Oxford Experimental Medicine Clinical Research Facility (Oxford EMCRF) Operational Policy

Oxford EMCRF aims to provide a world class multi-speciality clinical research facility and clinical research service for translational research at the University of Oxford and Oxford University Hospitals NHS Foundation Trust.

PURPOSE

This document aims to provide an overview of the Oxford Experimental Medicine Clinical Research Facility's Operational Policies.

Further details about each section can be found in the relevant SOPs. This manual is based on the UKCRF Network QA Workstream Quality Manual Guideline (V2). The guidance template details the minimum requirements for a CRF quality system. Hence Oxford EMCRF Operational Policy has been developed using a tool which is recognised by the Chief Scientist Office, UKCRF Network and NHS NIHR for this purpose.

Note for readers

Relevant policies and procedures have been signposted, rather than reproduced in this manual. A full list of Standard Operating Procedures (SOPs) and Work Instructions (WI) are available within the QMS. Refer to the current, approved detailed instructions when performing specific duties and tasks.

An Oxford EMCRF Study Visit SOP and EMCRF Building and Facilities Guide for Study Teams is available which details daily activities and procedures within Oxford EMCRF.

Note for SOP editors and line managers

This document should not require frequent updating. However, it is a key document to signpost the main quality measures which all staff and stakeholders need to be aware. When drafting a new or amended procedures please consider if the Operational Policy may need to be amended.

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1 INTRODUCTION

The Oxford EMCRF is part of the NIHR Oxford Clinical Research Facility. The NIHR Oxford CRF supports the delivery of experimental research projects to the highest standards of research and clinical governance. The infrastructure and processes ensure that quality and safety considerations are embedded throughout the facility and promote a culture of continual quality improvement. The facility has a documented and maintained quality management system in accordance with the principles of GCP and all applicable regulatory requirements. Oxford EMCRF also aims to work to the best practice principles outlined by the NIHR UKCRF Network workstream and current MHRA Guidance for CRF accreditation. It takes a risk adaptive approach to assuring participant safety.

2 SCOPE OF EMCRF

Oxford EMCRF is multi-user, multi-speciality facility for early phase and experimental clinical research involving both patients and healthy volunteers. EMCRF is an adult facility. Whether a study is suitable for EMCRF will be based on study specific risk assessments. The risk assessments will consider the participant group, intervention type and how these can be managed in the facility.

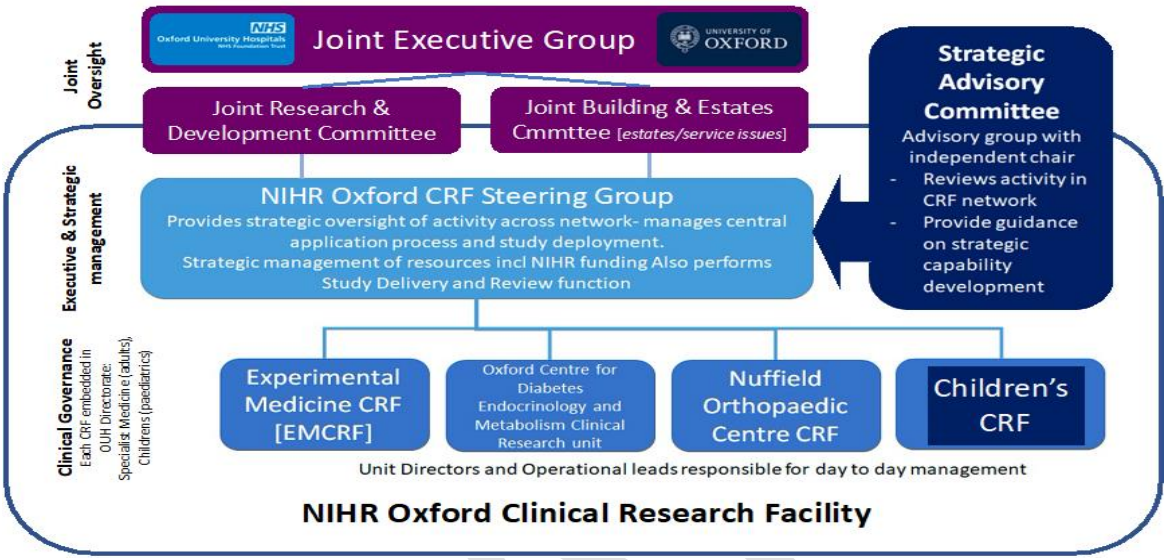
3 DEFINITIONS

Abbreviation	Definition
BRC	Biomedical Research Centre
CRF	Clinical Research Facility
HRA	Health Research Authority
ICH GCP	International Conference on Harmonisation Good Clinical Practice (E6 R2)
JEG	Joint Executive Group
JRO	Joint Research Office
MHRA	Medicines and Healthcare Products Regulatory Agency, UK
OUH	Oxford University Hospitals NHS Foundation Trust
Oxford EMCRF	Oxford Experimental Medicine Clinical Research Facility
QM	Quality Manual
QMS	Quality Management System
SDRC	Study Deliverability and Review Committee
SAC	Strategic Advisory Committee
SOP	Standard Operating Procedure
WI	Work Instructions

4 GOVERNANCE AND OVERSIGHT

Oxford EMCRF is a formal collaboration between the University of Oxford and the Oxford University Hospitals NHS Foundation Trust. A Collaboration Agreement exists detailing the legal components of the relationship and the division of responsibilities relevant to the relationship.

As a result of the collaboration, Oxford EMCRF has levels of management and responsibility through both institutions. These levels oversee the strategic objectives as well as the deliverability and conduct of the research. An organisational chart providing generic details is provided below to demonstrate the governance structure in the CRF.



* The organisational chart is approved by the Joint Executive Group (JEG) who oversee the collaborations of the University of Oxford and Oxford University Hospitals NHS Foundation Trust.

4.1 NUFFIELD DEPARTMENT OF ORTHOPAEDICS, RHEUMATOLOGY & MUSCULOSKELETAL SCIENCES (NDORMS)

The Nuffield Department of Orthopaedics, Rheumatology & Musculoskeletal Sciences (NDORMS) is the host department in the Medical Sciences Division at the University of Oxford for Oxford EMCRF. The facility sits within the Business Management systems of the department. NDORMS supports the facility by providing: a portal and system for financial transactions; patient and public involvement and engagement support; facilities management support; biological safety guidance and governance oversight representatives.

4.2 SPECIALIST MEDICINE DIRECTORATE

EMCRF is embedded within the Specialist Medicine Directorate for clinical governance purposes. This provides the organisation framework to ensure the CRF remains aligned with OUH clinical governance policies and procedures. EMCRF are represented at Directorate Executive Management and the Directorate Clinical Governance meetings.

4.3 EMCRF STAFFING

Oxford EMCRF employs a team of core staff who have been selected to ensure that they have the right qualifications, skills and competencies to carry out their roles. All core staff have clearly defined job descriptions.

All staff working with EMCRF are required to have either a substantive or honorary contract with OUH. In keeping with all substantive and honorary OUH staff, CRF staff will complete and maintain OUH Statutory and Mandatory training and, for clinical staff, an annual OUH appraisal will also be required.

5 MANAGEMENT RESPONSIBILITY AND ORGANISATIONAL STRUCTURE

5.1 STRATEGIC ADVISORY COMMITTEE (SAC)

A Strategic Advisory Committee (SAC) with an external independent chair has been established to provide strategic advice on capability development and to monitor the activity of the network of facilities. Details regarding roles and responsibilities are provided in OR-SOP-012_SAC_Charter.

5.2 NIHR OXFORD CRF STEERING GROUP

The NIHR Oxford CRF Steering Group provides executive and strategic management of the NIHR facilities. The Steering Group will provide the Scientific and Deliverability Review (SDRC) function by reviewing new business applications, conducting a proportionate risk assessment, and establish if studies can be effectively implemented in the facilities of the network. The Committee will also consider which facilities within the network are suitable for conduct of the proposed study. The committee is made up of representatives from: key stakeholders; the Joint Research Office (both University and Trust representatives); and Patient representatives. Details of the committee's role are provided in OR-SOP-005_Steering Group Charter.

5.3 OXFORD EMCRF OPERATIONS GROUP

The Oxford EMCRF Operations Group is primarily responsible for the implementation of the strategy for the facility and maintenance of the quality system and of day-to-day oversight of the operational policies within the EMCRF. Examples of the work of this committee include:

- Devise the implementation strategy for initiatives agreed at the SAC
- Review User Guidelines and SOPs
- Liaise with and report to the OUH Clinical Governance team regarding clinical activity in the facility
- Develop relevant SOPs
- Implement relevant SLA's for external services required
- Plan and respond to internal and external audits
- Review and respond to Customer Feedback and Complaints
- Provide oversight of Deviation Reports and CAPA projects relevant to the facility
- Identify and implement recommendations for improvement

5.4 OXFORD EMCRF DIRECTOR

The Oxford EMCRF Clinical Director shall act as the primary contact person for the OUH in relation to issues arising in connection with Oxford EMCRF, unless another postholder has been nominated in relation to a specific issue.

5.5 THE CLINICAL OPERATIONAL LEAD

The Oxford EMCRF Clinical Operational Lead is responsible for the activities of Oxford EMCRF. The post will be substantively employed by the OU, have honorary clinical research status in the OUH and will ensure relevant policies and procedures from both institutions are considered in the operational policy of the facility. They shall be the first point of contact for both the OU and OUH issues arising in connection with Oxford EMCRF.

6 QUALITY MANAGEMENT SYSTEM

The Operational Team and Steering Group are committed to resource the quality management system and operational policies to meet regulatory requirements and to maintain and improve the effectiveness of the quality management system and its processes. Policies from both the OUH NHS Foundation Trust and the University of Oxford have informed the operational processes of the facility.

6.1 Study Management models

Oxford EMCRF can provide a range of study site services by agreement with the trial PI and Sponsor. These will be decided via delegation and trial agreements. It offers three basic delegation models:

1. **Full:** All study site operations managed by Oxford EMCRF on behalf of the PI, includes site administration, management of participant visits and follow-up, liaison with monitor/ sponsors and provision of clinical cover.
2. **Partial:** A bespoke agreement by which study site responsibilities are shared between the PI study team and Oxford EMCRF.
3. **Minimal**: the PI study team arranges to use Oxford EMCRF to perform participant visit procedures and access specialist cover and resources.

Oxford EMCRF QMS and procedures will apply to any activity delegated or performed within it. These will include assurance that arrangements are feasible.

6.2 Internal Audits

The CRF will plan and conduct a regular programme of internal audit as per **OR-SOP-016 Internal audit.** The aim is to verify the QMS effectiveness in delivering the required operational standards and help achieve continuous quality improvement.

The internal audit programme will include all aspects of the CRF operations. Hence everyone is required to cooperate and participate in audit activities. The internal audit will address the CRF priorities and requirements.

6.3 Clinical Audits

The facility will participate in clinical audits as per OUH policy and procedures.

6.3.1 Third Party Audits

Oxford EMCRF may be required to accommodate audits conducted by third parties. These may be regulatory authorities or study specific audits. Reports will be sent to the Oxford EMCRF Management Committee and feedback filtered accordingly. Findings in these audits may inform policy and procedure reviews.

6.3.2 Training

The CRF ensures that all staff working in the CRF, including core staff and study team members, are appropriately qualified and have received adequate training to enable them to carry out their duties and the duties delegated to them by the PI.

6.4 Oxford EMCRF Induction

Induction is mandatory for everyone coming to work in the facility and will include:

- Registration onto the induction programme
- Provision of a welcome pack/user guide
- Attend the induction training/orientation session
- Provision and validation of required CV & GCP and other training documents
- Read and sign assigned Oxford EMCRF SOPs and policies
- Completion of mandatory role-based training plus any identified individual training or refresher needs
- Complete induction check list
- Agree on-going training/mentoring plan

7 Patient & Public Involvement and Engagement (PPIE)

PPIE in Oxford EMCRF will be undertaken in both an oversight capacity (as a representative on the SAC) and in working with research teams presenting with an “involvement gap”. Engagement and outreach work will be

conducted in collaboration with the research groups' own activities as well as Oxford EMCRF specific ones. The aim of engagement is to improve involvement through the research process in the facility. See the NIHR Oxford CRF PPIE Strategy for further details https://www.ndorms.ox.ac.uk/oxford-emcrf/patient-and-public-involvement-and-engagement-ppie-1.

8 Risk Management and Study Approval Process

PIs and study teams wishing to run their study in a CRF apply to do so. Study applications are risk assessed; reviewed by the SDRC and costed up accordingly. All studies will still process through standard OUH NHS Trust Research & Development Trust Management Approval process.

8.1 Risk Assessment & Study Review

The Risk Assessment and Study Review process is detailed in the Risk Assessment SOP OR-SOP-004. The review process identifies any mitigation measure considered important to conducting the study within EMCRF. The risk assessment will seek to distinguish between the risk associated with:

- The study intervention
- The study design and procedures
- Other feasibility and business considerations

The study will be reviewed by the Study Deliverability Review Committee (part of the Steering Committee). They will assess:

- Scientific merit and fit with current strategic objectives
- Operational considerations and deliverability – including participant safety
- Alignment with the clinical profile of participants and clinical procedures which EMCRF have capabilities to support (see Appendix 1 – EMCRF Clinical Procedures)

Issues to be resolved before the study is given the Green Light for the study will be communicated to the study team and PI. Satisfactory resolution of these issues is required and will be documented before the study is activated in the facility.

9 Study Conduct

9.1 Responsibilities

The PIs and their study teams remain responsible for the study conduct and activities in Oxford EMCRF.

9.1.1 Principle Investigators:

- Patient safety, the overall conduct of the study and for members of their research team
- Ensuring members of their research team have appropriate contracts with the host institution (research, honorary, substantive or letter of access)
- Ensuring their research team members have appropriate training
- Providing appropriate medical cover for their participants
- Provide CRF with protocol amendment details for review

The Oxford EMCRF team will inform PIs and their study teams about any changes to the facility resources and procedures.

9.1.2 Study teams

Principal Investigators will provide Oxford EMCRF with the contact details of all study staff who need to be granted access to the facility. Their induction needs to be completed as part of the study set-up procedure. Changes to study team personnel must be notified to Oxford EMCRF without delay to maintain continuity.

Study team members will be registered via the new user application form and an induction checklist opened. This explains the induction process and information needed to become an approved user with swipe card access.

9.2 Medical Cover

Oxford EMCRF will not provide medical cover for studies. This must be organised and agreed by the individual study teams, per study. The required level of cover and any special arrangements are assessed during the study onboarding process and agreed prior to green light. The name and contact details of study specific medical cover will be provided by the study team during the study set-up process.

9.3 Medical Emergency arrangements

Oxford EMCRF has an Emergency Transfer SOP which is used for studies that do not have protocol-defined arrangements. EMCRF may also develop guidance document for management of medical emergencies (e.g. cytokine release syndrome) as needs dictate.

9.4 Other Emergencies

The unit business continuity plan defines the actions to be taken in the event of complete or partial failure of key services (e.g. electrical, water).

9.5 Incident Reporting

Oxford EMCRF has an Incident Reporting SOP which details lines of responsibility in both the University and the OUH Trust; how different incidents will be reported and how they are managed. Clinical incidents, and incident involving OUH staff are reported via the OUH Ulysses system. Incidents related to the physical facility, laboratory incidents and incidents involving University staff are reported via the University's ISIS system.

9.6 Study Specific Safety Reporting

PIs and study teams are responsible for ensuring that all Adverse Events (AEs), Serious Adverse Events (SAEs) and Suspected Unexpected Serious Adverse Reactions (SUSARs) that occur within Oxford EMCRF are recorded and reported in compliance with the study protocol, Sponsor requirements and regulatory requirements.

9.7 Progress Reports

Study progress will be reviewed regularly by the NIHR Oxford Steering Group. The information in these reports will inform the deliverability and capacity for in-coming studies and also inform EMCRF stakeholder reports. Reports submitted to the Joint Research Office will be shared with EMCRF.

9.8 Trial closure and archiving

The Declaration of the End of Trial form (CTIMPs) or the HRA declaration of the End of Study form (non-CTIMPs) must be submitted to oxcrf@ndorms.ox.ac.uk once the study is completed. The study team retain responsibility for archiving of their study documents. There are no archiving capabilities within the facility.

9.9 Withdrawal of support

Oxford EMCRF reserves the right to suspend work on any project conducted in the facility should staff become concerned about participant or staff safety or research governance e.g. deliberate protocol violation or deviation or Oxford EMCRF processes and SOPs.

10 FINANCE

Both the University and OUHT have finance processes which need adhering to. Arrangements for charging studies; how funding flows between the two institutions and operational costs are detailed in EMCRF Finance SOPXXXX.

11 PREMISES

Oxford EMCRF provides and maintains adequate infrastructure needed to provide services to our users and conform to required regulations and local policies including:

- Buildings, workspace and associated utilities
- Process equipment (both hardware and software)
- Support services (i.e. communication etc.)

Facilities Management services for the capital building and equipment are provided through NDORMS and the University of Oxford Estates Services. Soft facility services are provided from both external service providers and the OUH NHS Trust. All facilities services are undertaken according to an agreed schedule and appropriately adhere to OUH NHS Trust or University standards.

12 PUBLICATIONS POLICY

Investigators must acknowledge Oxford EMCRF in publications and inform Oxford EMCRF of all publications that relate to work facilitated by the Oxford EMCRF, either physically or intellectually. The following statement must be included in all appropriate publications:

This study is funded/supported by the National Institute for Health and Care Research (NIHR) Clinical Research Facility (CRF). Conduct of the study was supported by the NIHR Oxford Clinical Research Facility. The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

13 REFERENCES

- ICH GCP Guideline (CPMP/ICH/135/95)
- EU Directive 2001/20/EC
- EU Directive 2003/94/EC
- EU Directive 2005/28/EC
- The Medicines for Human Use (Clinical Trials) Regulations 2004, as amended
- The Research Governance Framework for Health and Social Care, v3.3
- MHRAs guidelines: 'Guidance on the maintenance of regulatory compliance in laboratories that perform the analysis or evaluation of clinical trial samples'
- The clinical and research governance provisions of the Oxford University Hospital NHS Trust R&D Office and applicable Trust policies.
- The clinical and research governance provisions of Oxford University Research Governance, Ethics and Assurance (RGEA)

14 APPENDIX 1 – EMCRF CLINICAL PROCEDURES

Clinical Procedure	Description
Routine clinical procedures	
Weight and height	
Blood pressure	Taken using automated or manual machines
ECG	Specific equipment with battery back up
Venepuncture	Collection of blood from a vein
Cannulation	Insertion of small plastic cannula into vein
Lung function	Measurement of lung function using dedicated equipment
Drug administration:	All will follow OUH procedure
Injections- intramuscular, intradermal, subcutaneous	Delivered by hypodermic needle
Infusion – intravenous	Delivered through a cannula
Oral	
Suppository	
Intranasal	By instillation or spray
Intrathecal	Specialist procedure
Intra-articular	Specialist procedure
Specialist procedures	
Fine Needle aspiration (lymph nodes)	With or without ultrasound guidance
Local anaesthetic	
General anaesthetics will not be administered on EMCRF. Some procedures may involve light sedation	
Arterial line	Small cannula placed into artery- usually in arm. Sometimes use local anaesthetic
Lumbar puncture	Needle in back to collect fluid from around spinal cord. Local anaesthetic
Skin biopsy	Punch biopsy of skin. Local anaesthetic
Synovial biopsy	Needle biopsy of joint lining. Local anaesthetic. Ultrasound guidance
Joint injection	Needle injection into joint.
Lip biopsy	Small biopsy of lip under local anaesthetic
Laser Doppler assessment of skin blood flow	Non invasive assessment using a CE marked device
Future specialist procedures	
NB these procedures will be low throughput 1-2 procedures per morning or afternoon	
Flexible sigmoidoscopy	Telescope examination of lower bowel. Does not usually require sedation
Upper GI endoscopy	Telescope examination of stomach. Usually does not require sedation
Colonosopy	Telescope examination of full lower bowel. Sedation usually used
Bronchoscopy	Telescope examination of lungs. May include sedation