Reference Number: UHB 247 **Version Number:** 5.0	**Date of Next Review: 16/07/2029** **Previous Trust/LHB Reference Number:** UHB 135 &136

OVERSIGHT AND MONITORING IN CLINICAL RESEARCH STANDARD OPERATING PROCEDURE

Introduction and Aim

The procedure aims to provide detail regarding the oversight and monitoring arrangements for research sponsored by Cardiff and Vale University Health Board (CAVUHB) or Cardiff University (CU) and supports the Research Governance Policy (UHB 099) in ensuring that research conducted 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 for:

- CU Sponsored studies
- CAVUHB Sponsored studies
- Externally sponsored studies hosted by CAVUHB.

Objectives

To provide detail of all the activities required to oversee a study throughout the study period. To describe responsibilities when either CAVUHB or CU is acting as Sponsor or when CAVUHB is hosting the research.

Scope

This procedure applies to all individuals undertaking or involved in CU or CAVUHB Sponsored research and studies hosted within CAVUHB where the individual has any responsibility for oversight activities.
It also describes the responsibilities of the Chief Investigator (CI) and Principal Investigator (PI) in relation to study oversight activities. This includes those individuals:

- holding substantive or honorary contracts/titles with CAVUHB;
- holding substantive contracts or honorary titles with CU;
- holding ‘letters of access’ to CAVUHB;
- undertaking clinical research involving CAVUHB patients or staff;
- undertaking clinical research on CAVUHB 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) Cardiff University Code of Practice for Research Integrity and Governance **SOP-001-005 (UHB 543**) Joint SOP for Applying for Sponsorship of Higher Risk Studies (including Clinical Trials of Investigational Medicinal Products (CTIMPs) and Clinical Trials of Medical Devices (Medical Device Trials) **SOP-001-007 (UHB 525)** Joint SOP for Obtaining Sponsorship- Low and Medium Risk Studies
Approved by	Joint Research Governance Group

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

Disclaimer

If the review date of this document has passed, please ensure that the version you are using is the most up to date either by contacting the document author or the Governance Directorate.

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 TPL/002/01)
4	18/04/2024	06/06/2024	Naming conventions updated and confirmed. Minor changes around including new risk assessment process for all studies

5	16/07/2026	29/07/2026	Updated to reflect this is a joint SOP to cover CAVUHB and CU sponsored clinical research and in line with the amended UK Clinical Trial Regulations (effective from 28/04/26) and ICH GCP E6 (R3). Removal of requirement to provide Annual progress reports to REC Updated terminology; amendments are now referred to as modifications

Contents

1. ABBREVIATIONS AND DEFINITIONS

AE	Adverse Event
ARSAC	Administration of Radioactive Substances Advisory Committee
ATMP	Advanced Therapy Medicinal Product
C&C	Capacity and Capability
CAG	Confidentiality Advisory Group
CAVUHB	Cardiff and Vale University Health Board
CE	Conformité Européene (CE)
CI	Chief Investigator
CRO	Contract Research Organisation
CTIMP	Clinical Trials of Investigational Medicinal Products
CTU	Clinical Trials Unit
CU	Cardiff University
DMP	Data Management Plan
DSUR	Development Safety Update Report
GCP	Good Clinical Practice
HCRW	Health and Care Research Wales
HRA	Health Research Authority
IB	Investigator's Brochure
ICH	International Conference on Harmonisation
ICSR	Individual Case Safety Report
IMP	Investigational Medicinal Product
IMPD	Investigational Medicinal Product Dossier
IRAS	Integrated Research Application System
JRO	(Cardiff) Joint Research Office
MHRA	Medicines and Healthcare Products Regulatory Agency
MoU	Memorandum of Understanding
mNCA	Model Non-commercial Clinical Trial Site Agreement
OID	Organisation Information Document
PI	Principal Investigator
PIM	Project Initiation Meeting
PV	Pharmacovigilance
QMG	Quality Management Group
QMS	Quality Management System

RAF	Risk Assessment Framework
REC	Research Ethics Committee
RGT	Research Governance Teams (JRO)
R&D	Research and Development
RSI	Reference Safety Information
SAP	Sponsor Assessment Process
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SIV	Site Initiation Visit
SmPC	Summary of Product Characteristics
SOP	Standard Operational Procedure
SoE	Schedule of Events
SoECAT	Schedule of Events Cost Attribution Template
SSAR	Suspected Serious Adverse Reaction
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File
TMG	Tial Management Group
UKCA	UK Conformity Assessment
UK-CRC	UK Clinical Research Collaboration
UKPF	UK Policy Framework for Health and Social Care Research 2017 (as amended)
USM	Urgent Safety Measure

2. OVERSIGHT

In accordance with the UK Policy Framework for Health and Social Care (as amended), the Sponsor retains ultimate responsibility for the oversight of a clinical research study and is responsible for "...ensuring that effective procedures and arrangements are kept in place and adhered to for reporting (e.g. progress reports, safety reports) and for monitoring the research...". The level of Sponsor oversight will depend on the risk profile of the study, for example, whether the study is a Clinical Trial of an Investigational Medicinal Product (CTIMP) or other higher risk study as defined in UHB 543 *Cardiff Joint Research Office (JRO) Applying for Sponsorship of Higher Risk Studies (including Clinical Trials of Investigational Medicinal Products (CTIMPs) and Clinical Trials of Medical Devices (Medical Device Trials)).* For all CAVUHB or CU sponsored studies, the Sponsor risk and level of oversight will be reviewed

and determined during the Sponsor Assessment Process (SAP). Study oversight can consist of:

a) Monitoring
b) Auditing
c) Study initiation and close-down activity
d) Sponsor attendance at regular study meetings
e) External vendor assessments and oversight (including contracts and agreements)
f) Study tracking and reporting

If non-compliances are identified during Sponsor oversight activities (e.g. monitoring or audits), it may be necessary to escalate under the appropriate JRO procedures such as:

- Managing Breaches of Good Clinical Practice or the Study Protocol SOP (UHB 235);
- the CAVUHB procedure for Investigating and Handling Allegations of Research Misconduct SOP (UHB 145)
- the Research Governance Policy (UHB 099);
- Or the appropriate Cardiff University specific policies/Codes of Practice such as the Cardiff University Code of Practice for Research Integrity and Governance, the Academic Research Misconduct Policy and Procedures and/or applicable academic School or CTU SOPs and policies.

2.1 Oversight arrangements for CAVUHB or CU Sponsored higher risk studies

For CAVUHB or CU Sponsored CTIMPs and Medical Device Trials and other categories of Higher Risk studies (as defined in SOP/001/05 *Joint SOP for Applying for Sponsorship of Higher Risk studies (including CTIMPs and Medical Device Trials)*, it is expected that the type, frequency and intensity of these oversight activities will be determined by the study specific Risk Assessment Form (RAF). For CTIMPs and Medical Device Trials, monitoring requirements will be documented in a study specific Trial Monitoring Plan (TMP). Oversight activities will be reviewed and may be updated with any modifications made throughout the lifecycle of the study.

2.2 Oversight arrangements for CAVUHB or CU Sponsored medium and low risk studies

For CAVUHB or CU Sponsored studies meeting the JRO's criteria for medium or low risk (see SOP-001-007 (UHB 525) *Joint SOP for Obtaining Sponsorship-Low and Medium Risk Studies*), a JRO Sponsor Risk Assessment Template will be completed. Additional Sponsor monitoring and/or audit requirements may be determined based on the outcomes of the Sponsor Risk Assessment and following discussion with the JRO Senior Management Team (SMT). Oversight activities will be reviewed and may be updated with any modifications made throughout the lifecycle of the study.

3. 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 the case of CTIMPs, the current regulatory framework in the UK allows for a range of risk-adapted approaches. These adaptations are largely related to how much is known about the investigational medicinal product (IMP) and standard medical care.

In accordance with the MHRA guidance:
Clinical trials for medicines: guidance on quality and risk proportionality - GOV.UK ICH GCP E6 (R3) 3.10 states:

"The sponsor should adopt a proportionate and risk-based approach to quality management, which involves incorporating quality into the design of the clinical trial (i.e., quality by design) and identifying those factors that are likely to have a meaningful impact on participants' rights, safety and well-being and the reliability of the results (i.e., critical to quality factors as described in ICH E8 (R1))."

Sponsors should therefore move away from a "one size fits all" model of quality management as was previously common, and adopt trial-specific proportionate measures based on the intended design of the trial in order to:

- safeguard participant safety and rights
- maintain scientific validity and reliability of trial results

- avoid unnecessary complexity or burden

The risks associated with a study may change as modifications are implemented and the study evolves.

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

For CU and CAVUHB Sponsored CTIMPs and Medical Device Trials, Sponsor monitoring will be proportionate to the risk categorisation of the trial. The majority of trial monitoring activity will typically be delegated to the appointed CTU or CRO.

For CAVUHB and CU sponsored CTIMPs, Medical Device Trials and other categories of higher risk studies, (e.g. complex surgical trials), the risk assessment for the study is developed during Stage 2 of the SAP using the RAF. The completion and assessment of the RAF is normally delegated to the CTU/CRO, with input from the JRO Sponsor representative. From the completed RAF, a Trial Monitoring Plan (TMP) should be developed by the CTU and reviewed during the SAP. The RAF and TMP will be reviewed to determine the oversight and monitoring requirements for each study based on the perceived overall level of risk associated with the study. For CAVUHB and CU Sponsored higher risk studies which are not managed by a CTU, the JRO Sponsor Risk Template will be completed and will be reviewed by the relevant Research Governance team within the JRO.

The study RAF is a live document and must be kept updated throughout the study. The RAF is regularly reviewed as required by the CI/Sponsor/CTU e.g. following the implementation of a substantial modification or change of external provider. The study RAF should be completed and updated regularly in accordance with the relevant CTU SOPs and policies.

Studies determined by the JRO as presenting a higher level of risk, but which are not CTIMPs or Medical Device trials, may also be subject to additional monitoring requirements. This will be discussed with the CI and/or study team during the Sponsor assessment and study set-up process.

3.1 Responsibility for undertaking monitoring activity

For CTIMPs, Medical Device and some Higher Risk Studies Sponsored by CAVUHB or CU most monitoring duties will normally be delegated to a Clinical Trial Unit (CTU) and will be detailed in the Memorandum of Understanding (MoU) agreement or roles and responsibilities section of the agreement between each CTU and the sponsor organisation.

For all CAVUHB and CU sponsored studies, except CTIMPs and Medical Device Trials, monitoring and oversight responsibilities delegated to the CI are outlined and agreed in the JRO *Sponsor to CI Delegation of Roles and Responsibilities* (TPL/001/10), issued with the JRO Sponsorship in Principle letter.

For CAVUHB 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 CU or CAVUHB-Sponsored CTIMP has been delegated to the CI/PI/CTU, the appropriate Clinical Trials Pharmacist will review and approve the conditions. 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, CAVUHB/CU and/or CTU policies and procedures.

3.2 JRO monitoring arrangements for 'Notifiable' Trials and CTIMPs meeting the former Type A and Type B MHRA risk categories

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. This guidance describes three broad risk categorisations for CTIMPs based on the type of IMP in use in the trial:

- 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

UK CTIMPs approved prior to 28th April 2026 ('Old Rules Trials') will have been risk categorised by Sponsors in accordance with the above MHRA categories. CAVUHB and CU Sponsored CTIMPs will continue to be risk categorised in line with the above. The risk categorisation of a CTIMP will be included in the trial RAF.

From 28th April 2026, the MHRA has classified certain CTIMPs as 'Notifiable', as per regulation 11A of the amended UK Clinical Trial Regulations. Notifiable CTIMPs are trials which meet at least one of the eligibility conditions (see Appendix 1 of this SOP) set out in the MHRA's *Inclusion and Exclusion Criteria* and none of the exclusion criteria. Notifiable CTIMPs will be eligible for automatic approval from the MHRA (but will still require REC and HRA approval).

Sponsors are responsible for determining whether a CTIMP meets the MHRA's criteria for a Notifiable trial and this must be identified in the Clinical Trial application. The decision to submit a trial as a Notifiable trial should be made with the appointed Clinical Trials Unit (CTU) and the research team and recorded in the trial Risk Assessment.

Notifiable, Type A and some Type B trials (CTIMPS) should require less frequent monitoring than a Type C trial. For higher risk trials that may include any multicentre studies, the CI/CTU will usually need to convene an independent Study Steering or Data Monitoring Committee (DMC) to oversee study conduct and safety issues.

Typically no routine (scheduled) in-person Sponsor monitoring visits would be arranged for a Type A or Type B trial Sponsored by CU or CAVUHB. Instead, the CU or CAVUHB Sponsor representative will provide routine oversight and monitoring of the progress of the CTIMP or Medical Device Trial through the following methods and at the following trial timepoints:

i. **Prior to the trial commencing recruitment**: a formal Sponsor Initiation ('Sponsor Green Light') process will be conducted with the CTU and/or the Chief Investigator (CI). When all actions identified during the green light process have been satisfactorily resolved, a final Sponsor 'Approval to Commence' letter (or email) will be issued. No patients should be approached or recruited into the trial prior to this letter being issued (NB. Sponsor Green Light may be issued in stages, if appropriate to the design of the trial);

ii. **During the trial:** ongoing monitoring and oversight of the trial is achieved through regular Sponsor representative attendance at Trial Management Group meetings where relevant. It is anticipated that at least one Sponsor representative(s) will attend the majority of Trial Management Group (TMG) meetings which are held regularly throughout the trial. Ad-hoc meetings with the Trial Managers or the Chief Investigator will also be held as and when deemed necessary throughout the life of the trial;

iii. **During the trial:** the Sponsor representative will receive copies of site monitoring reports from the CTU/CRO upon request and as part of their membership of the TMG;

iv. **End of trial**: the Sponsor will receive copies of the Trial close-down paperwork from the CTU/CRO. A Close-Down meeting with the CTU/CRO may be held if deemed necessary, in line with Sponsor CTU Close Down procedures and relevant SOPs.

During the trial, the Sponsor may determine that a 'triggered' or 'for cause' Sponsor monitoring visit of the CTU, a trial site or an international trial coordination centres or sites (where relevant) is required during the trial.

3.3 JRO monitoring arrangements for Type C CTIMPs

Monitoring and Sponsor oversight of Type C CTIMPs and higher risk Medical Device Trials (e.g. trials of Class IIb implantable or long-term invasive, Class III or active implantable devices) will follow the same oversight processes as per Type A and Type B trials, but the JRO Sponsor representative will normally determine any additional Sponsor monitoring based on the safety profile of the IMP(s) and/or the complexity of the trial design. Additional Sponsor monitoring requirements will be discussed during Stage 2 of Sponsor Assessment Procedure (SAP) (SOP/001/05) and detailed in the Trial Monitoring Plan (finalised during Stage 3 of the SAP).

3.4 JRO criteria for 'triggered' or 'for cause' Sponsor monitoring or audit

As Sponsor, CU and CAVUHB reserve the right to conduct monitoring or audit of the trial as deemed appropriate. A 'triggered' or 'for cause' monitoring or audit visit may be scheduled where the JRO deems it is necessary to review trial processes and procedures in more detail. This could take place following a one-off, unexpected event, or where a series of systematic errors is identified. This might include:

- a major safety event (as reported by the CTU);
- major issues related to the IMP;
- a serious breach of GCP;
- repeated trial non-compliances or violations;
- if the study is selected for an external regulatory inspection;
- a wide-reaching data breach;
- a breach of the Human Tissue Act;
- an incidence of research misconduct;
- other issues related to the governance and/or ethical conduct of the trial;
- an ongoing failure to meet the trial milestones.

This is not an exhaustive list and the Sponsor may choose to conduct a monitoring or audit visit for other reasons not listed.

In the event of a 'triggered' monitoring or audit visit, the Sponsor (acting through the JRO Research Governance Teams) will notify the CTU Trial Managers, the Chief Investigator and the relevant trial site personnel (if relevant) of its intention to conduct a triggered monitoring or audit visit. The notification will be issued either by email or via a phone call with all relevant parties (in the case of the latter, this will be followed up with an email). The JRO Sponsor representative will clearly set out:

- the reasons for the triggered monitoring or audit visit;
- how the visit will be conducted;
- which members of staff are required to attend and provide documentation/responses;
- the information required by the JRO.

A JRO Sponsor Monitoring or Audit Report will be completed following all Sponsor Monitoring Visits, with any actions listed for the Trial Team. All actions and findings will be discussed with the relevant staff members before the Report is finalised. The JRO will then liaise with the relevant staff members to resolve all outstanding actions satisfactorily and in a timely manner(please refer to the CAVUHB SOP for Research Audit *SOP/009/01 (UHB 236)*).

3.5 Monitoring of externally Sponsored studies Hosted by CAVUHB

For all externally Sponsored (i.e. studies which are not Sponsored by CAVUHB or CU) research involving CAVUHB patients for whom CAVUHB retains the duty of care, study-specific monitoring arrangements as outlined in the study protocol and/or agreements are reviewed by the CAVUHB Research & Development (R&D) Office, which is part of the Joint Research Office (JRO), 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 CAVUHB's Research Governance requirements. C&C assessment is part of the UK-wide HRA/HCRW Approval process.

4. 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 CAVUHB.

The JRO reserves the right to conduct routine or 'for cause' audits of any research study for which CU or CAVUHB is acting as Sponsor or for which CAVUHB is acting as a Host Site.

5. STUDY TRACKING AND REPORTING

It is expected that the JRO will be aware of all studies being sponsored by CU and CAVUHB and those hosted by CAVUHB. The JRO is expected to ensure up to date information is held regarding active and closed CU and CAVUHB sponsored studies. Responsibility for uploading recruitment figures and study status for CAVUHB hosted and CAVUHB and CU Sponsored studies is delegated to local study teams. The Sponsor is accountable for ensuring periodic reports are submitted within appropriate timelines. For CTIMPS an annual Development Safety Update Report (DSUR) must be submitted to MHRA and a copy provided to the Sponsor representative (refer to the joint Safety Reporting SOP). Where CAVUHB or CU is the Sponsor, responsibility for compiling and submitting these reports has been delegated to the CI/CTU.

Further information on study and result reporting and transparency requirements is found in the JRO SOP for *Reporting and Transparency Requirements for CAVUHB and CU Sponsored Research* (SOP-012-02/ UHB 406).

6. TABULATION OF PROCEDURES FOR OVERSIGHT OF CAVUHB and CU SPONSORED STUDIES

(Please note throughout this table studies which fall into the category of a CAVUHB or CU 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 ' UHB 525 Applying for Sponsorship- Low and Medium Risk Studies Standard Operating Procedure (SOP) and **SOP-001-005 (UHB543**) *Joint SOP for Applying for Sponsorship of Higher Risk Studies (including Clinical Trials of Investigational Medicinal Products (CTIMPs) and Clinical Trials of Medical Devices (Medical Device Trials)* review and ensure oversight activities and frequency are appropriate for the risks associated with the study as shown in the relevant risk assessment form.	Sponsor (typically delegated to the JRO)	RGT/SMT	ALL
2	Develop a study specific TMP, detailing the frequency and intensity of oversight activities.	Sponsor (typically delegated to the CTU)	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 JRO)	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 ***SOP-001-005 (UHB543)*** *Joint SOP for Applying for Sponsorship of Higher Risk Studies (including Clinical Trials of Investigational Medicinal Products (CTIMPs) and Clinical Trials of Medical Devices (Medical Device Trials)*	Sponsor (typically delegated to the JRO)	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	Escalation process for CI/CTU/CRO who fail to complete actions post monitoring in reasonable timeframes	JRO	RGT	CTIMP*
6	Report monitoring activity to JRO	Monitoring service provider (typically CRO/CTU)	Appropriately trained monitor	CTIMP*
7	Report monitoring activity to Joint Research Governance Group (JRGG)	JRO	RGT	CTIMP*

	ACTIVITY	RESPONSIBILITY	UNDERTAKEN BY	CTIMP*/ ALL
AUDIT for CAVUHB sponsored				
1	First Patient First visit (FPFV) audits will be performed as outlined in the current audit plan	JRO	RGT	CTIMP*
2	'For Cause' audit may be performed where there are concerns in relation to the conduct of a study e.g. incidents, serious breach, or other	JRO	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	JRO	Contracts Manager /RGT	ALL
2	Confirm that the CI and/or CTU has signed Terms and Conditions of Sponsorship TPL/002/01 and/or *Sponsor to CI Delegation of Roles and Responsibilities* (TPL/001/10) or a Memorandum of Understanding (Roles and Responsibilities) with the Sponsor.	JRO	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	JRO	CI/RGT/CTU /CRO	ALL

	ACTIVITY	RESPONSIBILITY	UNDERTAKEN BY	CTIMP*/ ALL
STUDY TRACKING				
1	Conduct the agreed study tracking activities (from the agreed TMP) with the CI in order to track the progress of the study.	JRO	CI/RGT/CTU/CRO	Higher risk studies (including CTIMPs and Medical Device Trials)
2	Where requested by the JRO, 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 JRO of any changes made to the study after initial approval e.g. change of Principal Investigator, protocol modifications, 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 modifications, 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.	JRO	R&D/RGT	ALL

	ACTIVITY	RESPONSIBILITY	UNDERTAKEN BY	CTIMP*/ ALL
5	Review reports, record and store progress reports provided.	JRO	R&D/RGT	ALL
6	Confirm that the results have been publish on the necessary registries/databases as appropriate.	JRO	CI/CTU	ALL

7. TABULATION OF PROCEDURES FOR OVERSIGHT OF CAVUHB (HOSTED) EXTERNALLY SPONSORED STUDIES (excluding commercial contracts)

	ACTIVITY	RESPONSIBILITY	UNDERTAKEN BY	CTIMP*/ ALL
OVERSIGHT				
1	Conduct capacity and capability checks and review external agreements prior to confirmation of capacity and capability	Sponsor (typically delegated to the JRO)	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 JRO)	R&P	ALL
MONITORING				
1	The external 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 CAVUHB participants and staff	JRO	JRO	ALL

	ACTIVITY	RESPONSIBILITY	UNDERTAKEN BY	CTIMP*/ ALL
3	Report monitoring activity to the CAVUHB R&D office if requested by R&D	Monitoring service provider (typically CRO/CTU) **or research team**	Relevant monitor	CTIMP*
4	Report monitoring activity to JRGG or QMG as required	JRO	RGT	CTIMP*
AUDIT				
1	CAVUHB hosted studies will be risk assessed as part of Capacity and Capability review. Any studies identified to be high risk or medium high risk may require a FPFV audit (to be determined on a study-by-study basis).	JRO	RGT	CTIMP*
2	Up to 10% of hosted non-commercial CTIMPs will be audited (randomly selected)	JRO	RGT	CTIMP*
3	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.	JRO	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/**JRO**	Contracts Manager	ALL
2	Confirm that the PI has signed a COMA	JRO	R&P	CTIMP

	ACTIVITY	RESPONSIBILITY	UNDERTAKEN BY	CTIMP*/ ALL
STUDY TRACKING				
1	Inform the JRO of any changes made to the study after initial approval e.g. protocol modifications, extension of funding, changes to end dates ensuring confirmation of appropriate approvals	CI	PI/research team	ALL
2	Review of any changes made to the study after initial approval e.g. protocol modifications, extension of funding, changes to end dates ensuring confirmation of appropriate approvals	JRO	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 progress reports provided.	JRO	R&P	ALL

Appendix 1: Definitions

Notifiable trials

'Notifiable trials' are trials which have no significant safety concerns with any of the investigational medicinal products, as far as the sponsor is aware having made reasonable enquiries, and which meet certain defined conditions. These conditions include the investigational product being authorised for use, and used

in accordance with its authorisation, in the UK, and a trial involving a higher dose, frequency or duration having previously been approved in the UK.

These types of trial do not require assessment by the MHRA, as relevant safety features have previously been reviewed and approved, however they still require full review by the REC.

Notifiable trials must meet all of the inclusion criteria set out by the MHRA and none of the exclusion criteria to qualify.

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 or Cardiff University. 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).