Reference Number: UHB 247 **Version Number:** 3	**Date of Next Review: 28th April 2024** **Previous Trust/LHB Reference Number:** UHB 135 &136

OVERSIGHT AND MONITORING IN RESEARCH
STANDARD OPERATING PROCEDURE

Introduction and Aim

The procedure aims to provide detail regarding the oversight and monitoring arrangements for research conducted within Cardiff and Vale University Health Board (UHB) and supports the Research Governance Policy (UHB 099) in ensuring that research conducted within the UHB is of a high quality, complies with the law, is relevant, ensures that patient dignity, rights and wellbeing as well as financial probity is maintained.

Study oversight provides quality control checks and processes which enables studies, whether subject to planned monitoring or not, to have management and quality controls systems in place to protect the organisation in its role as sponsor or host.

The procedure is to be used when the UHB is either sponsoring or hosting externally sponsored research to enable all aspects of Research Governance oversight to be managed.

Objectives

- To provide detail of all the activities required to oversee a study throughout the study period. To describe responsibilities when the UHB is acting as Sponsor and when the UHB is hosting the research

Scope

This procedure applies to all individuals undertaking or involved in UHB Sponsored or hosted research within the UHB where the individual has any responsibility for oversight activities.
It also describes the responsibilities of the CI/PI in relation to study oversight activities This includes those individuals:

- holding substantive or honorary contracts/titles with the UHB;
- holding 'letters of access' to UHB;
- undertaking clinical research involving UHB patients or staff;
- undertaking clinical research on UHB premises

Equality Health Impact Assessment	An Equality Impact Assessment has been completed on the Research Governance Policy (UHB 099) under which this SOP sits. The Equality Impact Assessment completed for the policy found there to be no impact.

Documents to read alongside this Procedure	Research Governance Policy (UHB 099). Research Audit SOP (UHB 236) Managing Breaches of GCP or the Study Protocol SOP (UHB 235) Investigating and Handling Allegations of Research Misconduct SOP (UHB 145) Applying for C&V UHB Sponsorship SOP (UHB 457)
Approved by	Research Governance Group

Accountable Executive or Clinical Board Director	*Medical Director*
Author(s)	*Research Governance Manager*

Summary of reviews/amendments

Version Number	Date of Review Approved	Date Published	Summary of Amendments
1	20/01/15	26/03/15	Both of the existing monitoring SOPs UHB135 & UHB136 were due for renewal in October 14. This new SOP will replace both previous SOPs as an overarching oversight and monitoring SOP. Behind this SOP a suite of workplace instructions will detail the various stages of monitoring studies.
2	06/02/18	29/03/18	Review date 20/01/18 therefore this SOP has been reviewed and minor changes made throughout for consideration at RGG. The document has been placed in the most recent UHB template.
3	28/04/2021	22/06/2021	Minor changes: -updates of reference documents -update of author job title -removal of references to CaRRS and Host Quality Assurance Visits -removal of the requirement for a signed COMA for sponsored research studies (superseded by condition of sponsorship TR-RG-018)

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1. OVERSIGHT

All studies will have an element of oversight by the sponsor, which varies depending on the type of study (e.g. CTIMP, non CTIMPs) and in the case of UHB Sponsored CTIMPs, Sponsored Interventional Trials such as a surgical or device trials, the risk will be reviewed and determined during the Sponsor Assessment Process (SAP). Please refer to the document ‘Applying for Cardiff

and Vale University Health Board Sponsorship' SOP (UHB457) for further detail.

Study oversight can consist of:

a) Monitoring
b) Auditing
c) External Agreement oversight
d) Study tracking

For UHB Sponsored CTIMPs, surgical and device trials it is expected that the type, frequency and intensity of these oversight activities will be documented within a Trial Monitoring Plan (TMP) and study specific Risk Assessment Form (RAF).

If there is evidence of noncompliance with oversight activities such as monitoring, audit or other it may be necessary to manage the issues under the appropriate UHB policies and procedures such as Managing Breaches of Good Clinical Practice or the Study Protocol SOP (UHB 235), Investigating and Handling Allegations of Research Misconduct SOP (UHB 145), or the Research Governance Policy (UHB 099).

2. MONITORING

Monitoring is defined as 'the act of overseeing the progress of a clinical study, and of ensuring that it is conducted, recorded and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP) and the applicable regulatory requirement(s).'

In CTIMPs the current regulatory framework in the UK/EU allows for a range of risk-adapted approaches that may simplify the processes for initiating and conducting some clinical studies. These adaptations are largely related to how much is known about the investigational medicinal product (IMP) and standard medical care. The Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products was published in 2011 by the MRC/DH/MHRA to assist sponsor organisations to undertake risk assessment. Using a simple categorisation of three risk types (see below) it is possible to highlight, particularly for lower risk studies, where simplification is possible, resulting in a more risk proportionate approach.

- Type A = No higher than the risk of standard medical care
- Type B = somewhat higher than the risk of standard medical care

- Type C = markedly higher than the risk of standard medical care

The risk assessment for the study takes into consideration the type of study as well as the identification of areas of potential vulnerability in study design and planned methodology, which may require mitigation activities to ensure the reliability of the study results and to protect participants' rights.

For UHB sponsored CTIMPs, surgical and device trials the risk assessment for the study is developed during the Sponsor Assessment Process (SAP) using the Risk Assessment Form (RAF). From the completed RAF a proposed Trial Monitoring Plan (TMP) should be developed and reviewed during the SAP. The members of the SAP panel should review the RAF and TMP to determine the oversight and monitoring requirements for each study based on the perceived overall level of risk associated with the study.

Type A studies should require less frequent monitoring than a study assessed as Type B or C as detailed above. For Type C studies that may include any multicentre studies, the CI will usually need to convene an independent Study Steering or Data Monitoring Committee (DMC) to oversee study conduct and safety issues.

For CTIMPs, surgical and device trials sponsored by the UHB some monitoring duties will normally be delegated to a Clinical Trial Unit (CTU) and will be detailed in the agreement between each CTU and UHB. The detail will be transparent within the roles and responsibilities section of the study specific contract agreement.

For all sponsored studies, monitoring and oversight responsibilities delegated to the CI are outlined and agreed in the Terms and Conditions of Sponsorship (TR-RG-018).

For hosted non-commercial CTIMPs some monitoring duties will be delegated to the PI as part of normal day-today 'housekeeping', as agreed in the Conditions of Management Approval (COMA).

Monitoring activities can be delegated to external parties as set out in the study specific agreement but the sponsoring organisation is still accountable.

Where the IMP Management for a UHB-Sponsored CTIMP has been delegated to the CI/PI/CTU, the appropriate Clinical Trials Pharmacist will review and approve the conditions during the SAP. The Clinical Trial Pharmacist may carry

out monitoring of that particular area to ensure GCP compliant processes are being followed.

All monitoring activities such as site initiation, routine monitoring, close down visits and other monitoring activities will be conducted using the appropriate Sponsor, UHB and/or CTU policies and procedures.

For all research involving UHB patients for whom the UHB retains the duty of care, study-specific monitoring arrangements as outlined in the study protocol and/or agreements are reviewed by the R&D Office as part of the capacity and capability (C&C) assessment process. This is done prior to confirming that the site has the capacity and capability to deliver the study and ensures that the Sponsor's proposed monitoring arrangements meet the UHB's Research Governance requirements. C&C assessment is part of the UK-wide HRA/HCRW Approval process.

3. AUDIT

Audits are a mechanism for implementing quality assurance. The prime purpose is to evaluate study conduct and compliance with the protocol, SOPs, GCP and any other applicable regulatory requirements.

Auditing is a separate process from monitoring and acts as an assessment of compliance with the applicable standards at a specified point in time. Please refer to the Research Audit SOP (UHB236) which outlines the scope and procedure for research audit activity within the UHB.

4. AGREEMENT OVERSIGHT

The R&D office provides oversight support when required for the CI to ensure agreement obligations are met by other parties. When issues arise, the R&D office is expected to provide support and follow up on any actions given to the CI to resolve the issues.

For UHB sponsored CTIMP, surgical and device studies the potential issues and risks should be noted during the study set up as part of the SAP and documented in the TMP and RAF as detailed above in section 2. The RAF is kept updated throughout the study and reviewed as required by the CI/Sponsor/CTU e.g. substantial amendment, change of provider or other. Please refer to the document Applying for Cardiff and Vale University Health Board Sponsorship SOP (UHB457) for further detail.

5. STUDY TRACKING

It is expected that the R&D office will be aware of all studies being sponsored and hosted by the organisation. The R&D office is expected to ensure up to date information is stored regarding active and closed sponsored studies. The Sponsor is accountable for ensuring periodic reports are submitted within appropriate timelines. Annual reports must be reported to REC, and for CTIMPS an annual Development Safety Update Report must be submitted to MHRA. Where the UHB is the Sponsor, responsibility for compiling and submitting these reports has been delegated to the CI.

6. TABULATION OF PROCEDURE FOR OVERSIGHT OF UHB SPONSORED STUDIES

(Please note throughout this table studies which fall into the category of a C&V UHB Sponsored Clinical Trials of Investigational Medicinal Products (CTIMPs), surgical and device trials the acronym CTIMP will be used)*

	ACTIVITY	**RESPONSIBILITY**	**UNDERTAKEN BY**	**CTIMP*/ ALL**
OVERSIGHT				
1	During the Sponsor Assessment Process detailed in 'Applying for Cardiff and Vale University Health Board Sponsorship' SOP (UHB457) review and ensure oversight activities and frequency are appropriate for the risks associated with the study.	Sponsor (typically delegated to the R&D office)	Members of SAP	**ALL**
2	Develop a study specific Trial Monitoring Plan (TMP), detailing the frequency and intensity of oversight activities.	Sponsor (typically delegated to the R&D office)	CI/RGT/CTU	**CTIMP***

	ACTIVITY	RESPONSIBILITY	UNDERTAKEN BY	CTIMP*/ ALL
3	Ensure that all necessary arrangements are in place to deliver the study at this site prior to confirming capacity and capability	Sponsor (typically delegated to the R&D office)	RGT	**ALL**
MONITORING				
1	Monitoring activities delegated to a CRO/CTU must be agreed in writing prior to study start in a suite of documents RAF, TMP, Contract agreements. Please refer to the document Applying for Cardiff and Vale University Health Board Sponsorship SOP (UHB 457) for further detail	Sponsor (typically delegated to the R&D office)	CI/RGT/CRO /CTU	**CTIMP***
2	Conduct on site or central monitoring in line with agreed TMP and contract agreement	Monitoring service provider (typically CRO/CTU)	Appropriately trained monitor	**CTIMP***
3	Ensure any issues highlighted during monitoring are resolved through appropriate actions	Monitoring service provider (typically CRO/CTU **)**	CI/PI	**CTIMP***
4	Follow up with CI on actions which have arisen through monitoring activity	Monitoring service provider (typically CRO/CTU)	Appropriately trained monitor	**CTIMP***
5	Report monitoring activity to C&V R&D	Monitoring service provider (typically CRO/CTU)	Appropriately trained monitor	**CTIMP***
6	Report monitoring activity to C&V Research Governance Group (RGG)	R&D office	RGT	**CTIMP***

AUDIT				
1	For CTIMPs routine audits will be performed with priority to Type C studies followed by Type B & A. A subset of CTIMP* and non-CTIMP studies will be audited as per annual audit plan	R&D office	RGT	**ALL**
2	'For Cause' audit may be performed where there are concerns in relation to the conduct of a study e.g. incidents, serious breach, external audit findings or other	R&D office	RGT	**ALL**
AGREEMENT OVERSIGHT				
1	Ensure external agreements are signed as appropriate prior to the commencement of study at sites or at the start of contracted services	R&D office	Contracts Manager	**ALL**
2	Confirm that the CI has signed Terms and Conditions of Sponsorship TR-RG-018	R&D office	RGT	**ALL**
3	If an agreement/contract issue or risk arises during the study, escalate the matter and seek support from the relevant parties.	Sponsor (typically delegated to the CI)	CI	**ALL**
4	Manage the resolution of the risk/issue with the CI/CTU or research team in a proportionate way based on risk	R&D office	CI/RGT/CTU /CRO	**ALL**
STUDY TRACKING				
1	Conduct the agreed study tracking activities (from the agreed monitoring plan) with the CI in order to track the progress of the study. E.g. receipt of an annual report from the CI/PI.	R&D office	CI/RGT/CTU/CRO	**ALL**
2	Where requested by R&D, the CI must provide relevant study information e.g. recruitment figures, numbers of SAEs/other to comply with any other reporting requirements from National Bodies.	CI	CI/research team	**ALL**

3	Inform the R&D office of any changes made to the study after initial approval e.g. change of Principal Investigator, protocol amendments, extension of funding, changes to end dates ensuring confirmation of appropriate approvals.	CI	CI/research team	**ALL**
4	Review of any changes made to the study after initial approval e.g. protocol amendments, extension of funding, changes to end dates ensuring confirmation of appropriate approvals. For CTIMP,* updating RAF as appropriate as study is progressing to ensure the oversight/ TMP put in place at study start is still relevant to manage the risks associated with the study.	R&D office	R&D/RGT	**ALL**
5	Review reports, record and store annual reports provided.	R&D office	R&D/RGT	**ALL**

7.0 TABULATION OF PROCEDURE FOR OVERSIGHT OF UHB (HOSTED) EXTERNALLY SPONSORED STUDIES (excluding commercial contracts)

	ACTIVITY	**RESPONSIBILITY**	**UNDERTAKEN BY**	**CTIMP/ NON-CTIMP**
OVERSIGHT				
1	Conduct Research Governance checks and review external agreements prior to confirmation of capacity and capability	Sponsor (typically delegated to the R&D office)	R&P/Contracts Manager	**ALL**
2	Ensure all governance checks are satisfied (in line with HRA/HCRW guidelines) prior to confirmation of capacity and capability	Sponsor (typically delegated to the R&D office)	R&P	**ALL**

	ACTIVITY	RESPONSIBILITY	UNDERTAKEN BY	CTIMP/ NON-CTIMP
MONITORING				
1	The sponsor is responsible for monitoring hosted research.	Sponsor or delegate	Relevant monitor	**ALL**
2	Make available relevant SOPs/Guidance documents to ensure the safety of UHB participants and staff	R&D office	R&D office	**ALL**
3	Report monitoring activity to C&V R&D if requested by R&D	Monitoring service provider (typically CRO/CTU)	Relevant monitor	**CTIMP***
4	Report monitoring activity to C&V Research Governance Group (RGG)	R&D office	RGT	**CTIMP***
AUDIT				
1	PIs of externally sponsored non-commercial studies may complete a CTIMP self- audit as directed	R&D office	PI/Research team	**CTIMP**
2	Consider conducting a For-Cause audit where concern has been raised in relation to the conduct of a study e.g. incidents, breaches of GCP, or as a result of internal/external audit or monitoring findings.	R&D office	RGT	**ALL**
EXTERNAL AGREEMENT OVERSIGHT				
1	Ensure agreements are signed as appropriate prior to the commencement of study at sites or at the start of contracted services	Sponsor/R&D office	Contracts Manager	**ALL**
2	Confirm that the PI has signed a Conditions of Management Approval (COMA)	R&D office	R&P	**CTIMP**

STUDY TRACKING				
1	Inform the R&D office of any changes made to the study after initial approval e.g. protocol amendments, extension of funding, changes to end dates ensuring confirmation of appropriate approvals	PI	PI/research team	**ALL**
2	Review of any changes made to the study after initial approval e.g. protocol amendments, extension of funding, changes to end dates ensuring confirmation of appropriate approvals	R&D office	R&P	**ALL**
3	Where requested by R&D the PI must provide relevant study information e.g. recruitment figures, numbers of SAEs/other to comply with any other reporting requirements from National Bodies.	PI	PI/research team	**ALL**
4	Acknowledge reports, record and store annual reports provided.	R&D office	R&P	**ALL**

8.0 GLOSSARY OF TERMS

CaRRS -. Cardiff and Vale Research Review Service
CI - Chief Investigator
COMA- Conditions of Management Approval
CRO - Contract Research Organisation
CTIMP - Clinical Trial of Investigational Medicinal Product
CTIMP* - UHB Sponsored Clinical Trial of Investigational Medicinal Product, surgical or device trial
CTU- Clinical Trial Unit
DSUR- Development Safety Update Report
GCP - Good Clinical Practice
HCRW- Health and Care Research Wales
HRA- Health Research Authority
ICH - International Conference for Harmonisation
IMP - Investigational Medicinal Product
MHRA - Medicines and Healthcare products Regulatory Agency
PI - Principal Investigator
PV – Pharmacovigilance

RAF- Risk Assessment Form
R&D - Research & Development
R&P- Research and Permissions Manager
RGT- Research Governance Team
REC - Research Ethics Committee
SAE- Serious Adverse Event
SAM- Sponsor Assessment Meeting
SAP- Sponsor Assessment Process
SIV- Site Initiation Visit
SOP - Standard Operating Procedure
TMP – Trial Monitoring Plan
UHB - University Health Board

Chief Investigator -The investigator with overall responsibility for the research. In a multi-site study, the CI has co-ordinating responsibility for the research at all sites. The main application for ethical review should be submitted by the CI.

Principal Investigator - The investigator responsible for the research site where the study involves specified procedures requiring site specific assessment by the local R&D Office. For multi-site studies, there should be one PI for each research site. In the case of a single-site study, the CI and the PI will normally be the same person.

External Sponsor– This means any Sponsor of a CTIMP other than Cardiff and Vale UHB. An External Sponsor may be a Commercial organisation (e.g. a Pharmaceutical company) or a Non-Commercial organisation (e.g. another Local Health Board, NHS Trust or University, including Cardiff University).