian Information Governance. This may also be required if pseudonymised personal data is be shared with organisations out with the UK/EU depending on GDPR adequacy arrangements i.e. transfer of any personal data out with NHS Lothian should be described in the protocol and the PIS.

Data collected or generated by the study (including personal data) will not be transferred to any external individuals or organisations outside the sponsoring organisation(s) without participant consent, appropriate approvals (where applicable) and a data sharing agreement.

Where it is known that data will be shared, this should be explicit in the PIS e.g. what data, with whom (organisation, country).

## DATA CONTROLLER

A data controller is an organisation that determines the purposes for which, and the manner in which, any personal data are processed.

The University of Edinburgh and NHS Lothian are joint data controllers along with any other entities involved in delivering the study that may be a data controller in accordance with applicable laws (e.g. the site).

## DATA BREACHES

Any data breaches will be reported to the University of Edinburgh ([dpo@ed.ac.uk](mailto:dpo@ed.ac.uk)) and NHS Lothian ([Lothian.DPO@nhs.scot](mailto:Lothian.DPO@nhs.scot)) Data Protection Officers who will onward report to the relevant authority according to the appropriate timelines if required.

Please ensure you have read the [minimum and required reading](https://www.ed.ac.uk/infosec/information-protection-policies/information-security-required-reading) setting out ground rules to be complied with for incident management and adhere to the Information Security Standard for Incident Management <https://www.ed.ac.uk/infosec/information-protection-policies/information-security-required-reading>.

# STATISTICS AND DATA ANALYSIS

## SAMPLE SIZE CALCULATION

* Add in details of sample size calculation

Detail the sample size, precision or power calculation, dropout rates, relevant assumptions and justifications. Comment on an estimate of the recruitment period with justification that the required sample size will be achievable.

## PROPOSED ANALYSES

* Summary measures to be reported.
* Method of analysis.
* Plans for handling missing, unused and spurious data, non-compliers and withdrawals.
* Plans for pre-defined subgroup analyses.
* Statement regarding use of intention to treat analysis.
* Details of any interim analysis.

# ADVERSE EVENTS

Consider risk level for this study: although a non-CTIMP, should the protocol provide details of how adverse events will be dealt with/reported? ACCORD will provide further advice.

# OVERSIGHT ARRANGEMENTS

## INSPECTION OF RECORDS

Investigators and institutions involved in the study will permit study related monitoring and audits on behalf of the Sponsor, REC review, and regulatory inspection(s). In the event of audit or monitoring, the Investigator agrees to allow the representatives of the Sponsor direct access to all study records and source documentation. In the event of regulatory inspection, the Investigator agrees to allow inspectors direct access to all study records and source documentation.

## STUDY MONITORING AND AUDIT

The ACCORD Sponsor Representative will assess the study to determine if a study specific risk assessment is required.

If required, a study specific risk assessment will be performed by representatives of the Sponsor(s), ACCORD monitors and the QA group, in accordance with ACCORD governance and sponsorship SOPs. Input will be sought from the Chief Investigator or designee. The outcomes of the risk assessment will form the basis of the monitoring plans and audit plans.

If considered necessary, ACCORD clinical trial monitors, or designees, will perform monitoring activities in accordance with the study monitoring plan. This will involve on-site visits and remote monitoring activities as necessary. ACCORD QA personnel, or designees, will perform study audits in accordance with the study audit plan. This will involve investigator site audits, study management audits and facility (including 3rd parties) audits as necessary (delete where not required).

# GOOD CLINICAL PRACTICE

## ETHICAL CONDUCT

The study will be conducted in accordance with the principles of the International Conference on Harmonisation Tripartite Guideline for Good Clinical Practice (ICH GCP).

Before the study can commence, all necessary approvals will be obtained and any conditions of approvals will be met.

## INVESTIGATOR RESPONSIBILITIES

The Investigator is responsible for the overall conduct of the study at the site and compliance with the protocol and any protocol amendments. In accordance with the principles of ICH GCP, the following areas listed in this section are also the responsibility of the Investigator. Responsibilities may be delegated to an appropriate member of study site staff.

Delegated tasks must be documented on a Delegation Log and signed by all those named on the list prior to undertaking applicable study-related procedures.

### Informed Consent

The Investigator is responsible for ensuring informed consent is obtained before any study specific procedures are carried out. The decision of a participant to participate in clinical research is voluntary and should be based on a clear understanding of what is involved.

Participants must receive adequate oral and written information – appropriate Participant Information and Informed Consent Forms will be provided. The oral explanation to the participant will be performed by the Investigator or qualified delegated person, and must cover all the elements specified in the Participant Information Sheet and Consent Form.

The participant must be given every opportunity to clarify any points they do not understand and, if necessary, ask for more information. The participant must be given sufficient time to consider the information provided. It should be emphasised that the participant may withdraw their consent to participate at any time without loss of benefits to which they otherwise would be entitled.

The participant will be informed and agree to their medical records being inspected by regulatory authorities and representatives of the Sponsor(s) if applicable.

The Investigator or delegated member of the study team and the participant will sign and date the Informed Consent Form(s) to confirm that consent has been obtained. The original will be signed in the Investigator Site File (ISF). The participant will receive a copy of the signed consent form and a copy will be filed in the participant’s medical notes.

### Study Site Staff

The Investigator must be familiar with the protocol and the study requirements. It is the Investigator’s responsibility to ensure that all staff assisting with the study are adequately informed about the protocol and their study related duties.

### Data Recording

The Principal Investigator is responsible for the quality of the data recorded in the CRF at each Investigator Site.

### Investigator Documentation

The Principal Investigator will ensure that the required documentation is available in local Investigator Site files (ISFs).

### GCP Training

For non-CTIMP (i.e. non-drug) studies all researchers are encouraged to undertake GCP training in order to understand the principles of GCP. This is not a mandatory requirement unless deemed so by the Sponsor. GCP training status for all investigators should be indicated in their respective CVs.

### Data Protection Training

All University of Edinburgh employed researchers and study staff will complete the [Data Protection Training](https://www.ed.ac.uk/data-protection/training-events) through Learn.

NHS Lothian employed researchers and study staff will comply with NHS Lothian mandatory Information Governance Data Protection training..

Non-NHS Lothian staff that have access to NHS Lothian systems will familiarise themselves and abide by all NHS Lothian IT policies, as well as employer policies

### Information Security Training

All University of Edinburgh employed researchers, students and study staff will complete the [Information Security Essentials modules](https://www.ed.ac.uk/information-services/help-consultancy/is-skills/catalogue/capability-wellbeing/info-security-essentials)  and will have read the [minimum and required reading](https://www.ed.ac.uk/infosec/information-protection-policies/information-security-required-reading) setting out ground rules to be complied with.

NHS Lothian employed researchers and study staff will comply with NHS Lothian mandatory Information Governance IT Security training.

Non-NHS Lothian staff that have access to NHS Lothian systems will familiarise themselves and abide by all NHS Lothian IT policies, as well as employer policies.

### Confidentiality

All laboratory specimens, evaluation forms, reports, and other records must be identified in a manner designed to maintain participant confidentiality. All records must be kept in a secure storage area with limited access. Clinical information will not be released without the written permission of the participant. The Investigator and study site staff involved with this study may not disclose or use for any purpose other than performance of the study, any data, record, or other unpublished information, which is confidential or identifiable, and has been disclosed to those individuals for the purpose of the study. Prior written agreement from the Sponsor or its designee must be obtained for the disclosure of any said confidential information to other parties.

### Data Protection

All Investigators and study site staff involved with this study must comply with the requirements of the appropriate data protection legislation (including the UK General Data Protection Regulation legislation and Data Protection Act) with regard to the collection, storage, processing and disclosure of personal information.

Computers used to collate the data will have limited access measures via user names and passwords.

Published results will not contain any personal data that could allow identification of individual participants.

# STUDY CONDUCT RESPONSIBILITIES

## PROTOCOL AMENDMENTS

Any changes in research activity, except those necessary to remove an apparent, immediate hazard to the participant in the case of an urgent safety measure, must be reviewed and approved by the Chief Investigator.

Proposed amendments will be submitted to the Sponsor for classification, review and authorisation.

Amendments to the protocol must be submitted in writing to the appropriate REC and local R&D for approval prior to implementation and prior to participants being enrolled into the amended protocol.

## MANAGEMENT OF PROTOCOL NON-COMPLIANCE

### Protocol Waivers

Prospective protocol deviations, i.e. protocol waivers, will not be approved by the Sponsors and therefore will not be implemented, except where necessary to eliminate an immediate hazard to study participants. If this necessitates a subsequent protocol amendment, this should be submitted to the REC and local R&D for review and approval if appropriate.

### Management of Deviations and Violations

### Definitions

* **Deviation** - Any change, divergence, or departure from the study design, procedures defined in the protocol or GCP that does not significantly affect a subjects rights, safety, or well-being, or study outcomes.
* **Violation** - A deviation that may potentially significantly impact the completeness, accuracy, and/or reliability of the study data or that may significantly affect a subject’s rights, safety, or well-being.

Protocol deviations will be recorded in a protocol deviation log and logs will be submitted to the Sponsors every 3 months. Each protocol violation will be reported to the Sponsor within 3 days of becoming aware of the violation.

Deviation logs will be maintained for each site in multi-centre studies.

Deviation logs/violation forms will be transmitted via email to [QA@accord.scot](mailto:QA@accord.scot). Only forms in a pdf format will be accepted by ACCORD via email. Forms may also be submitted by hand to the office. Where missing information has not been sent to ACCORD after an initial report, ACCORD will contact the Investigator and request the missing information. The Investigator must respond to these requests in a timely manner.

An alternative frequency of deviation log submission to the Sponsors may be agreed in writing with the Sponsors.

## SERIOUS BREACH REQUIREMENTS

A serious breach is a breach which is likely to effect to a significant degree:

(a) the safety or physical or mental integrity of the participants of the study; or

(b) the scientific value of the study.

If a potential serious breach is identified by the Chief investigator, Principal Investigator or delegates, the Sponsor(s) ([qa@accord.scot](mailto:qa@accord.scot)) must be notified within 24 hours. It is the responsibility of the Sponsor(s) to assess the impact of the breach on the scientific value of the study, to determine whether the incident constitutes a serious breach and report to research ethics committees as necessary.

## END OF STUDY

The end of study is defined as the last participant’s last visit.

The Investigators and/or the Sponsor(s) have the right at any time to terminate the study for clinical or administrative reasons.

The end of the study will be reported to the REC, and R&D Office(s) and Sponsor(s) within 90 days, or 15 days if the study is terminated prematurely. The Investigators will inform participants of the premature study closure and ensure that the appropriate follow up is arranged for all participants involved. End of study notification will be reported to the Sponsor(s) via email to [resgov@accord.scot](mailto:researchgovernance@ed.ac.uk).

A summary report of the study will be provided to the REC and Sponsors within 1 year of the end of the study.

If the study has been registered on publicly accessible register then this should be updated and results posted where applicable.

## CONTINUATION OF TREATMENT FOLLOWING THE END OF STUDY

Detail arrangements for continuation of the intervention beyond the end of the study. If none, provide justification.

## INSURANCE AND INDEMNITY

The Sponsor(s) are responsible for ensuring proper provision has been made for insurance or indemnity to cover their liability and the liability of the Chief Investigator and staff.

The following arrangements are in place to fulfil the Sponsor(s)' responsibilities:

* The Protocol has been designed by the Chief Investigator and researchers employed by the University and collaborators. The University has insurance in place (which includes no-fault compensation) for negligent harm caused by poor protocol design by the Chief Investigator and researchers employed by the University.
* Sites participating in the study will be liable for clinical negligence and other negligent harm to individuals taking part in the study and covered by the duty of care owed to them by the sites concerned. The Sponsor(s) require individual sites participating in the study to arrange for their own insurance or indemnity in respect of these liabilities.
* Sites which are part of the United Kingdom's National Health Service will have the benefit of NHS Indemnity.
* Sites out with the United Kingdom will be responsible for arranging their own indemnity or insurance for their participation in the study, as well as for compliance with local law applicable to their participation in the study.

# AUTHORSHIP POLICY

Ownership of the data arising from this study resides with the study team.

## DATA SHARING

Detail procedures for data sharing (if any) – may be funder specific

# REFERENCES