UNIVERSITY OF SUSSEX

University of Sussex CTIMP Management Framework

Policy Reference	University of Sussex CTIMP Framework				
Authors	Caroline Brooks, Nicky Perry, Antony Walsh				
Approver	Prof Kevin Davies (Chair of Sponsorship Sub-Committee)	**Signature**		**Date**	28 July 2020
Version Number	**1.0**	**Version date**	28 July 2020		

This ***CTIMP Management Framework*** sets out the minimum expectations for management and oversight of University sponsored CTIMPs. Compliance with these requirements ensures adherence to the applicable legislation and guidance and ensures the University meets its legal obligations as Sponsor of CTIMPs. References to University of Sussex SOPs are correct at the time of implementation of the Framework but are subject to change during development of a Quality Management System.

Whilst references are provided to Brighton and Sussex CTU SOPs, when studies are supported by other CTUs, the equivalent documents will apply.

	Process	Regulatory Links	Principles	Elements of Sponsor Oversight
A1	Sponsorship Approval Process	SI 2004/1031 Part 3 12, 13, 17, 18, 19, 20, Schedules 3, 4 and 5	All clinical trials sponsored by University of Sussex are required to go through a central risk assessment and approval process. The partner CTU/CI is responsible for undertaking a risk assessment. This process will be carried out in two phases: prior to the funding application a high level risk assessment process will be completed by the partner CTU/CI; once the trial is funded the detailed sponsor application and approval process will be completed.	**Sponsorship in Principle** University of Sussex has a process ***University of Sussex SOP for Sponsorship Approval of CTIMPs (SOPRGO01)*** to accept the role of the Sponsors and will only accept trials which pose an acceptable level of risk to the University and that lie within its range of competence as Sponsor. Where the criteria laid out in ***University of Sussex SOP for Sponsorship Approval CTIMPs (SOPRG01a)*** **are met and the** ***Sponsor Risk Assessment Tool (RGA_1)*** does not highlight any significant risk areas, University of Sussex will usually, subject to approval by the Sponsorship Sub-Committee accept the role of Sponsor.

			The Sponsor approval process is managed by the Research Governance Officer.	Where the criteria laid out in ***University of Sussex SOP for Sponsorship Approval CTIMPs (SOPRG01a)*** are not met or the ***Sponsor Risk Assessment Tool (RGA_1)*** highlights significant issues. Under all circumstances, final decisions on Sponsorship in Principle are made by the Sponsorship Sub-Committee, taking account of the ***Sponsor Risk Assessment Tool (RGA_1)***. The Research Governance Officer will liaise with the CI and may take advice from the Chair of the Sponsorship Sub-Committee. It is expected that the Health Research Authority (HRA) CTIMP protocol template is used for new trials where appropriate. Where the HRA template is not used, this must be justified and confirmation is required that all elements contained within the HRA template are present, or justification provided for their absence.
				Confirmation of Sponsorship Confirmation of Sponsorship must be obtained prior to submission of regulatory applications as laid out in the ***University of Sussex SOP for Sponsorship Approval CTIMPs (SOPRG01a).***
B1	Contract, Delegation and Agreements	SI 2004/1032 3 (2)	**CIs** A **Delegation of Activities** is required for each trial.	The trial-specific ***University of* Sussex SOP for Delegation *of Roles and Responsibilities (SOPRG10)*** is agreed with the CI and CTU, which clearly details where operational delegation is to the CI and where the CTU are expected to provide support. Delegation must be made in writing prior to undertaking delegated activities, with the formal and comprehensive

				Delegation of Activities in place prior to commencement of recruitment and forms part of any protocol/contracts.
B1.1			**Co-Sponsorship** University of Sussex will consider Co-Sponsorship on a case-by-case basis.	University of Sussex will consider Co-Sponsorship on a case-by-case basis.
B1.2			**Service Providers** For services that are required for a clinical trial but cannot be provided by the University or a CTU, University of Sussex may enter into contracts with specialist providers.	Procurement and sub-contracts are managed by Finance's Procurement Team and Legal Services in accordance with their usual processes: ***http://www.sussex.ac.uk/finance/services/procurement***
B1.3			**CTUs**	
B1.4			**Participating Sites** Agreements are required for all participating sites.	The CI and CTU are responsible for ensuring that the Health Research Authority's ***model Clinical Trial Agreement*** is used and is in place before a participating site is authorised to open recruitment. The type of agreement will be determined by the level of activity by the sites. To be discussed by the Legal Team prior to submission to the HRA.
C1	Regulatory Applications	SI2004/1031 Part 3, Regulations 12/ 13, 17, 18, 19, 20. Schedules 3, 4, 5	All clinical trials sponsored by the University of Sussex are required to obtain relevant regulatory approvals before they will receive authorisation to commence. This includes a Clinical Trial Authorisation, favourable Ethical	Responsibility for obtaining all regulatory approval is delegated to the CI supported by the CTU and is carried out in accordance with ***CTU SOPs*** and the ***University of Sussex Delegation of Roles and Responsibilities (SOPRG10)*** (see section B1).

			Approval, HRA Approval and relevant site management approval.	
D1	Trial Master File (TMF)	SI 2004/1031 Part 4 31 A	CIs, supported by the CTU, are delegated responsibility for creating, maintaining and archiving a Trial Master File (TMF).	The TMF is managed in accordance with the Trial Master Files and Investigator Site Files SOP **(CTUSOP004).**
E1	Monitoring	SI 2004/1031 Part 4 28, 29 and Schedule 1	CIs, supported by the CTU, are delegated responsibility for day to day monitoring of trial conduct and participating sites. A standardised way of ensuring Sponsor oversight of the conduct of trials is in place to ensure compliance with Regulatory requirements and the principles of GCP.	The CI and CTU are expected to implement a risk-based trial-specific monitoring plan (for example, site monitoring in a multi-site study) in accordance with the trial protocol and trial-specific risk assessment. This is managed in accordance with the University of Sussex document ***Monitoring CTIMPs (SOPRG05A)*** A Sponsor monitoring procedure is detailed in University of Sussex document ***Monitoring CTIMPs (SOPRG05A)*** to ensure Sponsor oversight of regulatory matters and GCP.
F1	IMP Management	SI 2004/1031 Part 4 28, Part 6 36, 37, 43, Schedules 6, 7, 8 and part 7 46	University of Sussex does not manufacture Investigational Medicinal Products (IMPs) and does not have the facilities for storage or distribution from its premises. The CI and CTU are delegated responsibility for ensuring that adequate processes are put in place for managing the IMP(s).	It is expected that the MHRA's *Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products* will be applied as appropriate to the given trial and that advice is sought by the CI (or their delegate) as necessary from individuals with relevant expertise in IMP handling (for example a pharmacist) in accordance with the ***CTU's IMP Management SOPs*** **Supply and Management of IMP (CTU/SOP/013**) and ***Investigational Medicinal Product Labelling (CTUSOP014***)
G1	Serious breaches of GCP and the trial Protocol	SI 2004/2013 Part 4 29A and 30	The CI, CTU are responsible to reporting to the Sponsor and will expedite serious breach reports to the MHRA as required. University of Sussex ***SOP for***	CI and the CTU are required to retain records of any protocol deviations and potential serious breaches of the trial protocol or GCP, and the learning from them, and allow the Sponsor to undertake periodic review of the records. Issues of non-

			Sponsorship Approval CTIMPs (SOP/RGO/01a)	compliance are managed in accordance with University of Sussex document ***Notification of Serious Breaches of Good Clinical Practice or the Trial Protocol (SOPRG03)***. The Chair of the University of Sussex Sponsorship Sub-Committee (SSC) will review confirmed serious breaches.
H1	Amendments	SI 2004/1031 Part 3 22, 24, 25, 26	Preparation and submission of Amendments is delegated to the CI/CTU. Oversight of all Substantial amendments will be described below:	
H1.1			The Sponsor confirms categorisation of amendments as Substantial or Non-Substantial through review of a summary of the proposed changes.	The standard categorisation to be followed for amendments is described in the ***SOP Amendments, Urgent Safety Measures and Temporary Halt to a Trial (SOPRG16)***. The CI / CTU must provide a summary of the proposed changes and reasons for change to the Sponsor (through the Research Governance Office) who will confirm categorisation as Substantial or Non-substantial and ratify decisions of relevance to the MHRA- **(SOPRG16 - *Amendments, Urgent Safety Measures and Temporary Halt to a Trial*)**. Amendments must be authorised through the University of Sussex Sponsorship Sub-Committee (SSC).
I1	Data Management	SI 2004/1031 3A, part 5 32, 33, 24 and 35	Day to day data management, database design and maintenance is delegated to the CI and CTU.	The CTU'S Data Management SOP ***(CTUSOP027)*** describes the data management processes. ***(CTUSOP027)*** describes the set-up and management of the database and the data management plan (trial specific).
J1	Statistics		Statistical design and analysis is delegated to the CI and CTU.	The CTU'S Statistical Oversight SOP ***(CTUSOP030)*** describes the statistical design and analysis processes.

				All trials must convene a Data Monitoring Committee (DMC) and Trial Steering Committee (TSC). The DMC / TSC must agree the trial protocol and statistical analysis plan.
K1	Pharmacovigilance and Safety Reporting	SI 2004/1031 3A, Part 5 32, 33, 24 and 35	SAEs Suspected Unexpected Serious Adverse Reactions (SUSARs) Identification and reporting of SAEs and SUSARs is delegated to the CI and CTU.	The CI/CTU is required to notify the Sponsorship Sub-Committee (researchsponsorship@sussex.ac.uk) of any event meeting the definition of an SAE in accordance with University of Sussex Adverse Events in CTIMPs (***Sponsor SOPRG21***). To be included in the study progress report which is submitted to the SSC periodically. The CI/CTU is required to notify the Sponsorship Sub-Committee (researchsponsorship@sussex.ac.uk) of any event meeting the definition of an SUSAR in accordance with (***Sponsor SOP SOPRG21 - Adverse Events in CTIMPs ***). With immediate notification to the Chair of the SSC and escalated accordingly.
K1.1			**Development Safety Update Report (DSUR)** Completion of the DSUR is delegated to the CI and CTU for annual submission to the MHRA. An annual report of all the SAEs that occurred.	The DSUR/Reference Safety Information (RSI) must be copied to the Sponsorship Sub-Committee upon submission to the Regulatory Authorities in accordance with the CTU's SOP for DSUR handling ***(CTU SOP 19 - Reference Safety Information Definition and Updates:)***. This allows the Sponsor to assess any changes to the Risk: Benefit ration of the trial. Any areas of concern may be referred to the CI first for action, and if areas of concern continue to be identified by the Sponsor, these will be discussed at the Sponsorship Sub-Committee.
L1	End of trial	SI 2004/1031 27, Part 4 31A	Responsibility for submission of the ***End of Trial Notification*** (***or Notification of***	The notification of ***Close-Out of a CTIMP Research Study (SOPRGO09a***) (or *Notification of Early Termination*) must be

			Early Termination) is delegated to the CI and CTU.	copied to the Sponsor upon submission to the Regulatory Authorities. ***(CTU SOP 15: Trial Close Out Procedures)***.
L1.1			**Publication of results and end of trial report** The CI must ensure that clinical trial results are published in a timely manner, in a peer-reviewed and open access journal, and in accordance with funder requirements.	The end of study report must be copied to the Sponsor (researchsponsorship@sussex.ac.uk) ***US SOP Trial Reporting Project Publication and Dissemination (SOP/RG/35)***.
L1.2			**End of study reporting on EudraCT** The CI and CTU are delegated responsibility for reporting results on the EudraCT Results Database in accordance with regulatory requirements.	The Research Governance Officer has authority for the trial EudraCT accounts on behalf of the University. The Research Governance Officer gives access to appropriate individuals for preparation and submission of results.
L1.3			**Archiving** The CTU and participating sites will archive the study documents TMF and final dataset in line with the ethical approval for the study and in accordance with regulatory requirements. The TMF must be accessible in the event of audit or inspection.	On behalf of the Sponsor, a named individual will be identified who is responsible for archiving essential documents. Archiving is carried out in accordance with US SOP ***Archiving Paper Trial Documents for Sussex as a Sponsor (SOPRG33)***. Document Options Ltd will provide the archiving. Each research site is responsible for archiving their site documents.
M1	Audit		A system of Sponsor audit will oversee compliance with relevant regulatory and Sponsor processes.	Once the combined Quality Management System (QMS) is embedded, a Sponsor audit plan will be developed based on an assessment of trial risk.

				The Sponsors reserves the right to monitor or audit documentation relating to trials that it sponsors.
N1	Training	SI 2004/1031 Schedule 1 Part 2(2)	Individuals involved in the sponsorship of and management of clinical trials are expected to be adequately trained and / or experienced to perform their tasks.	
N1.1			**Sponsor**	Individual staff members are responsible for identifying training requirements within the team as applicable to their role. All new members of staff are required to read all SOPs relevant to their job role and maintain their own training file.
N1.2			**CIs, CTUs and Researchers** CTUs and CIs are responsible for identifying and addressing individuals' training needs within their trial teams as applicable to the trial. Training in new / complex Sussex Sponsor procedures may be undertaken as required.	Minimally, CIs and US research staff must be trained in the requirements of GCP, and this should usually be evidenced through a current (within the last 2 years) certificate. Where identified as required, the ***Research Governance Office*** will deliver training on Sussex's sponsorship processes on an ad hoc basis.

Section E References

Clinical Trials Regulations 2004 (SI 2004/1031)

http://www.legislation.gov.uk/uksi/2004/1031/pdfs/uksi_20041031_en.pdf

Section F List of SOPs cited in this Framework

RESEARCH & ENTERPRISE SERVICES
RESEARCH ETHICS, INTEGRITY & GOVERNANCE

Sponsor/Sussex SOPs

CTIMP MF Ref	**UK** SI 2004/1031 ref	**US SOP Ref**	**Document Name**
A1- Sponsorship Approval Process	Part 3 12, 13, 17, 18, 19, 20, Schedules 3, 4 and 5	SOPRG01a	Sponsorship approval CTIMPs
		SOPRG04	Risk Assessment
E1 - Monitoring	SI 2004/1031 Part 4 28, 29 and Schedule 1	SOPRG05a	Monitoring CTIMP research Studies
		SOPRG09a	Procedures for Close out of a CTIMP
B1- Contract, Delegation and Agreements	SI 2004/1032 3 (2)	SOPRG10	Delegation of roles and responsibilities
I1 - Data Management	SI 2004/1031 3A, part 5 32, 33, 24 and 35	SOPRG17	Data management
J1 - Statistics		CTU	Statistical review and analysis
G1 - Serious breaches of GCP and the trial Protocol	SI 2004/2013 Part 4 29A and 30	SOPRG03	Notification of Serious Breaches of Good Clinical Practice or the Trial protocol
		SOPRG20	Safety reporting in non-CTIMPs

			Code of Practice for Research
			Procedure for the Investigation of Allegations of Misconduct in Research
H1 - Amendments	SI 2004/1031 Part 3 22, 24, 25, 26	SOPRG16	Amendments, Urgent Safety Measures and Temporary Halt to a Trial
K1 - Pharmacovigilance and Safety Reporting	SI 2004/1031 3A, Part 5 32, 33, 24 and 35	SOPRG21	Adverse Events in CTIMPs
Quality Management System		SOPRG36	Writing SOPs
End of Trial	SI 2004/1031 27, Part 4 31 A	SOPRG33	Archiving Paper Trial Documents (for University of Sussex as a Sponsor)
		SOPRG35	Trial Reporting, Project Publication and Dissemination

Other SOPs

SOP on SOPs **SOPRG036**

Appendix 2 - CTU/ Brighton and Sussex CTU SOPs

CTIMP MF Ref	**UK** SI 2004/1031 ref	**Brighton & Sussex CTU SOP Ref**	**Document Name**
B1- Contract, Delegation and Agreements	SI 2004/1032 3 (2)	CTUSOP033	Sponsorship Contracts and Agreements
C1- Regulatory Applications	SI2004/1031 Part 3, Regulations 12/ 13, 17, 18, 19, 20. Schedules 3, 4, 5	CTUSOP005 CTUSOP006	Obtaining and Maintaining REC and HRA Approvals Application and maintenance of a Clinical trial Authorisation from the Competent Authority
D1- Trial Master File (TMF)	SI 2004/1031 Part 4 31 A	CTUSOP004	TMFs and ISFs

F1 - IMP Management	SI 2004/1031 Part 4 28, Part 6 36, 37, 43, Schedules 6, 7, 8 and part 7 46	CTUSOP013 CTUSOP014	IMP Supply and Management IMP Labelling
I1 – Data Management	SI 2004/1031 3A, part 5 32, 33, 24 and 35	CTUSOP027 CTUSOP028	Data Management Data Requests and Transfer
J1 - Statistics		CTUSOP030	Statistical Oversight
L1 – End of Trial	SI 2004/1031 27, Part 4 31A	CTUSOP015 CTUSOP017	Trial Closure Archiving

Section F Version Control details

Version	Date	Reason for change