

FLexor repAir and REhabilitation (FLARE) Trial

Associate Principal Investigator (API) Manual

Co-Chief Investigators: Matthew Gardiner and Emma Reay

Trial Manager: Liz Cook, York Trials Unit

Trial Coordinator: Emma Moatt, York Trials Unit

Trial Coordinator: Michelle Watson, York Trials Unit

1. Introduction

This manual provides information on the benefits, roles and responsibilities of a Specialty Trainee or other allied healthcare staff becoming an Associate Principal Investigator (API) with FLARE; how the role of the API in a clinical trial functions alongside the role of Principal Investigator (PI); the trial processes for FLARE; and the standards the trial team expect of participating PIs and APIs.

FLARE is registered with the NIHR scheme for API, which is aiming for junior doctors, nurses and allied health professionals to be the PIs of the future. APIs receive formal recognition of engagement in NIHR Portfolio research studies through the certification of API status, endorsed by the NIHR and Royal Colleges.

2. Background

Successful recruitment and retention of patients in research depends, to a considerable extent, on the structure and relationships within clinical research teams, in particular effective communication and recruitment skills. Treating clinicians play an important role in recruiting patients to a clinical trial. It is also our belief and aim that each patient should be considered by the clinician as a potential trial participant. We believe having dedicated APIs at each participating centre, with appropriate training and support provided by the PI, will help improve the patient experience of taking part in research, and improve recruitment and retention in trials.

3. The Associate Principal Investigator (API)

3.1 The role

A fundamental aspect of your role as API is to understand the role and responsibilities of a trial PI. You will not be required to undertake all these responsibilities fully, but they are listed in section 4 as an indication. As an API, you will be supporting the PI to achieve these tasks and responsibilities. This will help to integrate clinical research as part of your training and will help you to gain experience in local leadership of clinical trials, supported by mentors¹.

The NIHR scheme is **open to any junior doctor (FY1-ST8 or equivalent), nurse or other allied health professional** who is willing to make a significant contribution to the conduct and delivery of a surgical study at a local level¹. For FLARE, the API will work with the local consultant PI for the research study and to coordinate local trainee involvement. A commitment of at least 6 months will be required for gaining API status¹.

Trainees can be extremely effective in engaging and recruiting patients into clinical trials, particularly during out-of-hours work (evenings and weekends), when research teams may not be available. Secondary to this the API would be a source of information and advice locally within your hospital for Specialty Trainee (ST) colleagues. These local arrangements are at the discretion of the PI.

To register for the API scheme, first the applicants need to seek approval from the local PI and York Trials Unit (Trial Coordinator/Trial Manager), and follow the instructions provided on the NIHR API Scheme website¹.

3.2 Delegation of duties

The clinical trials regulations state: “A sponsor of a clinical trial, in accordance with this regulation may delegate any or all of his functions under these regulations to any person but any such arrangement shall not affect the responsibility of the sponsor”.

The principle of delegation of duties is that the duty can be delegated, but not the responsibility. This delegation may be from Sponsor to CI; CI to PI; PI to members of the site study team. At a study site, any duties that are delegated to the study team remain the responsibility of the PI. Each member of the team should perform their delegated duties adhering not only to research guidance and relevant legislation, but also to local Trust and professional body requirements.

The PI can delegate duties, but never the responsibility for the study at the site. The allocation of duties to appropriately qualified persons should be recorded in a study specific delegation log, with specimen signatures and the initials of all involved.

The API should expect to be guided by the PI on the conduct of FLARE at their site, where required. Team members must be appropriately trained before undertaking any delegated tasks on the study.

Please refer to the Site Staff Training section of the Trial Site Manual for further information regarding completing the FLARE delegation log.

3.3 Training

There are three training modules to complete, depending upon your role and responsibilities in the trial:

1. Trial Overview
2. Consent
3. Finger Range of Motion and Grip Strength Data Collection

The modules are accessible at www.flaretrial.com. **Everyone is expected to complete the Trial Overview training module.**

Please refer to Site Staff Training section of the Trial Site Manual for further information regarding completing training activities.

3.4 The Work

3.4.1 Recruitment

You may be involved in coordinating the recruitment of participants, particularly during out-of-hours clinical practice, when the trainee on call should identify potentially eligible patients and liaise with the API or PI to initiate the trial recruitment process. This does not mean you need to be in the hospital every weekend, but you will need to ensure that the on-call ST and other research staff are aware of the trial, the eligibility criteria, where the trial documentation is kept, and the processes for recruiting and randomising participants into the trial.

3.4.2 Consent

Once potentially eligible patients are identified for FLARE using screening/eligibility criteria through REDCap, it is expected that the API will facilitate eligibility confirmation by the treating clinician before initiating the trial consent and recruitment process.

You may be asked to determine the mental capacity of the patient – that is, their ability to receive, understand and weigh information and communicate a decision. Patients who lack mental capacity are not eligible for participation in this trial.

Potentially eligible patients with capacity will then be approached for voluntary, informed consent for the trial. The consent process will be coordinated by the API or a site research team member that has formal delegated duties to obtain consent for the trial, as detailed on the delegation log.

The API should instruct their trainee colleagues to identify potential patients for FLARE and pass on the details to the PI or local trial team. Eligible patients will be approached for trial consent by a designated member of the trial team.

3.4.3 Randomisation

Randomisation is completed online using REDCap. Randomisation must be completed by an unblinded member of the team. **Please ensure that you are familiar with the blinding arrangements at your site.**

3.4.4 Surgery

At the time of surgery, final eligibility will be assessed by a surgeon using the Eligibility and Randomisation instrument on REDCap. Ineligible patients will have their research participation stopped, be informed of this, and receive standard care.

Eligible patients will be randomised, and surgery will be completed by an unblinded member of the surgical team in accordance with their randomised treatment allocation. The repair of FDP alone or the repair of FDP and FDS should be completed as per standard practice.

To ensure the blind is maintained, please ensure the randomised treatment allocation is not discussed or recorded in any communications with the participant or blinded members of the team.

3.4.5 Follow-up activities

Unblinded team members who are aware of the participant's treatment allocation should not complete any of the participant's follow-up activities. Please note that blinded members of the surgical team can complete follow-up activities, provided they have not been involved with the participant's randomisation and surgery. Follow-up activities include obtaining finger Range of Motion (ROM) and grip strength measurements.

Please refer to the FLARE Trial protocol, trial site manual, and training modules for further information on the study processes.

3.5 Required Training, Knowledge & Documentation

3.5.1 Good Clinical Practice & Curriculum Vitae

To be eligible to work on the trial, research staff including APIs are required to have an authorised entry on the FLARE Trial Delegation Log (on REDCap), and go through the relevant training modules shared within the electronic investigator site file (eISF), or available online at www.flaretrial.com. You are also required to familiarise yourself with the key trial documents (such as the protocol, trial site manual, SIV slides, patient information sheet, informed consent form). After carrying out the above training, request a Study Specific Training certificate and record your FLARE Trial training, by clicking on 'Request your FLARE Study Specific Training Certificate' on the FLARE Trial website, completing the Google form and clicking submit. Access to the FLARE project on REDCap will then be granted by the YTU team. **Ensure the PI has authorised delegated tasks prior to completing any trial related activities.**

CV and GCP certificates are not required to work on this trial, except for PIs only.

Researchers are expected to maintain awareness of current standards through reference to published guidance and relevant policies. Study training and/or delegation logs should be updated when legislation has changed, new policies or practice have been implemented, different research activities are to be undertaken, or a significant period of time has elapsed since research activities have been conducted. NIHR has put together an API Toolkit to help potential APIs navigate the responsibility and support, available at

<https://sites.google.com/nihr.ac.uk/associatepi/scheme/toolkits/associate-pi-toolkit?authuser=0>

You should inform the PI and local research team of your last working day so that the Delegation Log can be updated. Also, you should then review and complete any pending tasks and paperwork; and handover to the PI/new API or members of the local research team as appropriate.

3.5.2 API Status Checklist and Certificate

The API Status Checklist should be completed during the API time period (available to download from NIHR Learn). Towards the end of the rotation or time period, the API should meet with the PI (and research delivery team) in order to review the checklist and if completed satisfactorily, the PI should sign it off. The checklist should then be forwarded to the York Trials Unit Trial Coordinator/Trial Manager for final confirmation that the activities described have been undertaken. When the checklist is fully signed, upload a copy via NIHR Learn. Once the checklist has been reviewed, if deemed to be successful, a certificate will be available for download.

3.6 The benefits

As the API, you will have the opportunity to be a named collaborator on the trial publication, which adds to your list of publications (please see the Collaborator Agreement and Points System section of the FLARE Trial Site Manual for further details of how to achieve this). Surgical Trainees can use it as part of the research requirements for CCT, depending on speciality. You will also gain valuable experience in trial processes which will be beneficial in your career.

3.7 API Scheme Alumni area within NIHR Learn

There is a dedicated API Scheme Alumni Area within NIHR Learn, which is open access to anyone with an NIHR Learn login (no application or enrolment key required). This area will further support an individual's pathway into research. Among other things, the resources available include:

- The Principal Investigator Learning Directory tile - which is available for those who are interested in gaining more research knowledge and are looking to take on the role of Principal Investigator in the future.
- The Making Local Connections tile - which will provide you with the details of Local Workforce Delivery Leads.
- An Alumni Forum, where APIs can connect with each other and share their experiences of the Scheme, what they have done since the Scheme and also share any ideas of what can be done after the API Scheme.

4. Principal Investigator

International Conference of Harmonisation GCP (ICH GCP) guidelines², define an investigator as “A person responsible for the conduct of the clinical trial at a trial site.” PIs are ultimately responsible for ensuring:

- The dignity, rights, safety, and wellbeing of participants are given priority at all times.
- The study follows the approved protocol.
- Procedures are in place to ensure the collection, processing, and storage of high-quality accurate data in accordance with the Data Protection Act 2018 and the Caldicott Principles (Please refer to sections 5.6 and 5.7)
- Each member of the research team is suitably qualified by education, training, and experience to conduct the study, and their qualifications and training details are documented.
- The study is conducted by the PI personally and/or members of your research team through authorised delegated duties.
- All necessary employment contracts, including honorary research contracts/letters of access, and other access arrangements are in place before the study starts.
- Students, new researchers, and those with delegated duties involved in the study have adequate supervision, support, and training.
- Appropriate arrangements are in place for obtaining informed consent for all participants, including those who cannot give consent themselves.

- If this is delegated to another member of the research team, it is the PI's responsibility to ensure this person has received adequate training to take informed consent.
- The relevant healthcare professionals or care staff will be adequately informed of subjects' participation in the study.
- Adverse events (AEs), serious adverse events (SAEs) and suspected unexpected serious adverse reactions (drug) (SUSARs) must be reported according to the Medicines for Human Use (Clinical Trials) Regulations 2004.
- Internal and external monitors/auditors are given access to documents, devices, and equipment as necessary.
- Arrangements are in place to archive the data when the research has finished, in line with the study requirements and local R&I / R&D policy.
- The API is supported in their role.

5. Relevant Legislation & Guidance

Listed below are some of the relevant legislations and guidance relating to the conduct of health and social care research in the UK, for your reference.

5.1 UK Policy Framework for Health and Social Care Research³

This policy framework sets out principles of good practice in the management and conduct of health and social care research in the UK.

These principles protect and promote the interests of patients, service users and the public in health and social care research, by describing ethical conduct and proportionate, assurance-based management of health and social care research, to support and facilitate high-quality research in the UK that has the confidence of patients, service users and the public. It is for organisations and individuals that have responsibilities for health and social care research. This includes funders, sponsors, researchers and their employers, research sites and care providers.

5.2 Mental Capacity Act⁴

The Mental Capacity Act (MCA) is designed to protect and empower individuals who may lack the mental capacity to make their own decisions about their care and treatment. It is a law that applies to individuals aged 16 and over. Examples of people who may lack capacity include those with unconsciousness caused by an anaesthetic or sudden accident.

5.3 Medicines for Human Use (Clinical Trials) Regulations 2004⁵

The Medicines for Human Use (Clinical Trials) Regulations 2004, set out the legal requirements for pharmacovigilance in clinical trials involving UK participants. The regulations cover:

- Definitions of adverse events
- The responsibilities of investigators for recording of adverse events and the notification of adverse events to sponsors
- The responsibilities of sponsors for reporting to competent authorities and ethics committees, including expedited reports of SUSARs and annual safety reports.

To comply with the regulations, those taking on pharmacovigilance responsibilities must ensure that the necessary quality standards are observed in case documentation, data collection, validation, evaluation, reporting and archiving of adverse events. This includes devising Standard Operating Procedures (SOPs) or equivalent written policies/guidelines.

5.4 HRA Guidance on Submission of Curriculum Vitae (CV)⁶

The template documents are highly recommended for use. See link in references ⁷.

5.5 The EU General Data Protection Regulation⁷

The EU GDPR is the most important change in data privacy regulation in 20 years and came into force in May 2018. Its aim is to protect all EU citizens from privacy and data breaches in an increasingly data-driven world. The UK Data Protection Act (2018) has been updated to follow the EU GDPR principles.

5.6 Data Protection Act 2018⁸

The Data Protection Act 2018 controls how personal information is used by organisations, businesses, or the government. The Data Protection Act 2018 is the UK's implementation of the General Data Protection Regulation (GDPR). Everyone responsible for using personal data has to follow strict rules called 'data protection principles'.

5.7 Caldicott Guardians & Principles⁹

Caldicott Guardians are the experts on confidentiality issues and access to patient records who are on-site to give you advice on any concerns that you may have about a case. The 'Caldicott' principles and recommendations apply specifically to patient-identifiable information, and emphasise the need for controls over the availability of such information and access to it. In particular, a Caldicott Guardian, appointed in each NHS organisation, has specific responsibilities to oversee an ongoing process of audit, improvement and control.

The eight Caldicott principles are:

- Justify the purpose(s) for using confidential information
- Use confidential information only when it is necessary
- Use the minimum necessary confidential information
- Access to confidential information should be on a strict need-to-know basis
- Everyone with access to confidential information should be aware of their responsibilities
- Comply with the law
- The duty to share information for individual care is as important as the duty to protect patient confidentiality
- Inform patients and service users about how their confidential information is used

6. References

1. National Institute for Health and Care Research (NIHR), Applying to be an Associate Principal Investigator
<https://www.nihr.ac.uk/health-and-care-professionals/career-development/applying-to-be-an-associate-principal-investigator.htm#eligible>
2. International Council for Harmonisation, Good Clinical Practice, n.d. 14th March 2017
<http://www.ich.org/products/guidelines/efficacy/efficacy-single/article/good-clinical-practice.html>
3. UK Policy Framework for Health and Social Care Research, last updated 30 October 2020,
<https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/>
4. Mental Capacity Act, 2005: <http://www.legislation.gov.uk/ukpga/2005/9/contents>
5. The Medicines for Human Use (Clinical Trials) Regulations 2004
<http://www.legislation.gov.uk/uksi/2004/1031/contents/made>
6. Health Research Authority, Prepare study documentation:
<https://www.hra.nhs.uk/planning-and-improving-research/research-planning/prepare-study-documentation/>
7. The EU General Data Protection Regulation. <https://eur-lex.europa.eu/legal-content/en/ALL/?uri=CELEX%3A02016R0679-20160504>
8. Data Protection. <https://www.gov.uk/data-protection>
9. The Caldicott Principles. <https://www.gov.uk/government/publications/the-caldicott-principles>