STANDARD OPERATING PROCEDURE FOR THE LOCAL MANAGEMENT REVIEW OF AMENDMENTS TO STUDIES

SOP NUMBER:	**Fife R&D SOP40**
AUTHOR:	**Penny Trotter**
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1. PURPOSE

This SOP describes the procedure for the Local Management review and approval of amendments to clinical research studies sponsored or hosted by NHS Fife.

It is the responsibility of all staff using this SOP to ensure they are using the latest version of it. The latest version is available via StaffLink, the R&D section of the NHS Fife website (www.nhsfife.org/research) and EDGE (https://www.edge.nhs.uk). For guidance, contact the R&D Department via fife.randd@nhs.scot.

2. APPLICABILITY

This SOP applies to all staff involved in the conduct of clinical research studies and members of the NHS Fife R&D Department involved in the process for Local Management review and approval of amendments to clinical research studies.

3. PRINCIPLES

3.1 Researchers wishing to make amendments to research conducted by NHS Fife must obtain NHS Local Management Approval (also referred to as R&D Approval). This approval must be in place before any amendments can be implemented. The only exception to this is if the amendment introduces an Urgent Safety Measure. Amendments that are Urgent Safety Measures must still go through the amendment review and approval process but must be implemented immediately.

3.2 All amendments for research projects should be submitted online using the Integrated Research Application System (IRAS) Amendment Tool.

The Amendment Tool categorises the amendment and provides tailored guidance on how to submit. It will identify any review bodies the amendment needs to be sent to, based on the changes that are being made to the trial.

The Amendment Tool and full guidance on its use can be found at http://www.myresearchproject.org.uk/help/hlpamendments.aspx.

3.3 The Amendment Tool classifies amendments into the following types:

- *Substantial:* A substantial amendment is a change to the terms of the request for clinical trial authorisation or the ethics committee application, or to the accompanying particulars or documents, which significantly affects one of the following:
  - The safety or physical or mental integrity of study participants
  - The conduct or management of the study
  - The scientific value of the study
  - The quality or safety of any investigational medicinal product or device used in the study.

- *Non-substantial:* amendment is defined as a change to the details of the study which will have no significant implications for participants, the scientific value, conduct or management of the trial, or quality and safety of the product or device used in the study.

- *Non-notifiable:* an amendment that does not require online amendment submission to REC or MHRA (via the IRAS online amendment portal) and does not need Local Management review, however local research teams need to be informed.

3.4 The Amendment Tool allocates amendments into the following categories:

- *Category A*: Has implications for, or affects, all participating NHS/Health and Social Care organisations hosting the research project therefore needs to be considered and may need change control actions.

- *Category B*: Has implications for, or affects, specific participating NHS/HSC organisations hosting the research project. Only at these organisations does it need to be considered and any change control actions required.

- *Category C*: Has no implications that require management or oversight by the participating NHS/HSC organisations hosting the research project. However, the amendment should still be submitted for information.

- *Not Applicable:* These are changes that don't require a categorisation. It might be something that doesn't impact on NHS sites (such as an Investigational Medicinal Product Dossier (IMPD) update) or changes that would be a non-notifiable amendment (such as translated documents).

3.5 The R&D Approvals Team may be informed of an amendment either by the Chief Investigator (CI), NHS Research Scotland Permissions Coordinating Centre (NRSPCC), by a study contact, or by the local Principal Investigator (PI) / R&D Research Nurse.

3.6 For multicentre studies, the Local Management Review process commences once the NRSPCC makes the appropriate documentation available to the NHS Fife R&D Approvals Team via the Scottish Research Database Application (SReDA).

For single centre studies, where NHS Fife is the only site, notification of the amendment is not received from NRSPCC. The Sponsor completes the Amendment Tool and emails a copy directly to NHS Fife R&D Approvals Team to start the Local Management Review process.

3.7 For studies supported by an R&D Research Team, implementation of amendments by the R&D Research Team occurs *after* Local Management Approval is issued, and at a date specified by the Sponsor (See *WI38 – Implementing Study Amendments*).

3.8 Once the NRSPCC has confirmed that a Category A or B amendment is complete and valid, they will provide the Sponsor with a 35-day "Implementation Date".

Note "Implementation Date" above does not mean the date when the change will be implemented at the site, or Regulatory Green Light (RGL) for the amendment implementation.

The 35-day Implementation Date is the date by which the site must inform the Sponsor that there are issues: either (a) before the amendment can be implemented or (b) therefore the amendment cannot be implemented.

The **Sponsor** can implement the amendment once **all** the following conditions are met:

- After the 35-day Implementation Date **unless** the site has communicated to the Sponsor that there are issues.
- External approvals are received.
- NHS Fife Local Management Approval is issued.
- PI / Local Study Team / Support Departments have confirmed they are ready to IMPLEMENT the amendment.

Or at an alternative date confirmed to the Local Study Team by the Study Coordinator or CI once the conditions above are in place.

If the site **has** communicated to the Sponsor that there are issues, the amendment can only be implemented at the site once Local Management review and approval of the amendment has been completed.

3.9 The local research team are responsible for ensuring that all Support Departments involved in the study (other than the Clinical Trials Pharmacy Team) are aware of the amendment, if it relates to activities they carry out.

3.10 Although a complete document set does not have to be provided immediately; approval cannot be granted until all appropriate documents are in place.

3.11 Local Management Approval for substantial amendments (all categories) cannot be issued until the external approval documents have been received, with the exception of PBPP approval, if relevant.

3.12 Local Management Approval for an amendment must be issued before any changes to data collection/research activity can be implemented within NHS Fife.

4. PROCEDURE

4.1 For Category A and Category B Amendments which affect NHS Fife

4.1.1 On receipt of an Amendment Notification from NRSPCC (multi-centre studies) or CI (single centre study) the R&D Approvals Team must add the following workflows to EDGE:

- *'Approvals - Amendments – CAT A / CAT B*'
- 'Research Team – Amendment Implementation' for R&D Research Nurse Team supported studies.
- '*Pharmacy – Amendment Implementation'* if the study is a Clinical Trial of Investigational Medicinal Product (CTIMP).
- 'Finance – Amendment Finance Review' if there are potentially any costings implications, as a result, of the amendment.

The R&D Approvals Team must send an email to the PI, Senior Research Nurse, Clinical Trials Pharmacy Team (for CTIMPs), R&D Business Accountant and Lead R&D Research Nurse (where there are possible costings implications) to request that they review the amendment (with the Amendment Tool and documents attached). The local team assess if there are foreseeable capacity or capability issues. Their email responses are filed in EDGE and the comments added to the '*Approvals - Amendment – CAT A / CAT B'* workflow.

4.1.2 The R&D Approvals Team must scrutinise the details of the amendment and carry out the checks, record the outcome in the workflow and escalate issues that arise.

4.1.3 Once the '*Approvals – Amendments – CAT A / CAT B*' Workflow is authorised by the Assistant Director RIK on EDGE the Local Management Approval letter is issued (Doc Ref 40-03).

For CTIMPs and Medical Device Clinical Investigations (MDCIs) the Medical Director Delegate as an Authorised Signatory of Fife Health Board signs off the Local Management Approval letter.

For Non-CTIMPs and Non-MDCIs the Local Management Approval letter signatory is the Assistant Director RIK on behalf of the Medical Director.

4.1.4 The Local Management Approval letter and associated amendment documentation must be emailed to the PI or CI, Senior R&D Research Nurse (where the study is being supported by an R&D Research Team), Clinical Trials Pharmacy Team (CTIMPs only) and Sponsor representative.

4.2 For Category B Amendments not applicable to NHS Fife:

4.2.1 Where the study is being supported by an R&D Research Team, check the *'Research Team - Study Summary Checklist'* workflow to access instructions from the Sponsor or research nurse regarding ISF filing arrangements. If the Sponsor has instructed that Amendments CAT B N/A Fife should be filed in the ISF, or if their requirements are not yet established, the R&D Approvals Team must:

- Add the *'Research Team – Amendment Implementation'*
- Send an email notification to the PI, Senior R&D Research Nurse and Clinical Trials Pharmacy Team (CTIMPs only) to inform them of the amendment and implementation workflow, should they require to record or update files.
- Add a note to EDGE:

  - Title: amendment reference; amendment date; category.
  - Text: "notification by NRSPCC but no action by NHS Fife required".

4.3 For Category C Amendments

4.3.1 On receipt of an Amendment Notification from NRSPCC (multi-centre studies) or CI (single centre study) the R&D Approvals Team must add the following workflows to EDGE:

- *'Approvals - Amendments – CAT C'*
- 'Research Team – Amendment Implementation' for R&D Research Nurse Team supported studies.
- *'Pharmacy – Amendment Implementation'* if the study is a Clinical Trial of Investigational Medicinal Product (CTIMP).

4.3.2 The R&D Approvals Team must scrutinise the details of the amendment and carry out the checks, record the outcome in the workflow and escalate issues that arise.

4.3.3 Where documents from external bodies are pending, the R&D Approvals Team must send an email notification to the PI, Senior R&D Research Nurse (where the study is being supported by an R&D Research Team) and Clinical Trials Pharmacy Team (CTIMPs only) informing them that formal acknowledgement will be issued on receipt of all external approval documents.

4.3.4 Once all the study documentation has been reviewed, all queries have been resolved satisfactorily, the *'Approvals – Amendments – CAT C'* Workflow must be completed.

Substantial Category C amendment workflows must be reviewed and confirmed by the R&D Research Coordinator prior to the issue of the acknowledgement email (Doc Ref 40-04).

Category C amendments do not require authorisation by the Assistant R&D Director or sign off by either the Assistant R&D Director or the Medical Director's authorised signatory.

4.3.5 The R&D Approvals Team must send an email as soon as possible acknowledging the Amendment has been received and there are no implications for the ongoing Local Management Approval, to the PI, Senior R&D Research Nurse (where the study is being supported by an R&D Research Team), Clinical Trials Pharmacy Team (CTIMPs only) and Sponsor representative.

4.4 For Category N/A Amendments

4.4.1 On receipt of an Amendment Notification from NRSPCC (multi-centre studies) or CI (single centre study) the R&D Approvals Team must add the following to EDGE:

- 'Research Team – Amendment Implementation' for R&D Research Nurse Team supported studies.
- Add a note to EDGE,
  - Title: amendment reference; amendment date, category.
  - Text: "Notification by NRSPCC but no action by NHS Fife required".

4.4.2 The R&D Approvals Team must send an email notification to the PI, Senior R&D Research Nurse (where the study is being supported by an R&D Research Team) and Clinical Trials Pharmacy Team (CTIMPs only) to inform them of the amendment and implementation workflow, should they require to record or update files. Any external approval documents related to the amendment that are received, at a later date, must be forwarded to the Research Team.

4.5 The Local Management Approval letter, Acknowledgement email or any other associated documentation must be stored in *S:\Research\PROJECTS\2 PROJECT DOCUMENTATION\APPROVAL STUDY FOLDERS* and uploaded to EDGE.

4.6 Honorary Contracts and Letters of Access must be issued by HR and the R&D Approvals Team, if required once Local Management Approval is granted (See *R&D SOP24*).

5. ASSOCIATED DOCUMENTS

R&D SOP24 - Research Passports, Honorary Research Contracts, Letters of Access and Other Processes for External Researchers

R&D WI38 - Implementing Study Amendments

R&D Doc Ref 40-03 – Amendment Approval Letter Template

R&D Doc Ref 40-04 – Text for Cat C Amendment Acknowledgement Email.

6. REFERENCES

NHS/HSC R&D – UK PROCESS FOR MANAGEMENT OF AMENDMENTS (http://www.hra.nhs.uk/nhshsc-rd-uk-process-management-amendments/)

7. ABBREVIATIONS

CI	Chief Investigator
CLO	Central Legal Office
CTIMP	Clinical Trial of Investigational Medicinal Product
IRAS	Integrated Research Application System
MDCI	Medical Device Clinical Investigation
MHRA	Medicines and Healthcare Products Regulatory Agency
NRSPCC	NHS Research Scotland Permissions Coordinating Centre
PI	Principal Investigator
REC	Research Ethics Committee
RGL	Regulatory Green Light
SOP	Standard Operating Procedure
SReDA	Scottish Research Database Application (https://www.reda.org.uk/)

8. DOCUMENT HISTORY

Version Number:	Edited by (job title):	Effective Date:	Details of Revisions Made:
1	Allyson Bailey R&D Commercial Manager Julie Aitken R&D Trials Facilitator	16 Sept 2017	N/A – new SOP
2	Aileen Yell R&D Research Coordinator	27 Sept 2019	Format updated in line with current SOP template and minor changes to text for clarity. Clarification added that advice may be required from Information Governance if the amendment involves changes to the way data is accessed/handled/stored or if there will be any new data linkage.

Version Number:	Edited by (job title):	Effective Date:	Details of Revisions Made:
			Clarification added that Support Departments must be made aware of all amendments. Associated Documents Doc Ref 40-01 and Doc Ref 40-02 added.
3	Aileen Yell R&D Research Coordinator	07 Dec 2021	Doc Ref 40-01 and Doc ref 40-02 deleted and reference to EDGE Workflows added. Process clarified regarding issue of LMA for Category A and B amendments and acknowledgment of Category C amendments.
4	Penny Trotter R&D Research Coordinator	04 Mar 2024	Text re-organised to distinguish between principles and procedure. Added background information on the process for submission of amendments via the IRAS Amendment Tool and describing how the Amendment Tool classifies and categorises Amendments. Clarified that for single centre studies where NHS Fife is the only site, the Amendment Tool is sent directly to the Approvals Team and not via NRSPCC. Reference to WI38 added and clarification of the timing of Amendment Implementation. Highlighted that the local research team are responsible for making Support Departments aware of any amendments that impact activities they are involved in. Details added to clarify the procedures to be followed and EDGE Workflows to be added for each category of Amendment. Added requirement for Substantial Category C Amendments to be reviewed by the Research Coordinator prior to issuing the Acknowledgment email. Clarified that LMA letters and acknowledgement emails will be sent to the PI, Lead R&D Research Nurse (if appropriate), Clinical Trials Pharmacy

Version Number:	Edited by (job title):	Effective Date:	Details of Revisions Made:
			Team (CTIMPs only) and Sponsor representative only. Doc Refs 40-03 and 40-04 created to provide version control of the LMA letter and acknowledgement email.

9. APPROVAL

APPROVED BY	Date
Professor Frances Quirk, Assistant Director RIK, NHS Fife Signature: 	04 March 2024