STANDARD OPERATING PROCEDURE FOR SETTING UP STUDIES SPONSORED BY NHS FIFE

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AUTHOR:	**Julie Aitken**
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1. PURPOSE

This document describes the procedure used for setting up a research study sponsored by NHS Fife to ensure compliance with Good Clinical Practice (GCP).

It is the responsibility of all researchers using this SOP to ensure they are using the latest version of it. The latest version is available via the Research & Development (R&D) pages on the NHS Fife Intranet or, for guidance, contact the R&D Department via fife-uhb.randd@nhs.net

2. APPLICABILITY

Unless otherwise specified in a clinical study agreement, this document applies to all research studies sponsored by NHS Fife and to all staff who have a role or responsibility in study set-up including those who manage, coordinate or advise on set-up and/or start-up procedures.

3. POLICY

3.1 It is a legal requirement for Clinical Trials of Investigational Medicinal Products (CTIMPs) to be set up and conducted in accordance with the Medicines for Human Use (Clinical Trials) Regulations 2004 and 2006 (the UK Clinical Trial Regulations) and the Principles of GCP, however, the pertinent issues of GCP are also relevant to all other types of studies.

3.2 The responsibility for set-up is the Sponsor's however the performance of specific set-up duties will be delegated by the Sponsor to the Chief Investigator (CI) by way of a Sponsorship Agreement (Doc Ref 06-02) between the Sponsor and the CI.

3.3 This SOP should be read together with R&D SOP06 that describes the process for obtaining Sponsor agreement from NHS Fife and R&D SOP11 that describes the process for obtaining Local Management Approval for studies conducted in NHS Fife.

4. PROCEDURE

4.1. Funding

4.1.1 The CI must secure resources to finance the study.

4.1.2 If the study is externally funded, the R&D Approvals Team, on behalf of the Sponsor, must ensure an agreement is in place to confirm financial flow and oversight between the holder (recipient) of the funding and the Sponsor prior to the start of the study.

4.2. Insurance/Indemnity

4.2.1 The NHS Fife R&D Department must confirm that adequate insurance and/or indemnity arrangements are in place to cover study liabilities.

4.2.2 The CI must ensure that evidence of insurance is held in the Study Master File (SMF).

4.3. Sponsorship

4.3.1 The CI must ensure that Sponsorship is in place (see R&D SOP06).

4.3.2 The CI will be required to sign a Study -Specific Sponsorship Agreement and Chief Investigator Declaration (Doc Ref 06-02) which sets out the duties delegated by the Sponsor to the CI, and the duties retained by the Sponsor, to ensure the set-up and conduct of the study is to the appropriate standards and Regulatory/legislative requirements.

4.4. SOPs

4.4.1 The CI must adhere to the pertinent NHS Fife SOPs and Policies available via the R&D pages on the NHS Fife Intranet. These will be designated at Risk Assessment (See R&D SOP07) and highlighted to the CI by the R&D Approvals Team.

4.4.2 Where the CI wishes to use SOPs other than NHS Fife SOPs, this must be reviewed and agreed as part of the Risk Assessment (see R&D SOP07. Approval will be given only for non NHS Fife SOPs which are study or group specific and additional to NHS Fife SOPs.

4.4.3 A Study SOP Log (Doc Ref 28-01) must be maintained in the SMF and Investigator Site File (ISF), if appropriate.

4.5. Establishing Study Files

4.5.1 The R&D Research Coordinator is responsible for setting up and maintaining the Sponsor File in accordance with the Sponsor File Index. The Sponsor File contains confidential documents and must be kept in the R&D Office in a locked cupboard in a locked room with restricted access. All pertinent correspondence concerning the study must be filed in the Sponsor File including monitoring visit reports and actions lists from monitoring.

4.5.2 The CI or delegate is responsible for establishing the SMF (see R&D SOP03).

4.5.3 The Principal Investigator (PI), or delegate, at external Sites is responsible for establishing an ISF.

4.5.4 It is the responsibility of the CI and PI(s) or delegates to ensure that all essential documents, as described in the NHS Fife SMF/ISF Index, are filed in the SMF and ISF as appropriate.

4.5.5 All study-related documents, including the SMF and ISF, should be stored securely and in a manner that protects confidentiality.

4.5.6 The SMF and ISF should be maintained in a ready-state manner to allow for inspection, audit or monitoring on request.

4.6. Protocol

4.6.1 The CI must write the protocol using the latest version of the appropriate NHS Fife Protocol Template (See R&D WI36 - Writing a Protocol to the Standards of ICH-GCP, which is available on the R&D pages on the NHS Fife Intranet).

4.6.2 The CI and research team must conduct the study in compliance with the protocol approved by the Sponsor, MHRA, other Regulatory Authorities, Research Ethics Committee (REC) and NHS Fife R&D Office.

4.6.3 The CI and research team must not deviate from or amend the protocol without agreement from the Sponsor and subsequent approval from the MHRA, REC, NHS Fife R&D and any other relevant bodies, as appropriate (see R&D SOP20).

4.6.4 The CI and research team must notify the Sponsor promptly of any potentially serious breaches of protocol or GCP (see R&D SOP22) using the NHS Fife Potential Serious Breach Notification Form (Doc Ref. 22-02).

4.6.5 The CI must take into account all protocol deviations and any serious breaches in the final study analysis and publication.

4.7. Designing Case Record Forms (CRFs) and/or Data Collection Tools.

Where required, the CI or delegate must design the CRF/Data Collection tools in accordance with R&D WI41 – Designing and Maintaining Case Report Forms (CRFs) for Use in Clinical Research.

4.8. Writing Participant Information Sheets and Informed Consent Forms

The CI or delegate must write Participant Information Sheets and Informed Consent Forms in accordance with R&D WI35.

4.9 Third Party Agreements

4.9.1 The R&D Approval Team, on behalf of the Sponsor, must ensure that Agreements (contracts) or Statements of Services with third party organisations providing services such as (but not limited to); laboratory work, statistics, supply of equipment, study management, data management, are approved by the Central Legal Office (CLO), or the East Node Legal Services Manager and signed off by the NHS Fife Medical Director or delegate.

4.9.2 All agreements must be reviewed and agreed by the Assistant R&D Director or the CLO/ East Node Legal Services Manager and the Sponsor must be a signatory to these contracts/agreements.

4.9.3 The CLO/ East Node Legal Services Manager must be notified of any changes to any agreements and all changes must be approved by the CLO/ East Node Legal Services Manager and signed off by the R&D Director or delegate.

4.9.4 The R&D Approval Team, on behalf of the Sponsor, must ensure that all staff appointed to work on the research who are not employees of the Sponsor (contracted staff) have appropriate employment contracts.

4.9.5 The R&D Approvals Team, on behalf of the Sponsor, must ensure that all staff participating in the research on behalf of the Sponsor hold substantive or NHS Honorary Contracts/Letters of Access as appropriate.

4.10. Material Transfer Agreement (MTA) and Tissue

4.10.1 The CI must ensure that where required a Material Transfer Agreement (MTA) is in place for the transfer and storage of human tissue prior to any participant being enrolled in the study. MTAs must be approved by the CLO/ East Node Legal Services Manager prior to sign off. If the study is non-commercial and non-interventional, the appropriate appendix to the Organisation Information Document (OID) can be used.

4.10.2 The CI must be aware of, and adhere to, all obligations and requirements for the storage and transfer of tissue.

4.10.3 The CI, or PIs at external sites, must obtain agreement from all labs for any processing, storage and handling of tissue and bloods prior to recruiting the first participant.

4.10.4 The CI, on behalf of the Sponsor must ensure that any Central Labs used in the research hold the necessary license / accreditation.

4.10.5 For multi-centre research, the CI must ensure that the MTA and study Protocol contain clear instructions for processing, storage and handling of tissue, blood or any other bodily material and that these are provided to each participating site.

4.11. Approvals

4.11.1 The CI must ensure that the following approvals have been obtained prior to any approach regarding the study or screening procedure for the study and prior to the first participant being consented and entered into the study:

- Sponsor Approval
- REC favourable opinion (if required)
- NHS Fife R&D Local Management Approval. In addition, for multi-centre studies each participating site requires a letter of Local Management Approval from each site NHS R&D Office.
- Any other necessary approvals or authorisation.

4.12. IRAS Applications

4.12.1 All applications for permissions and approvals for health and social care or community care research in the UK must be made using the Integrated Research Application System (IRAS) online application form (https://www.myresearchproject.org.uk/).

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

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

4.12.3 The CI or delegate must complete an IRAS form and complete all relevant sections for the REC, NHS R&D, and any others as required. An outline OID and Schedule of Events (or SoECAT if available) must be included in the study-wide submission.

The localised OIDs must then be provided for each site except PICs.

If any non-NHS Site is involved, all sites must be listed in Part C of the IRAS form.

The Sponsor contact on the IRAS form should be detailed as the NHS Fife Assistant R&D Director and the R&D Approvals Team must arrange for the IRAS form to be signed by the Medical Director or an appropriately senior delegate.

4.12.4 The CI or delegate should submit the completed IRAS forms and all essential documents to REC, MHRA via the Common European Submission Portal (CESP), NHS Fife R&D Office and any other necessary Regulatory Authorities. In addition, evidence of NHS Fife Support Department(s) approvals must be provided to NHS Fife R&D Office.

4.12.5 For multi-centre studies, the CI should submit the IRAS R&D form and all essential documents to National Research Scotland Permissions Co-ordinating Centre (NRS-PCC). Permissions for multi-site studies are managed in line with NRS-PCC SOPs.

4.12.6 Copies of all communications and documentation should be sent to the R&D Research Co-ordinator for the Sponsor File and copies must be filed in the SMF.

4.12.7 NHS R&D Office(s) at other participating sites will review the study for Local Management Approval and issue an approval letter/provisional approval letter once Sponsorship, a favourable ethical opinion and any other essential approvals are in place/in process.

4.12.8 The CI or delegate should notify the NHS Fife R&D Research Co-ordinator when the first participant is consented to the study.

4.13. Training

The CI / PI must ensure that all research staff involved with the study are fully trained in the study procedures (see R&D SOP42)

4.13.1 Training must include but not be limited to:

- The protocol and any amendments
- Case Report Form
- The informed consent procedure (see R&D SOP14), consent form, participant information sheet and other study documents
- Adverse event reporting (refer to R&D SOP31)
- Completion of source documents particularly patient's hospital or GP medical records/casenotes
- Responsibility to report Serious Breaches (see R&D SOP22)

4.13.2 Training may be given during pre-study investigator meetings or during pre-study visits and during the course of the study.

4.13.3 The CI/PI must keep a record of study specific training to confirm that all members of the research team are trained.

4.13.4 Although there is no legal requirement, it is highly recommended that staff taking part in research have GCP training (See NHS Fife Wide Procedure for Good Clinical Practice (GCP) Training - FWP-GCPT-01).

4.13.5 The CI/PI must ensure that, where appropriate, the SMF/ISF contains up-to-date GCP certificates and CVs (signed and dated) for all research staff involved with the study. If held separately, the location should be File Noted in the SMF or ISF.

4.13.6 All research staff should maintain a training log in their personal training folder recording details of all training undertaken.

4.13.7 If new staff join a study after it has begun, the CI or PI must ensure that they receive the appropriate training (see R&D SOP42).

4.14. Study Delegation and Signature Log

4.14.1 All significant duties or tasks such as taking consent, assessing eligibility, prescribing or dispensing IMP, physical examinations etc. can be delegated by the CI, or PI, to those who have the necessary education, training and experience. If the CI or PI delegates tasks to other team members, the CI and PI still retains responsibility for the study at Site.

For a CTIMP the following duties can only be delegated to a study clinician:

- assessing the eligibility of study participants
- performing medical examinations
- signing-off completed SAE forms
- reviewing safety information such as line listings or SUSARs
- reviewing clinical information such as lab results, ECGs and imaging reports
- responding to medical queries
- approving IMP prescriptions

4.14.2 The CI or PI is responsible for the completion and maintenance of the Delegation of Duties & Signature Log (Doc. Ref 13-01) in the SMF or ISF, prior to and during the study. The Log should confirm all research staff involved with the study and all their duties which have been delegated to them by the CI or PI.

4.14.3 The CI and PI must ensure that no staff member is added to the Delegation of Duties & Signature Log without appropriate training.

4.14.4 The Delegation of Duties & Signature Log must contain the signature and initials of study staff to ensure they can then be identified on study documents such as CRFs, casenotes and prescriptions.

4.14.5 When staff leave the study and/or new staff join, the Delegation of Duties & Signature Log must be appropriately updated.

4.15. Participant Screening Log and Participant Identification Log

4.15.1 The CI (or delegate) is responsible for keeping a list of all potential participants screened for the study, those that were eligible to be recruited and those that were recruited (see Doc Ref WI22-04 - Participant Screening Log).

4.15.2 The CI/PI (or delegate) is responsible for keeping a confidential Participant Identification Log (see Doc Ref WI22-05) with names of all participants consented for participation , to allow the CI/PI to reveal the identity of participants if necessary. This is the only place where the full name, CHI number and contact details (optional) of study participants are documented. Participants should only be referred to by their initials and/or study number on CRFs, data collection tools or elsewhere.

4.15.3 The CI or delegate must notify the R&D Approvals Team (fife-uhb.fiferesearchapprovals@nhs.net) of the date when the first participant signs an Informed Consent Form.

4.16. Study Equipment

4.16.1 The CI, PI or delegated team member is responsible for confirming that all equipment used in the study has been properly maintained (see R&D WI26). This may include fridges, freezers, centrifuges, weighing scales and equipment used for medical procedures.

4.16.2 The CI is responsible for ensuring that appropriate indemnity arrangements are in place for any equipment loaned for use in the study (see R&D WI26).

4.16.3 All equipment must be logged by NHS Fife Medical Physics and, if it is supplied from mains electricity will require an Electrically Safety Test (contact Estates via Quicklinks on the NHS Fife Intranet).

4.17. Study Meetings

4.17.1 Regular team meetings must be held involving staff working on the study. Meetings should be minuted or notes made of all significant decisions and follow-up actions. Copies of minutes or notes must be kept in the SMF.

4.17.2 For large multi-centre studies Study Oversight Committees e.g. a Study Management Group, Data Monitoring Committee and Study Steering Committee should be set up by the CI or the NHS Fife Approvals Team in order to review study data and oversee study management at regular pre-defined intervals during the study.

Minutes of all meetings must be maintained in the SMF.

5. ASSOCIATED DOCUMENTS

Doc Ref 06-02 - Study -Specific Sponsorship Agreement and Chief Investigator Declaration
Doc Ref 13-01 - Delegation of Duties & Signature Log
Doc Ref 22-02 - Potential Serious Breach Notification Form
Doc Ref WI22-04 - Screening Log Template
Doc Ref WI22-05 - Participant Identification Log Template
Doc Ref 28-01- Study SOP Log
R&D SOP03 - Establishing and Maintaining a Study Files
R&D SOP07 - Assessment of Risk Associated with Research Sponsored by NHS Fife
R&D SOP14 - Obtaining Informed Consent
R&D SOP20 - Management of Study Amendments
R&D SOP22 - Escalation and Notification of Breaches of GCP or the Study Protocol for Clinical Research
R&D SOP31 - Adverse Event Reporting for non-CTIMPs
R&D WI26 - Management of Equipment for Use by R&D Staff
R&D WI35 - Writing a Patient Information Sheet and Informed Consent Form
R&D WI36 - Writing A Protocol to the Standards of ICH-GCP
R&D WI41 - Designing and Maintaining Case Report Forms (CRFs) for Use in Clinical Research
R&D SOP 42 - Creating and Maintaining a Training Record for Research Staff.
FWP-GCPT-01 - NHS Fife Wide Procedure for Good Clinical Practice (GCP) Training

6. ABBREVIATIONS

CI	Chief Investigator
CLO	Central Legal Office
CRF	Case Report Forms
CTIMP	Clinical Trial of Investigational Medicinal Product
GCP	Good Clinical Practice
ISF	Investigator Site File
MTA	Material Transfer Agreement
OID	Organisation Information Document
PI	Principal Investigator
REC	Research Ethics Committee
R&D	Research and Development
SMF	Study Master File
SOP	Standard Operating Procedure

7. REFERENCES

UK Policy Framework for Health and Social Care Research (2017)
https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/

ICH Harmonised Tripartite Guideline - Guideline for Good Clinical Practice
E6(R1), 1996.
(*http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf*)

8. DOCUMENT HISTORY

Version Number:	Edited by (job title):	Effective Date:	Details of editions made:
1.0	Julie Aitken R&D Trials Facilitator	30/03/2015	New - Adapted from TASC SOP 18, version 3
2.0	Julie Aitken R&D Trials Facilitator	08/01/2018	Updated for clarity and to reflect current practice.
3.0	Julie Aitken R&D Quality & Performance Lead	19 Feb 2020	Updated in line with format of Current SOP template. Watermark removed and replaced with statement indicating document uncontrolled when printed. Section on Clinical Trial Pharmacy removed. Process for completion of IRAS form, OID and SoECAT updated to reflect current practice.

8. APPROVAL

APPROVED BY	Date
Professor Alex Baldacchino, Research & Development Director, NHS Fife Signature: 	19 Feb 2020