UNIVERSITY OF BIRMINGHAM

Clinical Trial Management

UoB QMS reference number: UoB-CLN-SOP-001

Purpose:

The purpose of this procedure is to explain how clinical trials should be conducted within the University of Birmingham (UoB). It maps out all aspects of clinical trial management, and explains how different departments within the UoB work together.

Scope:

All UoB staff members involved in clinical trials sponsored and managed by the UoB should follow this procedure, focussing on those aspects of this procedure that cover their day to day work. Where clinical trials are (co-)sponsored and/or (partially) managed by another institution, this procedure should be followed as far as possible.

Implementation plan:

The initial implementation period has been set to 6 months to allow for the procedure to be embedded in the UoB structures, with the note that over this period of time all staff members should start to follow this procedure where possible.

Thereafter -

- ☐ For new trials identified prior to any grant application, follow the processes from 'Idea' onwards.
- ☐ For trials in the phase of grant application, follow the processes from 'award receipt & distribution' onwards, and follow any previous processes as far as possible.
- ☐ For trials in their set up phase, ensure any regulatory requirements are met, follow the processes 'throughout the project' and onwards, and follow any previous processes as far as possible.
- ☐ For ongoing trials and trials in the closure phase, ensure any regulatory requirements are met, follow the process 'Amendments', and supply information to Sponsor as requested on the process map 'throughout the project'.

Date of implementation:

01-Dec-2012

Abbreviations and Definitions:

Term	Description
ARSAC	Administration of Radioactive Substances Advisory Committee
Chief Investigator	Chief Investigator means: (a) in relation to a clinical trial conducted at a single trial site, the investigator for that site (b) in relation to a clinical trial conducted at more than one trial site, the authorised health care professional (doctor, dentist, nurse or pharmacist), whether or not he is an investigator at any particular site, who takes primary responsibility for the conduct of the trial
CI	See 'Chief Investigator'
Clinical research	Any health related research on humans.
Clinical study	Any health related research study on humans. This includes: • 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)
Clinical trial	**For clinical trials using an Investigational Medicinal Product:** Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy. **For all other clinical trials:** A set of procedures in medical research and drug development that are conducted to allow safety (or more specifically, information about adverse drug reactions and adverse effects of other treatments) and efficacy data to be collected for health interventions. Examples include devices, surgery and radiotherapy trials.
CTIMP	A Clinical Trial of an Investigational Medicinal Product
CTOC	Clinical Trials Oversight Committee
CTU	Clinical Trials Unit
DSUR	Development Safety Update Report
ERN	Ethics Registration Number; an internal number assigned to a project following completion of a UoB Ethical Review of Research Self Assessment Form
IRAS	Integrated Research Application System; set up to streamline the research application process in the UK
IRMER	The Ionising Radiation (Medical Exposure) Regulations 2000
LES	College of Life and Environmental Sciences

MDS	College of Medical and Dental Sciences
NIHR	National Institute for Health Research
NIHR CSP	NIHR Coordinated System for gaining NHS Permission
PF2 / PF3 Form	Forms used by the Research Governance Team for request for Sponsorship
Pink Form	College of Medical and Dental Sciences Application for Research Grants and Contracts Approval Form; this is a college specific form that facilitates the review, approval and tracking of any new grant proposals and is commonly known as 'Pink Form'. *Note: for trials set up in LES an equivalent form (or forms) are set up to ensure the same information is captured and reviewed. At the time of writing, the actual name of this form (or forms) is not yet known; please liaise with the LES Research Support Partner to obtain the latest information.*
PI	See 'Principal Investigator'
Principal Investigator	The investigator is responsible for the conduct of a clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the leader responsible for the team and may be called the Principal Investigator.
R&KT Office	Research & Knowledge Transfer Office
RA1 Form	Research Activation Form used by the Research Finance Office to document that an account has been set up and listing the account code.
REC	Research Ethics Committee
RG Number	Research Governance Number; the number that the Research Governance Team will assign to any project put forward for UoB Sponsorship
Research Facilitator	The Research Facilitator acts as the central contact point in project development, initiation and conduct. The Research Facilitator liaises with relevant contacts e.g. Finance Office, peer review and any other internal or external bodies which may be able to assist. Research Facilitators work closely with Head of School to ensure compliance with the UoB Code of Practice for research and other regulations especially with regard to more junior researchers or those working outside of a Clinical Trials Unit. Different Colleges may use different job titles for the same role.
SAE	Serious Adverse Event
SAF	UoB Ethical Review of Research Self Assessment Form
SUSAR	Suspected Unexpected Serious Adverse Reaction
UKCRN	UK Clinical Research Network
UoB	University of Birmingham
UoB CTU	One of the three UKCRN fully registered University of Birmingham Clinical Trials Units, i.e. Cancer Research UK Clinical Trials Unit (CRCTU), Birmingham Clinical Trials Unit (BCTU) or the Primary Care Clinical Research and Trials Unit (PC-CRTU).
UoB Lead	The UoB Lead is a (senior) person in the UoB who takes responsibility for the conduct and delivery of those parts of the study which are either carried out at or managed/overseen by the UoB. Normally this would be an academic researcher, but in some cases it may be a senior member of a UKCRC registered UoB CTU.

See also the Glossary of Terms.

Responsibilities:

Given the complexity of this procedure, a colour coding has been used to identify individuals/teams and their role in the procedure. Below is a summary of their responsibilities and the colour coding used for the individual/team.

Chief Investigator or delegate

The Chief Investigator (CI) is responsible for the initiation, conduct and completion of the clinical trial. They may however delegate tasks. Delegates may include trial team members, who may be based in a Clinical Trials Unit (CTU). Where the CI does not hold a contract with the UoB and the UoB takes on trial management, it would be expected they work together with a UoB Lead, who may also be delegated certain tasks.

Specific tasks are indicated in black.

Research Officer, Research Facilitator, Research Support Partner, College of Medical and Dental Sciences Research & Knowledge Transfer Office, Clinical Research Compliance Team

The College of Medical and Dental Sciences (MDS) Research & Knowledge Transfer (R&KT) Office provides practical support and guidance to researchers. Members of the office include the Research Officer (a central administrative post) and the Research Facilitators (who work closely together with the researchers). In the College of Life and Environmental Sciences (LES) the post of Research Officer is covered by the Research Support Partner, who also fulfils the role of Research Facilitator, alongside other LES Research Facilitators.

The Clinical Research Compliance Team also forms part of the MDS R&KT Office, and is responsible for developing an infrastructure for researchers involved in clinical trials. In addition, the team takes on responsibilities relating to Sponsor oversight such as audits and quality checks.

Specific tasks are indicated in red.

Research Governance Team

The Research Governance Team is responsible for Sponsorship decisions and confirmation of Sponsorship on behalf of the UoB, signing-off any applications for approval/authorisation as Sponsor representative, issuing Trial Specific Template Site Agreements, and for maintaining Sponsor oversight.

Specific tasks are indicated in light blue.

Research Finance Office

The Research Finance Office is responsible for providing staff costs and advice on funder rules for research applications, setting up trial accounts, and all other pre- and post award financial administration.

Specific tasks are indicated in purple.

Insurance Administrator / Insurance Office

The Insurance Administrator is responsible for processing any requests for clinical trial insurance, in liaison with the Insurance Office. The Insurance Office is responsible for the complete insurance portfolio within the UoB.

Specific tasks are indicated in dark green.

Research Ethics Team

The Research Ethics team is responsible for the operation of the University's internal ethical review processes, including the administration of the UoB Ethical Review of Research Self Assessment Form (SAF) and the co-ordination of applications requiring further review by an internal ethical review committee.

Specific tasks are indicated in dark blue.

Research Contracts Team

The Research Contracts team is responsible for drafting, reviewing and negotiating contracts with funders and other collaborating parties, ensuring that the University and individual researchers are protected from contractual risks and liabilities. The team is also responsible for approving the final agreement for signing by an authorised signatory (usually the Deputy Director of Finance or Head of Research Support Group).

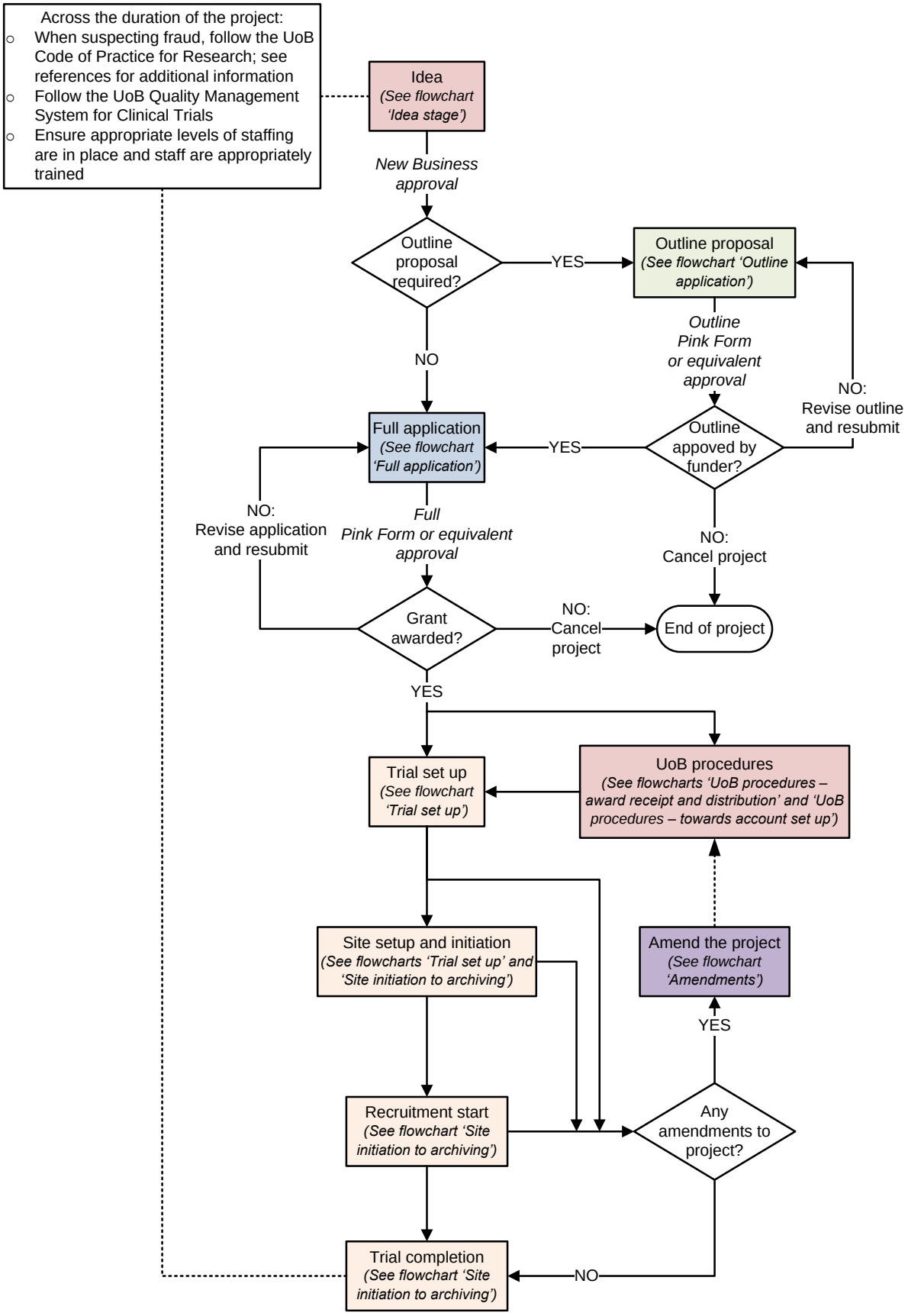
Specific tasks are indicated in orange.

Procedure:

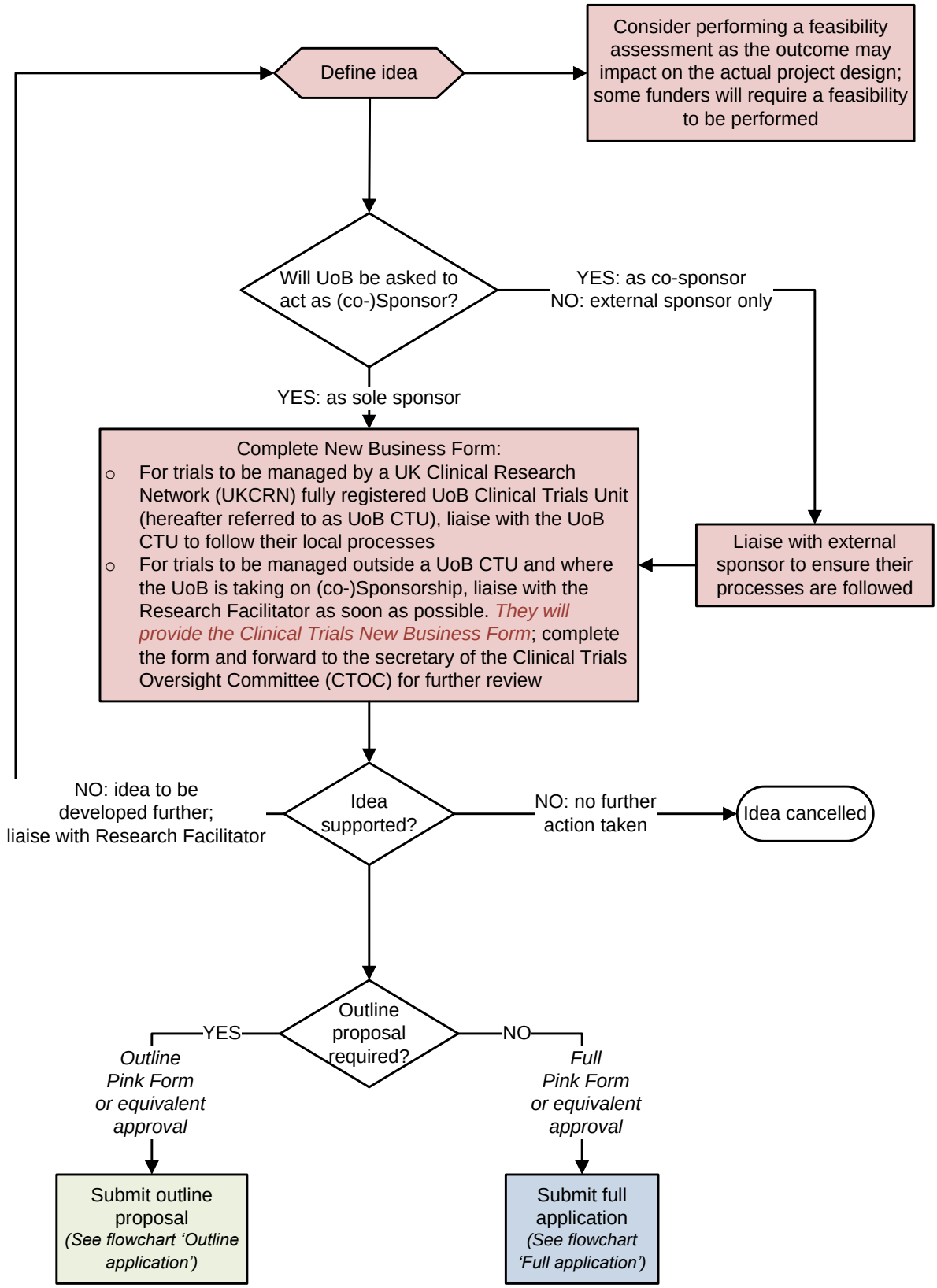
Explanatory notes

- ☐ The procedure consists of several flowcharts. The first flowchart is a summary; with each coloured box being detailed further in subsequent flowcharts.
- ☐ Throughout the document references are made to the Pink Form or equivalent. For trials set up in MDS a College of Medical and Dental Sciences Application for Research Grants and Contracts Approval Form must be completed; this is commonly known as the Pink Form. For trials set up in LES an equivalent form (or forms) is set up to ensure the same information is captured and reviewed. At the time of writing, the actual names of this form (or forms) is not yet known; please liaise with the LES Research Support Partner to obtain the latest information.
- ☐ The flowcharts contain a few timelines. These are put in place where teams/offices within the UoB are responsible for undertaking specific tasks in the procedure; the timeline will give the CI and their team clarity as to when they can expect results.
- ☐ Where (aspects of) this procedure are not followed, this has to be justified in writing and the justification kept in the Trial Master File.

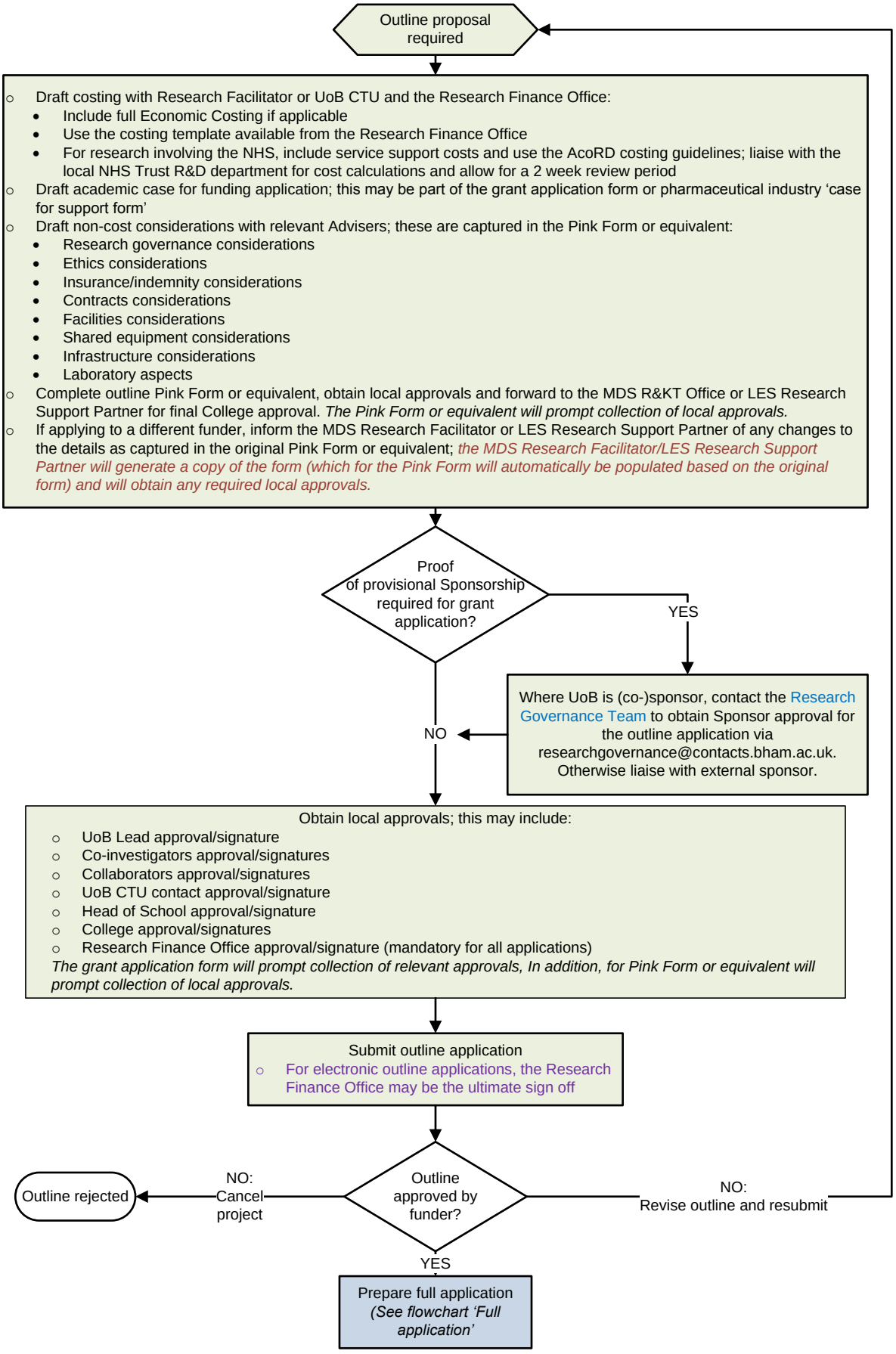
Procedure summary



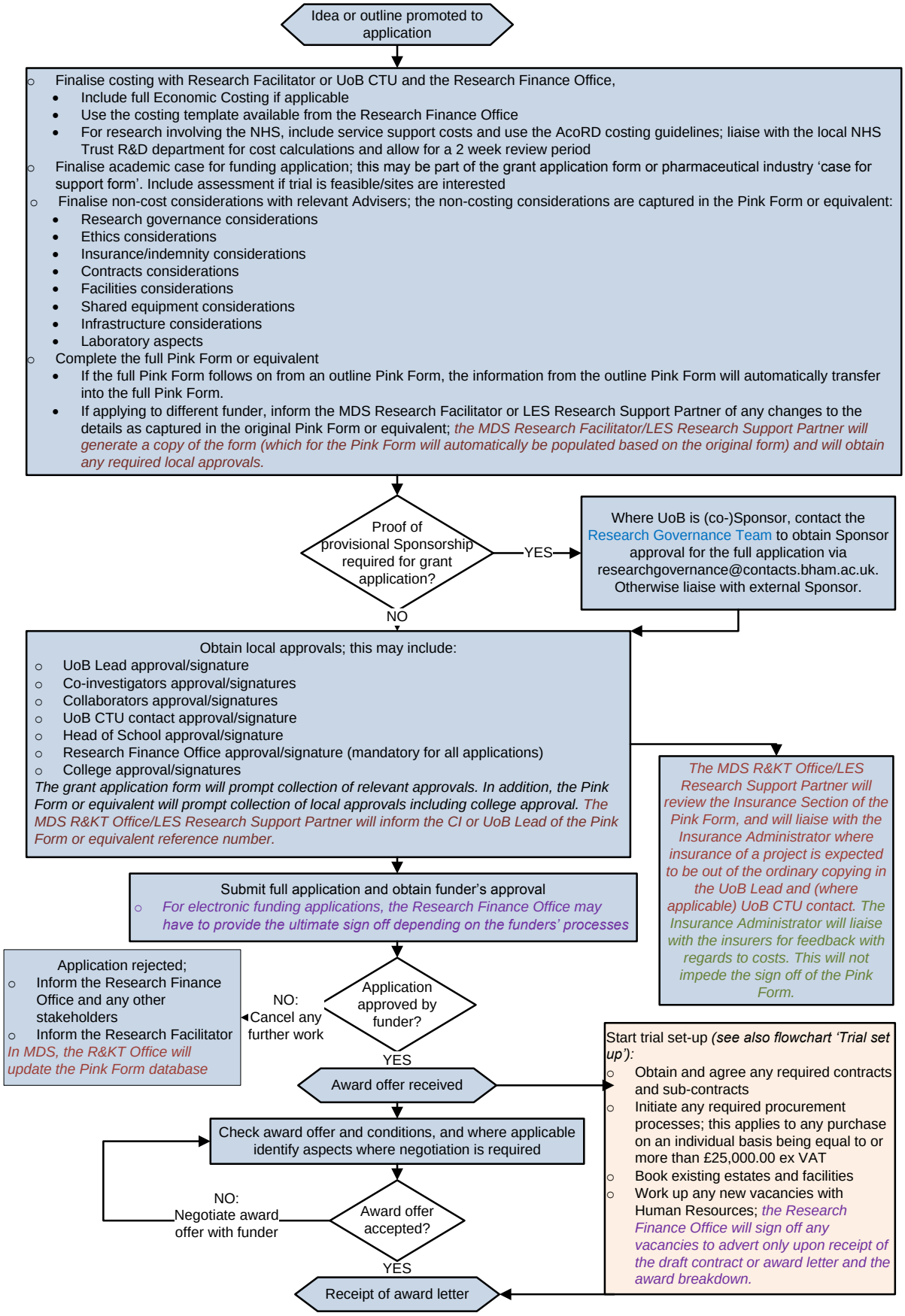
Idea stage


Define idea
Consider performing a feasibility assessment as the outcome may impact on the actual project design; some funders will require a feasibility to be performed
Will UoB be asked to act as (co-)Sponsor?
YES: as co-sponsor
NO: external sponsor only
YES: as sole sponsor
Complete New Business Form:
For trials to be managed by a UK Clinical Research Network (UKCRN) fully registered UoB Clinical Trials Unit (hereafter referred to as UoB CTU), liaise with the UoB CTU to follow their local processes
For trials to be managed outside a UoB CTU and where the UoB is taking on (co-)Sponsorship, liaise with the Research Facilitator as soon as possible. They will provide the Clinical Trials New Business Form; complete the form and forward to the secretary of the Clinical Trials Oversight Committee (CTOC) for further review
Liaise with external sponsor to ensure their processes are followed
NO: idea to be developed further; liaise with Research Facilitator
Idea supported?
NO: no further action taken
Idea cancelled
Outline proposal required?
YES
NO
Outline Pink Form or equivalent approval
Full Pink Form or equivalent approval
Submit outline proposal (See flowchart 'Outline application')
Submit full application (See flowchart 'Full application')

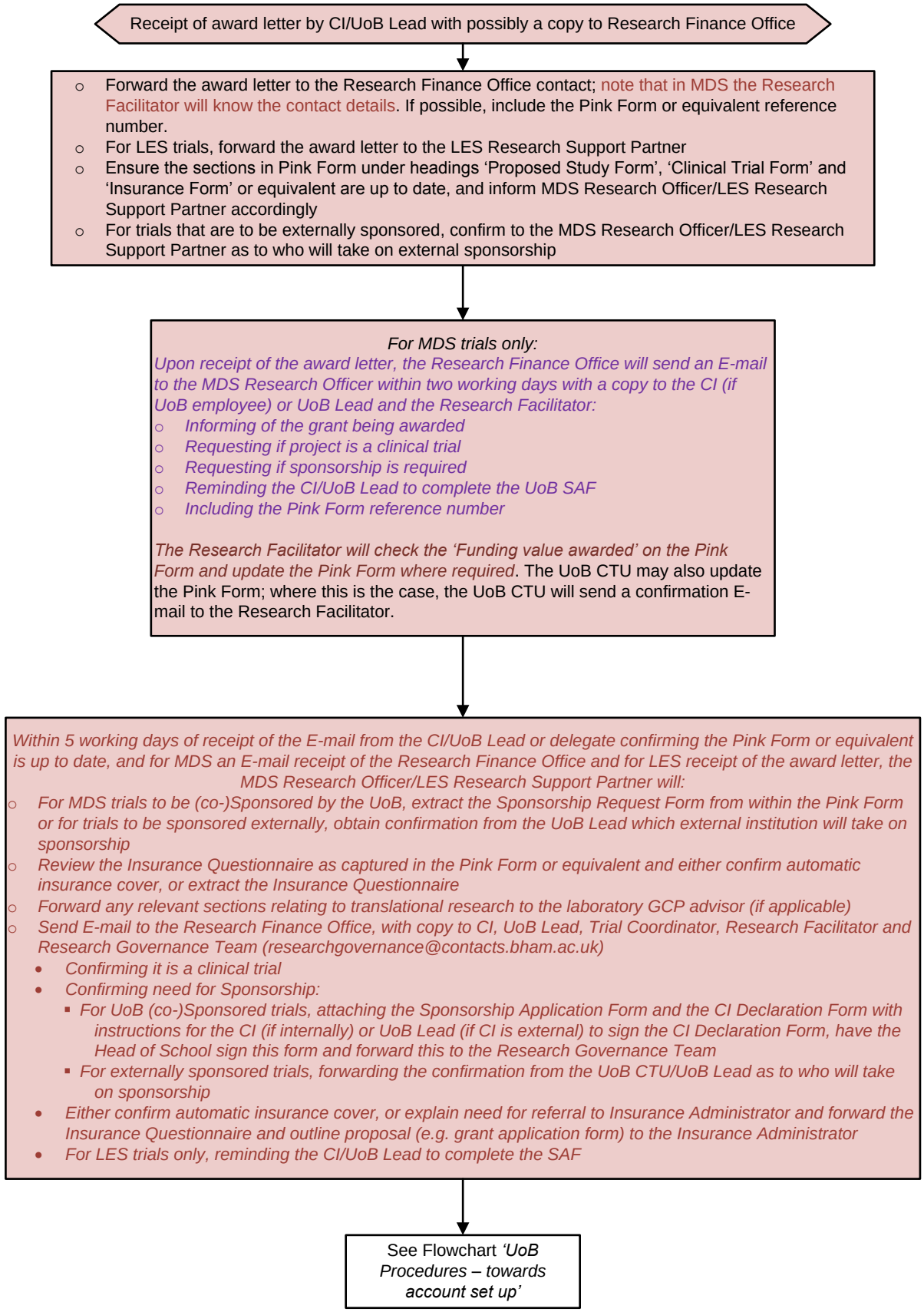
Outline application



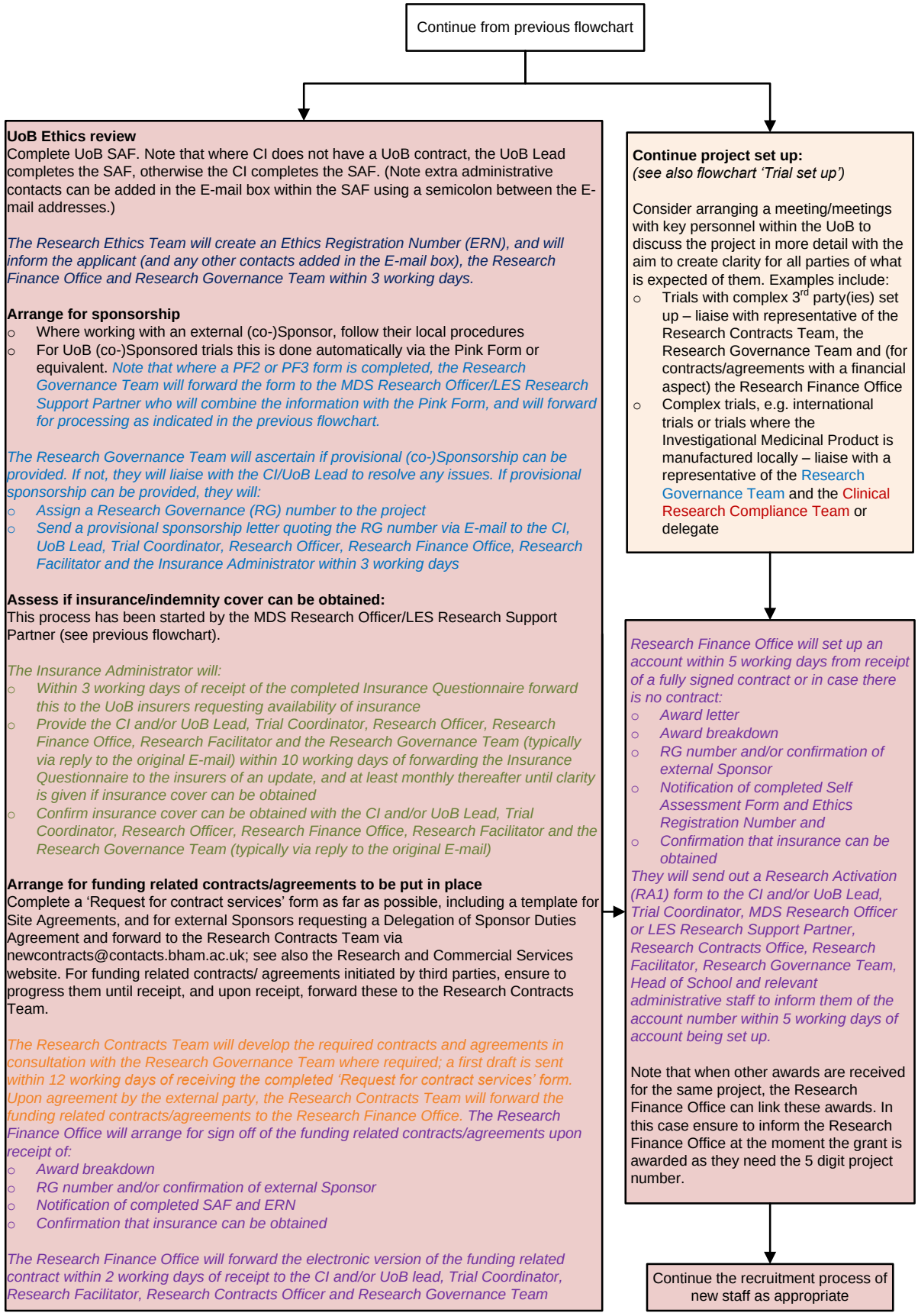
Full application



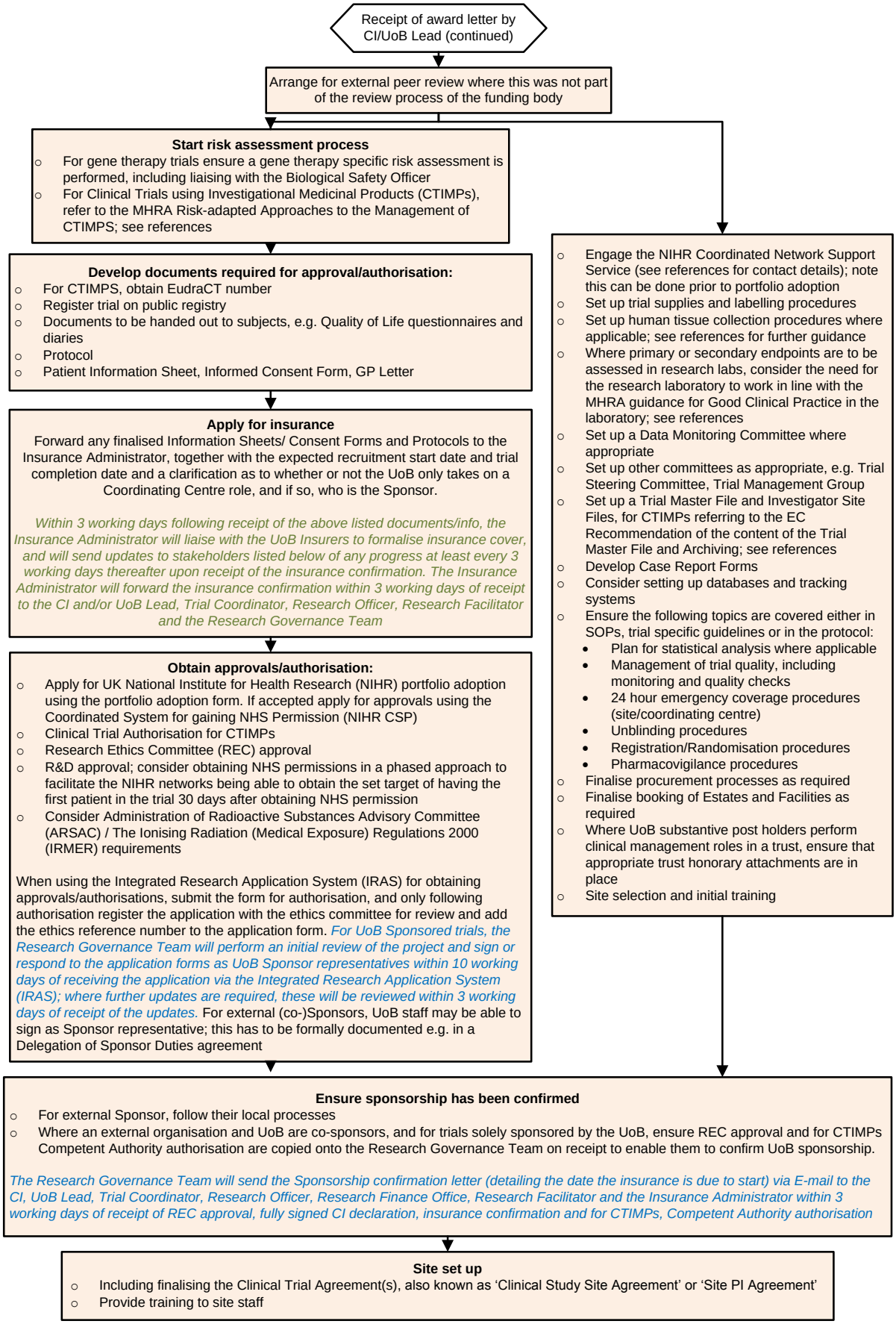
UoB procedures – award receipt and distribution



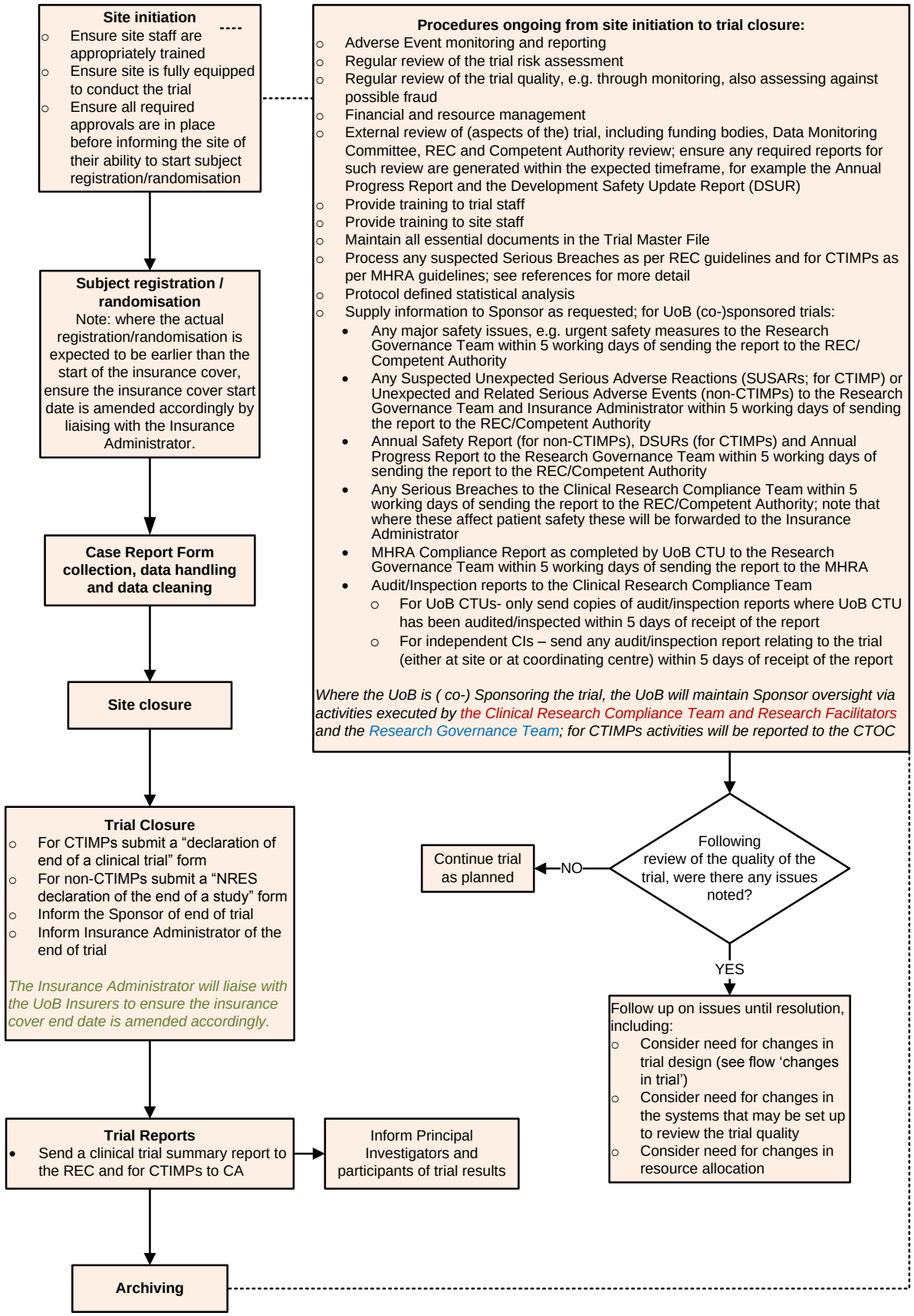
UoB procedures – towards account set up



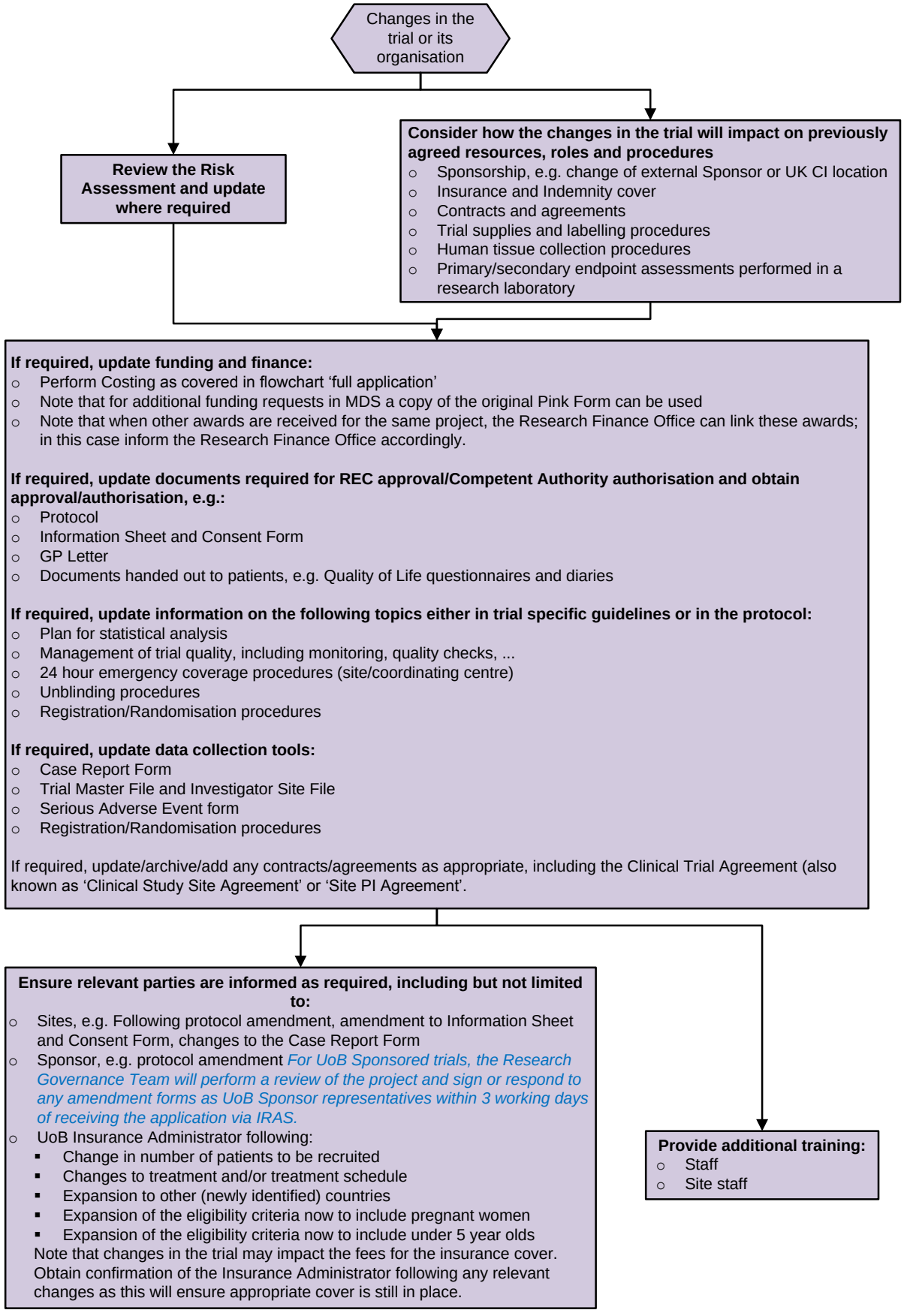
Trial set up


Receipt of award letter by CI/UoB Lead (continued)
Arrange for external peer review where this was not part of the review process of the funding body
Start risk assessment process
For gene therapy trials ensure a gene therapy specific risk assessment is performed, including liaising with the Biological Safety Officer
For Clinical Trials using Investigational Medicinal Products (CTIMPs), refer to the MHRA Risk-adapted Approaches to the Management of CTIMPS; see references
Develop documents required for approval/authorisation:
For CTIMPS, obtain EudraCT number
Register trial on public registry
Documents to be handed out to subjects, e.g. Quality of Life questionnaires and diaries
Protocol
Patient Information Sheet, Informed Consent Form, GP Letter
Apply for insurance
Forward any finalised Information Sheets/ Consent Forms and Protocols to the Insurance Administrator, together with the expected recruitment start date and trial completion date and a clarification as to whether or not the UoB only takes on a Coordinating Centre role, and if so, who is the Sponsor.
Within 3 working days following receipt of the above listed documents/info, the Insurance Administrator will liaise with the UoB Insurers to formalise insurance cover, and will send updates to stakeholders listed below of any progress at least every 3 working days thereafter upon receipt of the insurance confirmation. The Insurance Administrator will forward the insurance confirmation within 3 working days of receipt to the CI and/or UoB Lead, Trial Coordinator, Research Officer, Research Facilitator and the Research Governance Team
Obtain approvals/authorisation:
Apply for UK National Institute for Health Research (NIHR) portfolio adoption using the portfolio adoption form. If accepted apply for approvals using the Coordinated System for gaining NHS Permission (NIHR CSP)
Clinical Trial Authorisation for CTIMPs
Research Ethics Committee (REC) approval
R&D approval; consider obtaining NHS permissions in a phased approach to facilitate the NIHR networks being able to obtain the set target of having the first patient in the trial 30 days after obtaining NHS permission
Consider Administration of Radioactive Substances Advisory Committee (ARSAC) / The Ionising Radiation (Medical Exposure) Regulations 2000 (IRMER) requirements
When using the Integrated Research Application System (IRAS) for obtaining approvals/authorisations, submit the form for authorisation, and only following authorisation register the application with the ethics committee for review and add the ethics reference number to the application form. For UoB Sponsored trials, the Research Governance Team will perform an initial review of the project and sign or respond to the application forms as UoB Sponsor representatives within 10 working days of receiving the application via the Integrated Research Application System (IRAS); where further updates are required, these will be reviewed within 3 working days of receipt of the updates. For external (co-)Sponsors, UoB staff may be able to sign as Sponsor representative; this has to be formally documented e.g. in a Delegation of Sponsor Duties agreement
Engage the NIHR Coordinated Network Support Service (see references for contact details); note this can be done prior to portfolio adoption
Set up trial supplies and labelling procedures
Set up human tissue collection procedures where applicable; see references for further guidance
Where primary or secondary endpoints are to be assessed in research labs, consider the need for the research laboratory to work in line with the MHRA guidance for Good Clinical Practice in the laboratory; see references
Set up a Data Monitoring Committee where appropriate
Set up other committees as appropriate, e.g. Trial Steering Committee, Trial Management Group
Set up a Trial Master File and Investigator Site Files, for CTIMPs referring to the EC Recommendation of the content of the Trial Master File and Archiving; see references
Develop Case Report Forms
Consider setting up databases and tracking systems
Ensure the following topics are covered either in SOPs, trial specific guidelines or in the protocol:
Plan for statistical analysis where applicable
Management of trial quality, including monitoring and quality checks
24 hour emergency coverage procedures (site/coordinating centre)
Unblinding procedures
Registration/Randomisation procedures
Pharmacovigilance procedures
Finalise procurement processes as required
Finalise booking of Estates and Facilities as required
Where UoB substantive post holders perform clinical management roles in a trust, ensure that appropriate trust honorary attachments are in place
Site selection and initial training
Ensure sponsorship has been confirmed
For external Sponsor, follow their local processes
Where an external organisation and UoB are co-sponsors, and for trials solely sponsored by the UoB, ensure REC approval and for CTIMPs Competent Authority authorisation are copied onto the Research Governance Team on receipt to enable them to confirm UoB sponsorship.
The Research Governance Team will send the Sponsorship confirmation letter (detailing the date the insurance is due to start) via E-mail to the CI, UoB Lead, Trial Coordinator, Research Officer, Research Finance Office, Research Facilitator and the Insurance Administrator within 3 working days of receipt of REC approval, fully signed CI declaration, insurance confirmation and for CTIMPs, Competent Authority authorisation
Site set up
Including finalising the Clinical Trial Agreement(s), also known as 'Clinical Study Site Agreement' or 'Site PI Agreement'
Provide training to site staff

Site initiation to archiving



Amendments


Changes in the trial or its organisation
Review the Risk Assessment and update where required
Consider how the changes in the trial will impact on previously agreed resources, roles and procedures
Sponsorship, e.g. change of external Sponsor or UK CI location
Insurance and Indemnity cover
Contracts and agreements
Trial supplies and labelling procedures
Human tissue collection procedures
Primary/secondary endpoint assessments performed in a research laboratory
If required, update funding and finance:
Perform Costing as covered in flowchart 'full application'
Note that for additional funding requests in MDS a copy of the original Pink Form can be used
Note that when other awards are received for the same project, the Research Finance Office can link these awards; in this case inform the Research Finance Office accordingly.
If required, update documents required for REC approval/Competent Authority authorisation and obtain approval/authorisation, e.g.:
Protocol
Information Sheet and Consent Form
GP Letter
Documents handed out to patients, e.g. Quality of Life questionnaires and diaries
If required, update information on the following topics either in trial specific guidelines or in the protocol:
Plan for statistical analysis
Management of trial quality, including monitoring, quality checks, ...
24 hour emergency coverage procedures (site/coordinating centre)
Unblinding procedures
Registration/Randomisation procedures
If required, update data collection tools:
Case Report Form
Trial Master File and Investigator Site File
Serious Adverse Event form
Registration/Randomisation procedures
If required, update/archive/add any contracts/agreements as appropriate, including the Clinical Trial Agreement (also known as 'Clinical Study Site Agreement' or 'Site PI Agreement'.
Ensure relevant parties are informed as required, including but not limited to:
Sites, e.g. Following protocol amendment, amendment to Information Sheet and Consent Form, changes to the Case Report Form
Sponsor, e.g. protocol amendment For UoB Sponsored trials, the Research Governance Team will perform a review of the project and sign or respond to any amendment forms as UoB Sponsor representatives within 3 working days of receiving the application via IRAS.
UoB Insurance Administrator following:
Change in number of patients to be recruited
Changes to treatment and/or treatment schedule
Expansion to other (newly identified) countries
Expansion of the eligibility criteria now to include pregnant women
Expansion of the eligibility criteria now to include under 5 year olds
Note that changes in the trial may impact the fees for the insurance cover. Obtain confirmation of the Insurance Administrator following any relevant changes as this will ensure appropriate cover is still in place.
Provide additional training:
Staff
Site staff

Related documents:

Links below were correct at time of writing:

- ☐ Clinical Trials New Business Form: available from the Research Facilitator or equivalent
- ☐ Costing template: available from the Research Finance Office
- ☐ College of Medical and Dental Sciences Application for Research Grants and Contracts Approval Form (Pink Form): http://intramed.bham.ac.uk/Login.aspx?ReturnUrl=%2fdefault.aspx
- ☐ Sponsorship Application Form (PF2 and PF3) and the CI Declaration Form: https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Governance/UoB-Sponsorship.aspx
- ☐ UoB SAF: https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Ethics/Ethical-Review-Forms.aspx
- ☐ Insurance Questionnaire: https://intranet.birmingham.ac.uk/finance/insurance/Clinical-Trials.aspx
- ☐ Request for Contract Services. https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Contracts/Request-a-Contract.aspx
- ☐ MHRA Template for Serious Breaches http://www.mhra.gov.uk/Howweregulate/Medicines/Inspectionandstandards/GoodClinicalPractice/News/CON084915
- ☐ DSUR Template can be obtained from the Clinical Research Compliance Team and the Research Governance Team
- ☐ Annual Progress Report (of NRES). http://www.nres.nhs.uk/applications/after-ethical-review/annual-progress-reports/
- ☐ Declaration of end of a Clinical Trial Form. http://www.nres.nhs.uk/applications/after-ethical-review/endofstudy/
- ☐ NRES Declaration of the end of a Clinical Study Form. http://www.nres.nhs.uk/applications/after-ethical-review/endofstudy/

References:

- ☐ Department of Health. (2012, May 04). *Attributing the costs of health and social care Research & Development (AcoRD).* Retrieved October 15, 2012, from DoH Publications Policy and Guidance: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_133883.pdf
- ☐ European Committee. (2006, July). *Recommendation of the content of the Trial Master File and Archiving.* Retrieved September 10, 2012, from http://ec.europa.eu/health/files/eudralex/vol-10/v10_chap5_en.pdf
- ☐ MHRA. (2009, July). *Good Clinical Practice Guidance on the maintenance of regulatory compliance in laboratories that perform the analysis or evaluation of clinical trial samples.* Retrieved September 13, 2012, from http://www.mhra.gov.uk/home/groups/is-insp/documents/websiteresources/con051910.pdf
- ☐ MHRA. (2011, October 10). *Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products.* Retrieved February 21, 2012, from http://www.mhra.gov.uk/home/groups/l-ctu/documents/websiteresources/con111784.pdf
- ☐ NIHR CRN CC. (2012). *Coordinated Network Support Service (previously known as the Lead Network Service)*. Retrieved September 10, 2012, from http://www.crncc.nihr.ac.uk/about_us/ccrn/bbc/rmg/Coordinated+Network+Support+Service
- ☐ University of Birmingham. (2011-2012). *Code of Practice for Research.* Retrieved March 20, 2012, from http://www.birmingham.ac.uk/Documents/university/legal/research.pdf

See also the Clinical Trials Quality Manual for references to the applicable regulations and (inter)national guidance relating to clinical trials.

Acknowledgements:

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Development summary:

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Date:	See original copy		

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