Guidance on the use of Model Clinical Trial Agreement (mCTA) and Contract Research Organisation Model Clinical Trial Agreement (CRO-mCTA)

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Contents

Introduction 2
Structure of the Guidance 2
1. Use of the mCTAs 2
2. Guidance on the Provisions in the mCTAs 6
Contact Points for Advice and Assistance 27
3. Background and Change History 28
Background 28
Change History 29
Summary of Key Changes in April 2026 29
Summary of Key Changes in July 2025 34
Summary of Key Changes in May 2025 34
Summary of Key Changes in December 2023 36
Summary of Key Changes in October 2023 36
Summary of Key Changes in May 2022 38
Summary of Key Changes in January 2021 39

Introduction

The first model Clinical Trial Agreement (mCTA) for pharmaceutical research was drawn up and published by the Department of Health and Social Care (DHSC) and The Association of the British Pharmaceutical Industry (ABPI) in 2003, with the intention that a template agreement would make the contracting process more straightforward and efficient. The first Clinical Research Organisation model Clinical Trial Agreement (CRO-mCTA) was published in 2007.

Since 2003, the mCTAs have been refined and developed to take account of a changing regulatory regime and clinical trial environment. The mCTAs are for use with NHS[1] organisations across all four UK nations. Detailed information about the development of the mCTAs is provided in Section 3.

The mCTAs have been developed through consultations between the various stakeholder groups, including representatives from the DHSC, the Health Research Authority, the National Institute for Health and Care Research, the Medical Research Council, the Devolved Administrations, the NHS, life sciences trade associations and national and global heads of research from bio-pharmaceutical companies and contract research organisations.

The mCTAs have been devised to meet the needs of the companies Sponsoring clinical trials and contract research organisations managing sites and to reflect the duty of care that Trial Sites have for their patients and other research participants under their care.

This guidance provides an introduction to the mCTAs, outlining when and how they should be used, summarising some of their key provisions, as well as providing an overview of the change history of the mCTAs.

Structure of the Guidance

This guidance is in three parts:

1. **Section 1 provides an overview of how the mCTAs should be used.**
2. **Section 2 is an overview of some of the provisions within the mCTAs.**
3. **Section 3 provides background on the development of the mCTAs, including a change history.**

1. Use of the mCTAs

1.1 What are the mCTAs?

The mCTA is the standard form contract for use by industry Sponsors and NHS[2] Trial Sites (but see 1.3 below for relationship between the mCTAs and the Hub

[1] Throughout, references to NHS should be read to include references to Health and Social Care (HSC) in Northern Ireland

[2] The mCTAs are intended for use in NHS organisations, not with independent contractors of primary care NHS commissioned services. Primary Care mCTA is provided for such circumstances.

and Spoke Agreements) running contract clinical trials of investigational medicinal products (CTIMPs).

The CRO-mCTA is the standard form contract used by industry Sponsors, the contract research organisations (CROs) separately contracted by them to undertake site management responsibilities, and NHS Trial Sites (but see 1.3 below for relationship between the mCTAs and the Hub and Spoke Agreements) running contract CTIMPs.

Contract CTIMPs in the NHS are industry funded and sponsored CTIMPs in which NHS patients, or healthy volunteers under an NHS duty of care, receive Investigational Medicinal Products ("IMPs").

All references in this guidance to "clinical trial" should be read as a reference to a contract CTIMP.

1.2 When should the mCTAs be used?

The mCTA is intended to be used for all phases of contract clinical trials, including Phase I trials in NHS patients or healthy volunteers under an NHS duty of care.

The CRO-mCTA is intended to be used as above but where, in addition, the Sponsor has contracted with a contract research organisation (CRO) to be responsible for aspects of trial management at the Trial Site.

When the Sponsor has contracted a CRO to manage or oversee aspects of trial conduct at the Trial Site, it is the Sponsor's responsibility to decide whether to contract with the Trial Site using the mCTA or CRO-mCTA. If the Sponsor chooses to use the mCTA, it takes responsibility for the actions of its CRO and passes down its contractual responsibilities to the CRO as its Agent (as applicable). Where the CRO-mCTA is used, it forms a tri-partite agreement between the Sponsor, CRO and Trial Site.

The mCTAs should be used with NHS Trial Sites undertaking research activities overseen by a Principal Investigator at that Trial Site. Where a Principal Investigator oversees research activity at multiple Trial Sites, the relevant mCTA should be used to contract the Lead Trial Site, with Other Trial Sites subcontracted by Hub and Spoke Agreements (see 1.3 below).

The mCTAs are not for use in non-commercial studies funded or sponsored by charities, government departments or research councils, whether or not such studies involve NHS patients or healthy volunteers and whether or not they are carried out by NHS organisations. The Model Agreement for Non-Commercial Research in the Health Service (mNCA) or non-commercial Organisation Information Document (as appropriate) should be used for non-commercial studies.

The mCTAs are for managing site arrangements and are not for use to manage the collaboration between organisations in collaborative clinical research trials. NHS, commercial (and, where applicable, academic) collaborations should be managed, as necessary, via a collaborator agreement and the resultant research studies separately contracted between sponsor and site using the appropriate UK

template (which would be an mCTA for a commercial CTIMP, the mNCA or Organisation Information Document, for non-commercially sponsored collaborative studies).

The mCTAs are not designed for use with any phase of contract Clinical Trial of investigational advanced therapy medicinal products (ATMPs). Commercial studies which are ATMPs should be contracted using the ATMP-mCTAs.

The mCTAs are not designed for the purposes of any Contract Clinical Trials (Phases I to IV) performed by private institutions with patients recruited independently of their treatment within the NHS.

The mCTAs are not for use with independent contractors of NHS primary care services. Commercial studies with NHS patients in independent contractor primary care should be contracted using the Primary Care model Clinical Trial Agreement (PC-mCTA).

The mCTAs are not for use in investigator-initiated, non-commercially sponsored, trials. The Model Agreement for Non-Commercial Research in the Health Service (mNCA) should be used for this purpose.

The mCTAs are not for use in clinical investigations of medical devices (commercially sponsored device studies should use mCIA), or for non-interventional studies (for which mNISA should be used if commercial or the organisation information document if non-commercial).

1.3 Investigator Sites, Trial Sites and Hub and Spoke Agreements

The mCTA takes account of and aligns with UK guidance on the set up of research activity at NHS organisations (interventional research). Accordingly, the Party contracted by the Sponsor to conduct the Clinical Trial is defined as the Trial Site.

The above referenced set-up guidance defines a Trial Site as “a legal entity responsible for some element of an interventional research study for which PI oversight is required”. It also clarifies that one PI may oversee more than one trial site, or that one trial site may need more than one PI to ensure effective oversight.

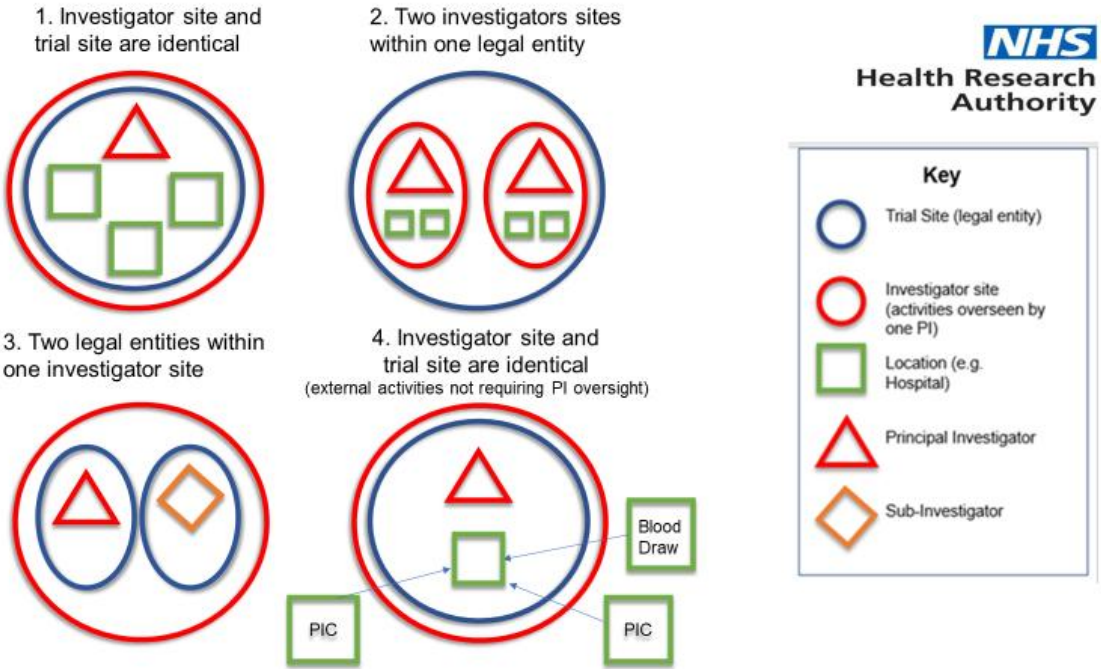
The guidance (and the mCTAs) uses the term Investigator Site for “the activities (regardless of their location) with effective oversight by one Principal Investigator”.

A clinical trial may therefore be delivered with one (or a combination of) the following PI oversight arrangements;

- one Investigator Site per Trial Site. That is to say that there is one PI overseeing research activity at one legal entity (see figure 1.1), or;
- More than one Investigator Site within the one Trial Site. That is to say that there is more than one PI for research activity occurring within the one legal entity, each PI having oversight for specific activities within that entity (see figure 1.2), or;

- More than one Trial Site within the one Investigator Site. That is to say that one PI oversees research activities occurring within more than one legal entity (see figure 1.3);
- There may also be other legal entities involved in the Clinical Trial that are undertaking activities not needing PI oversight, for example general practices undertaking simple blood draws, Participant Identification Centres and so on (see figure 1.4).

FIGURES 1.1 – 1.4



Where there is more than one Investigator Site within the one Trial Site, one mCTA per Investigator Site should be agreed between the Parties. Whilst this means that the same Trial Site has more than one contract for the same clinical trial, each contract would cover the activities specifically contracted to be overseen by one PI. Clause 16.4 facilitates this approach. The mCTA should not be altered to attempt to use one contract to cover more than one Investigator Site within the same Trial Site.

Where there is more than one Trial Site within the one Investigator Site, the mCTAs have been drafted to allow the Lead Trial Site (that which employs the PI) to contract with the Sponsor using the mCTA. The Lead Trial Site then subcontracts to Other Trial Sites the aspects of the Clinical Trial that they will conduct, overseen by the Lead Trial Site PI. A commercial hub and spoke template has been published for use alongside the mCTA in such circumstances, allowing the Lead Trial Site to subcontract with Other Trial Sites in a consistent manner.

1.4 Alterations to the mCTAs

The mCTAs have been developed through many years of negotiation and discussion between a wide stakeholder group.

Prior to execution of a clinical trial agreement, it is necessary for trial-specific information to be appended to, or options selected within, the mCTAs. The information required / options are identified on the front page of the mCTAs (and throughout the mCTAs in yellow highlight). Other than the need to add or select information as specified, it is strongly recommended by all the UK Health Departments that the mCTAs should be used without alteration. Any request by a sponsor or CRO to alter the mCTAs and / or to use any agreement to contract with a site other than the appropriate mCTA, should be disclosed in the IRAS submission (a version of the template proposed for use, with tracked changes, and detailed justification should be provided).

In England and Wales, NHS organisations are required to use only an unaltered mCTA or CRO-mCTA (as appropriate and applicable). In exceptional circumstances this requirement may be waived by the letter of HRA and HCRW Approval for the Clinical Trial. Such waivers require UK agreement from the UK Four Nations Contracting Leads Group. Similarly, proposals for alterations to mCTAs for use with sites in Scotland or Northern Ireland will also be escalated to the UK Group.

Sponsors should be aware that proposing alterations to template agreements is likely to result in significant delay and does not oblige NHS organisations to agree the altered agreement, even where a waiver is centrally agreed for its use. Any waiver issued would allow the NHS organisation to propose and negotiate its own alterations. Unaltered use is strongly recommended.

2. Guidance on the Provisions in the mCTAs

2.1 Contracting Parties

In order to comply with research and clinical governance requirements and expectations, and to establish the correct lines of accountability for health care professionals practising in the NHS, all contract clinical trials must be governed by contracts between the Sponsor and NHS organisation (or, where appropriate, a subcontract between NHS organisations). This remains the case even when, for example, the investigator is employed by a university and holds an honorary contract with the NHS organisation.

The agreement must list the name and address of the organisation acting as the UK Sponsor for the clinical trial. This organisation must match the Sponsor named in IRAS, but it does not need to be the same as the global Sponsor named in the Protocol. The UK Sponsor could be contracted by the global Sponsor. It also does not need to be based in the UK.

Where a Sponsor has legally delegated to another organisation the power to contractually bind the Sponsor by signing the Agreement on its behalf, evidence of this delegated authority should be attached as Appendix 8 of the mCTA or Appendix 9 of the CRO-mCTA. The other organisation could be a corporate affiliate of the Sponsor, or another organisation such as a CRO. This evidence is required by the NHS as an assurance that the delegated entity is empowered by the Sponsor to sign on behalf of the Sponsor and thereby bind the Sponsor as Party to the agreement.

Where a Sponsor is not established in the UK or EEA, their UK / EEA Legal Representative for the purposes of the clinical trial regulations should be named in the recitals of the agreement but will not be a separate signatory or Party to the agreement in their capacity as Legal Representative.

Where the Sponsor has contracted a CRO to manage aspects of the clinical trial, the CRO may be made a Party to the Agreement through the use of CRO-mCTA. Where CRO-mCTA is used, the separation of responsibilities between the Sponsor and CRO should be set out clearly, including evidence of the delegated activities appended at Appendix 8 of the CRO-mCTA. If the CRO has been legally empowered by the Sponsor to sign on behalf of the Sponsor to bind the Sponsor as party to the Agreement, this should be clearly evidenced in this appendix. Alternatively, a sponsor that has contracted a CRO to manage some aspects of the clinical trial on its behalf may prefer to exclude the CRO from the contract with Trial Sites through use of the mCTA. In this instance, the CRO is reflected in the mCTA as an Agent of the Sponsor. In either case, the Sponsor is ultimately responsible for ensuring both it and the CRO perform their duties in line with the Agreement.

Participating NHS organisations have an obligation to inform medical academics' substantive employers, which are usually universities, about clinical trials in which they are to take part. The mCTAs should not be altered to form a tripartite agreement with an academic institution as a third party.

In no case should a clinical trial Sponsor enter into a contract with an individual employee of either an NHS organisation or a university in a personal capacity to undertake a clinical trial involving NHS patients or healthy volunteers under NHS care. This prohibition applies to contracts governing the conduct of clinical trials (including the mCTAs). Chief Investigators may be separately contracted for their services either personally (if acting in a personal, non-NHS capacity), or via their employing organisation using one of the model Commercial Chief Investigator Agreements (mCCIAs).

2.2 Clause 1: Definitions: Sub-Investigator

The definition of a Sub-Investigator is taken from ICH-GCP E6 R3. Sub-Investigators may perform activities on behalf of the Principal Investigator once delegated to them, as appropriate. This includes making important Clinical Trial-related decisions and carrying out significant Clinical Trial-related procedures. These decisions and activities could include confirmation of eligibility against the Protocol where this is unclear to the person screening the potential Participant, or standing in temporarily during short periods of absence by the Principal Investigator. Where activities are undertaken by a Sub-Investigator (or other Personnel), these remain the responsibility of the Principal Investigator, and appropriate oversight should be in place.

2.3 Clause 2: Principal Investigator and Personnel

The Principal Investigator is not to be a signatory to the mCTAs. Clause 2 makes clear the obligation of the Trial Site to procure the performance of the Principal Investigator with respect to the Trial Site's obligations under the Agreement. Since the March 2020 version, this obligation has extended to procuring the services of

Sub-Investigators and other personnel (which, from the May 2022 version onwards may extend to include those at Other Trial Sites). The mCTAs do not seek to amend the well-understood and established obligations of Principal Investigators. Trial Sites should bring these responsibilities to the attention of Principal Investigators in the course of research governance training.

As the obligations of the Trial Site will be fulfilled through the work of the Principal Investigator, it is important that the Trial Site incorporates the obligations of the Principal Investigator and other investigators set out in the mCTAs, into a separate agreement (in a form that is at the discretion of the Trial Site) between the Trial Site and the Principal Investigator.

It is prudent for the clinical trial activities to be included in the work plans of the Principal Investigator and any Sub-Investigators and (as applicable) any other Personnel. The Trial Site may seek assurances from the Principal Investigator and any Sub-Investigators to satisfy the conditions of the mCTAs.

2.4 Clause 2.5: Attendance at Investigator Meetings and Reimbursement of Expenses

Clause 2.5 sets out an obligation on the Principal Investigator and / or the personnel to attend meetings reasonably requested by the Sponsor (or CRO). It should be noted that no compensation will be paid for attendance at such meetings and any expenses incurred will be paid at the rate of fair market value, subject to documentation evidencing the expenses incurred being in sufficient detail for the Sponsor's financial reporting purposes (or those of the CRO, as applicable), provided that this is not overly burdensome for the Trial Site.

2.5 Clause 3.2 and 3.3: Governance

These Clauses set out the minimum compliance requirements for the conduct of trials, including in respect of domestic law and investigational new drug (IND) in respect of trials conducted by US companies. However, it is essential that Sponsors (or CROs, where applicable) notify Trial Sites of specific requirements that relate to the performance of trials and that arise from such laws.

2.6 Clause 3.3.4: Declaration of Helsinki

The legal requirement is for Sponsors to follow the principles of the 1964 Declaration of Helsinki. Sponsors may choose to only follow the principles of the 1964 Declaration, and not to place any further obligations upon themselves, CROs (where applicable) or Trial Sites.

Two options are presented for the Sponsor to choose whether and how it will follow a full version of the Declaration of Helsinki in addition to the legal requirement. The Sponsor should delete both of these options if it will only follow the principles in the 1964 Declaration of Helsinki, or if it will expect a full version of the Declaration of Helsinki to be followed it should delete the non-applicable version.

The 1996 Declaration of Helsinki was the version which was legally required to be followed prior to the Medicines for Human Use (Clinical Trials) (Amendment)

Regulations 2025. Sponsors may choose contractually to continue to adhere to this version. It places no obligation on the Sponsor to make provision for any intervention to be provided to Participants post-trial.

The 2024 Declaration of Helsinki is the most recent version and therefore contains the most up to date global ethical expectations. Including this version in the Agreement places a contractual obligation on Sponsors to continue to provide an intervention to Participants post-trial where this is found to be "beneficial and reasonably safe" unless the ethics committee agrees to waive this requirement.

In all instances, the Declaration of Helsinki specified should be followed unless it contravenes UK law.

2.7 **Clause 3.3.7: WHO Ethical Principles**

This reference to the WHO Ethical Principles is intended for use where the clinical trial involves transplantation of human cells, tissue or organs. It is an optional reference, to be deleted if not applicable to the Clinical Trial.

2.8 **Clause 3.6.1: Adverse Event Reporting**

To facilitate use of the mCTAs for Phase I trials in NHS patients or healthy volunteers under NHS care, clauses setting out obligations in relation to adverse event reporting have been included. These clauses are only applicable where the Clinical Trial is a Phase I clinical trial and should be deleted if not applicable.

2.9 **Clause 3.6.2: Quality Control of Data in Phase I Dose Escalation Trials**

To facilitate use of the mCTAs for Phase I dose escalation trials in NHS patients or healthy volunteers under NHS care, a clause setting out obligations in relation to adverse event reporting has been included. This clause is only applicable where the Clinical Trial is a Phase I dose escalation clinical trial and should be deleted if not applicable.

2.10 **Clause 3.7: Anti-Bribery and Corruption**

Alterations to this clause to reference the Foreign and Corrupt Practises Act of the USA, or any other foreign law, should not be proposed and will not be agreed. Compliance with the Bribery Act 2010 should provide adequate assurance to foreign Sponsors (and CROs) in relation to their own compliance with foreign law.

2.11 **mCTA Clause 4.6 (CRO-mCTA Clause 4.7): No Supply of Trial Drugs by the Sponsor (or CRO) Prior to Approval**

Clause 4.6 (CRO-mCTA Clause 4.7) requires Sponsors (and CROs, as applicable) to delay supply of Trial Drugs supplied by the Sponsor to the Trial Site, and / or to withhold authorisation to the Trial Site to use the Trial Site's own stock as Trial Drugs for the purpose of the Clinical Trial, until all regulatory approvals have been obtained and the Sponsor has received confirmation from the Public Registry that it has been published or accepted onto it. There is an obligation on the Trial Site to ensure that no clinical interventions arising from the Protocol take place before receipt of all relevant approvals.

2.12 mCTA Clause 4.7 (CRO-mCTA Clause 4.8): modifications to the Protocol

Clause 4.7 (CRO-mCTA Clause 4.8) requires the Principal Investigator to have reviewed any modifications to the Protocol which impact the conduct of the Clinical Trial at the Trial Site, and to have confirmed that they and the Personnel can implement the modifications. This ensures that the Principal Investigator understands the requirements of the Clinical Trial and can provide effective oversight. The review and confirmation provided by the Principal Investigator needs to be auditable, and should be proportionate in relation to the modifications. Examples of the auditable trail can include a file note, minutes of meetings, or an email trail with the Sponsor or Trial Site's R&D office discussing the modification.

The review and confirmation by the Principal Investigator does not relieve the Trial Site of its overall obligations to ensure that the modification can be implemented at the Trial Site. The Trial Site, as the Party to the Agreement, is responsible for ensuring that the contract is varied (if applicable) in line with Clauses 16.2 and 16.3 of the Agreement, and that the modification is implemented as soon as possible. It is expected that the Trial Site and Principal Investigator work together to ensure timely review and implementation of modifications.

2.13 mCTA Clause 4.10 (CRO-mCTA 4.11): Reimbursement to Trial Site when purchasing Trial Drugs

This Clause details the reimbursement of the Trial Site when it purchases Trial Drugs for use in the Clinical Trial. Reimbursement includes any VAT the Trial Site incurs when it purchases the Trial Drugs. The Sponsor is not responsible for paying VAT on the purchase at the point of purchase, though where the Trial Site has incurred VAT charges when it has purchased the Trial Drugs, the Sponsor is contractually required to reimburse them for this.

2.14 mCTA Clause 4.12 (CRO-mCTA 4.13): Supply and end of Clinical Trial management of Trial Drugs

Clause 4.12 (CRO-mCTA Clause 4.13) allows the Sponsor to specify which Party it expects to provide Trial Drugs for use in the Clinical Trial. The Sponsor may use the information in the Pharmacy Assurance Pharmacy Technical Review Form to state how the Trial Drugs will be provided (see Section 10 Product Information for each Trial Drug, Product Source section). Alternatively, discussion may be needed with the Trial Site about how it will provide any Trial Drugs, if it is determined that Trial Site will provide them.

This Clause also allows the Sponsor to specify how any unused Trial Drugs will be managed at the end of the Clinical Trial. Examples are provided of ways in which unused Trial Drug might be managed.

Where the Sponsor has provided Trial Drugs itself and it expects these unused Trial Drugs to be returned, it should ensure that appropriate practical arrangements are in place to support this. Return of Trial Drugs could be inspected by the MHRA. Arrangements may need to include consideration of issues such as quarantine, temperature control and monitoring, maintenance of chain of custody, and licensing and ability of the Sponsor to hold prescription medications under the law.

Similarly, where the Sponsor has provided Trial Drugs itself and it expects these unused Trial Drugs to be destroyed on its behalf by the Trial Site, the Parties should ensure that the chain of custody maintained by pharmacy is clear throughout.

Where the Trial Site has provided Trial Drugs from its own supplies, unless it is purchased in bulk and taken out of those supplies for quarantine, it cannot be returned to the Sponsor or destroyed at the end of the Clinical Trial and will remain in the Trial Site's own stocks.

2.15 **mCTA Clause 4.14 (CRO-mCTA 4.15)**

Reflecting different types of clinical trial and differing Sponsor requirements, mCTA 4.14 (CRO-mCTA 4.15) requires that the Sponsor specifies whether the local recruitment target should be expressed as number(s) enrolled, dosed or randomised. Enrolled means that the Participant has consented to be a participant in the clinical trial. Dosed means that the Participant has received their first dose of Investigational Drug. Randomised means that the Participant has been randomised to an arm of the Clinical Trial, or equivalent, in accordance with the Protocol. The local recruitment target is specified either a) as an agreed number of participants or b) as a minimum agreed number of participants to aim to enrol, dose or randomise. Target ranges of participants to be enrolled, dosed or randomised are not acceptable.

2.16 **mCTA Clause 4.15.2 (CRO-mCTA 4.16.2): Enrolment Targets**

mCTA Clause 4.15.2 (CRO-mCTA Clause 4.16.2) makes clear that payment will only be made for Participants who have been enrolled into the Clinical Trial prior to the date of receipt of the notice.

2.17 **mCTA Clause 4.16 (CRO-mCTA Clause 4.17): Transparency Requirements**

Clause 4.16.5 (CRO-mCTA Clause 4.17.5) includes three optional sub-clauses to reflect that a deferral has not been requested or issued (option 1), a deferral has been issued for all of the Transparency Requirements (option 2) or a deferral has been issued for only the publication of results and provision of a lay summary (option 3). Options 2 and 3 include sub-options to specify how the deferral is provided to the Sponsor. Where the deferral is provided to the Sponsor by email, this should be included in Appendix 9 (CRO-mCTA Appendix 10).

2.18 **mCTA Clause 4.18 (CRO-mCTA Clause 4.19): Access, Research Misconduct and Regulatory Authorities**

Reflecting the strict regulatory environment faced by Sponsors (and CROs), representations have been included to confirm that the Trial Site is unaware of any restriction on the Principal Investigator or the Personnel that would prevent that (those) individual(s) from having a role in the Clinical Trial. The representation made by the Trial Site must be made only after reasonable due diligence on its part to ensure that the Sponsor may take adequate assurance from this representation. The clause clarifies that where the Trial Site does not substantively employ the Principal Investigator, or any of the Personnel, the due

diligence shall extend to ensuring there are no restrictions in place with their substantive employer.

Additionally, Trial Sites and Principal Investigators are required to notify the Sponsor of any restrictions being applied to the Trial Site, any Other Trial Site, the Principal Investigator and any Sub-Investigators for five years after the termination or expiry of the Agreement. This time period reflects MHRA expectations to ensure that the Results produced by the Investigator Site are reliable.

Detailed provisions covering the Sponsor's (and CROs) access to the Trial Site and handling of possible misconduct have been agreed and these include various reporting requirements.

2.19 **mCTA Clause 4.18.9 (CRO-mCTA Clause 4.19.9): Retention Period**

This clause sets out the Retention Period for Clinical Trial records. In line with the Medicines for Human Use (Clinical Trial) (Amendment) Regulations 2025, if the Clinical Trial is a "new rules" Clinical Trial and was (or will be) submitted on or after 28 April 2026, the minimum legal retention period is 25 years. If the Clinical Trial is an "old rules" Clinical Trial and was submitted before 28 April 2026, the minimum legal retention period under the Medicines for Human Use (Clinical Trials) Regulations is 5 years. The two sub-clauses clarify when there is a legal requirement to extend the Retention Period and how updates will be managed by the Sponsor.

2.20 **mCTA Clause 4.18.10 (CRO-mCTA Clause 4.19.10): Destruction of records**

This clause clarifies the management of Clinical Trial record destruction in line with the Regulations and Sponsor instruction. Clause 4.18.10.a (CRO-mCTA Clause 4.19.10.a) allows the Trial Site to destroy Clinical Trial records where the Retention Period has expired and it has asked the Sponsor to destroy the records but has not received a response within the contractual timeframe. This position is in line with guidance received from the MHRA.

2.21 **mCTA Clause 4.18.11 (CRO-mCTA 4.19.11): Archiving**

This sub-clause allows for circumstances in which archiving is in line with the Trial Site's usual arrangements, or circumstances in which the Sponsor (or CRO, where applicable) assist the Trial Site to make alternative arrangements for archiving. Costs associated with archiving may be reimbursed by the Sponsor (or CRO, where applicable), and should be charged to it by the Trial Site as a one-off cost.

Where physical archiving is required, the one-off cost is charged at close-down of the Clinical Trial. The minimum charge of £750 per box includes all overheads but excludes VAT. It is not negotiable but as it is a pass-through cost the Trial Site can charge the Sponsor more than this to recoup the additional costs only which the Trial Site is charged at Investigator Site Trial Completion.

Where electronic archiving is required, the one-off cost is charged when the electronic Investigator Trial Master File is established by the Trial Site. The charge of £1000 covers both the establishment of the electronic Investigator Trial Master

File and its archiving. It includes all overheads but excludes VAT; it is not negotiable and cannot be increased.

The one-off fee Sponsors will be charged is to cover archiving of physical boxes and / or digital records for the agreed Retention Period, destruction, the anticipated number of retrievals during the Retention Period, and any other relevant factors. No other fees related to archiving should be charged.

2.22 **mCTA Clauses 4.18.12, 4.18.13 and 4.18.14 (CRO-mCTA Clauses 4.19.12, 4.19.13 and 4.19.14): Use of Material**

The mCTAs define "Material" as "…any clinical biological sample, or portion thereof, derived from Participants, including information related to such material, obtained, stored or analysed by the Trial Site or Other Trial Site in accordance with the Protocol, or otherwise supplied under Appendix 6 (where applicable) to the Sponsor or its nominee." mCTA Clauses 4.18.12 and 4.18.14 (CRO-mCTA 4.19.12 and 4.19.14) distinguish between the situations where a Trial Site (or Other Trial Site(s) should this be subcontracted) analyses material, and situations where a Sponsor takes that responsibility and it is carried out either in the Sponsor's own laboratory or through a third party laboratory.

mCTA Clause 4.18.12 (CRO-mCTA 4.19.12) should be deleted where no analysis of Material will take place at the Trial Site (or, as applicable, Other Trial Site(s)).

mCTA Clause 4.18.14 (CRO-mCTA 4.19.14) should be deleted where no transfer of Material from the Trial Site (or, as applicable, Other Trial Site(s)) will take place for analysis by the Sponsor or their nominee.

Both clauses should remain where analysis of Material will be undertaken by **BOTH** the Trial Site (and / or, as applicable, Other Trial Site(s)) **AND** by the Sponsor or their nominee.

Appendix 6 sets out general responsibilities with respect to the handling and use of Material transferred to the Sponsor (or their nominee) by the Trial Site / Other Trial Site(s), applicable to both Parties and is applicable only where Clause mCTA 4.18.14 (CRO-mCTA 4.19.14) applies.

mCTA Clause 4.18.13 (CRO-mCTA 4.19.13) should be deleted where the Trial Site neither stores nor destroys Material during the course of the Clinical Trial. This clause clarifies management for storage and destruction. It also confirms that where destruction of Material would be in breach of the Trial Site's legal and clinical obligations, the Trial Site shall not destroy this Material. Retaining Material for clinical requirements could be necessary, for example, for ongoing patient care, audit or for future testing for alternative treatment options.

Additional requirements relating to the use of Material in any specific clinical trial are also captured in the Integrated Research Application System (IRAS) Form required to obtain approval for the Clinical Trial. Sponsors and Trial Sites (and CROs, where applicable) are strongly encouraged to review both the IRAS question relating to use of Material and Participants in order to determine the feasibility (or otherwise) of use / participation in multiple Clinical Trials, as well as the accompanying notes which place restrictions on the use of Material.

2.23 mCTA Clause 4.20 (CRO-mCTA Clause 4.21): Hub and Spoke Agreement

This optional clause is for use when the mCTA is used as a head agreement for subcontracting between the Lead Trial Site and Other Trial Site(s) (that is to say where the PI at the Lead Trial Site is overseeing activities at other legal entities, which are therefore part of the same Investigator Site and subcontracted as such).

Clause 4.20.1 (CRO-mCTA 4.21.1) is also optional and is for use where the Sponsor has agreed the inclusion of Other Trial Sites in advance of execution of the Agreement. Clause 4.20.1 (CRO-mCTA 4.21.1) should be duplicated as needed, with one sub-clause per Other Trial Site.

2.24 mCTA Clause 4.21 (CRO-mCTA Clause 4.22): Home health care visit providers

This optional clause is for use where the Sponsor has separately contracted with a home health care visit provider which will support Clinical Trial activities at the Investigator Site, and the Trial Site and Principal Investigator have agreed that this is appropriate. The Sponsor is required to share details with the Trial Site of the services which have been contracted to the home health care visit provider and which will be delivered on behalf of the Investigator Site.

Notwithstanding the Sponsor's contract with the home health care visit provider, the Principal Investigator is still responsible for oversight of all activities at the Investigator Site – including those conducted by the home health care visit provider – for the health of Participants under their care and for the data collected during the Clinical Trial. It is therefore still their responsibility to ensure that the home health care visit provider is an appropriate organisation to deliver these services, and that the Personnel employed by the home health care visit provider are suitably qualified, and have the appropriate registration and skills to conduct the activities which the Principal Investigator delegates to them. The Trial Site should support the Principal Investigator as necessary to seek any reassurance the Principal Investigator needs when assessing suitability of the home health care visit provider and Personnel as part of due diligence. This due diligence may include working with the Sponsor, or other activities without Sponsor input as necessary.

The Sponsor, home health care visit provider, Trial Site and Principal Investigator should agree which activities will be delegated for delivery by the home health care visit provider under the oversight of the Principal Investigator, and how oversight will be provided, before the mCTA (or CRO-mCTA) is executed. This should be documented accordingly with reference as needed to the contracts between Sponsor and home health care visit provider, and Sponsor and Trial Site (and CRO), though the documentation will not be a contract in itself as the respective contracts should reflect the required contractual relationships and obligations.

In addition to the Sponsor's contractual ability through its separate contract to postpone, suspend or discontinue the services of the home health care visit provider, the Trial Site and Principal Investigator also retain the right under the mCTA (or CRO-mCTA) to postpone, suspend or discontinue the provision of home healthcare services by the home health care provider at the Investigator

Site. In line with the above, the Principal Investigator is responsible for ensuring that the home health care provider continues to be an appropriate organisation to deliver home health care visit services, and that the Personnel employed by the home health care provider are appropriately qualified and skilled to continue to conduct Clinical Trial activities delegated to them. Where the services of the home health care visit provider are postponed, suspended or discontinued, the Trial Site and Sponsor (and CRO) shall ensure that home health care services can continue to be provided on behalf of the Investigator Site, or alternative arrangements made to ensure continued participation and safety of Participants in line with the Protocol.

2.25 **Clause 5: Liabilities and Indemnities**

It is essential that Sponsors and Trial Sites (and CROs, where relevant) indemnify each other for any liabilities other than those covered under the ABPI Indemnity Agreement, in case participation in a clinical trial results in damage to a party's property and facilities. Hospitals' non-clinical liabilities in relation to research are not usually covered by existing NHS litigation schemes and it is unlikely that their management would authorise the taking on of unquantified and potentially unlimited liabilities, such as might arise from an intellectual property rights claim.

The liabilities of Trial Sites to Sponsors (and CROs, where applicable) have been capped at two different levels depending on the nature of the breach. The first cap, covering (a) wilful and / or deliberate breaches of the agreement and (b) any breach related to Clauses 6, (Data Protection), 7 (Freedom of Information), 8 (Confidential Information), 10 (Publications) and 11 (Intellectual Property), provides for the Trial Site's liability to be limited to a maximum of twice the value of the agreement, as defined in clause 5.5. The second cap covers all other breaches of the agreement by the Trial Site and limits the Trial Site's liability to the maximum value of the contract.

While for a number of types of possible breaches these provisions might not fully compensate the Sponsor (or CRO) for their loss, it is considered that the risk of paying compensation on this basis provides an additional incentive for Trial Sites to take every reasonable precaution to prevent a breach of the agreement. These precautions could include: (i) having in place robust research governance arrangements; (ii) instituting training programmes for researchers undertaking commercial trials; (iii) emphasising to staff the importance of protecting the integrity of Sponsors' (and CROs) confidential information; and taking disciplinary action in the event of a wilful or reckless breach of the provisions of clinical trial agreements.

Under The Medicines for Human Use (Clinical Trials) Regulations 2004, Sponsors must either have appropriate clinical trials insurance or indemnity in place to cover their liabilities which may arise in relation to the Clinical Trial. Sponsors must ensure that there are no exclusions or conditions on the policy which would impact on the provision of coverage for the Clinical Trial – for example, where paediatric Participants are included, the insurance or indemnity must cover these Participants. It is expected that Sponsors conducting clinical trials in the UK will not self-insure or self-indemnify, unless they can clearly demonstrate that they have established a separate and adequate fund to meet their insurance

obligations which would provide compensation to Participants even if the Sponsor ceases to trade. In the unlikely event that a Sponsor intends to self-indemnify or self-insure, it must make this clear in the application to the research ethics committee for their consideration. Trial Sites will wish to be assured either that sufficient insurance cover has been purchased, or that the Sponsor has provided an indemnity covering potential liabilities to Participants participating in the relevant clinical trial. Research ethics committees that provide an opinion on the trial proposal may therefore take a view, in relation to the risks posed by a specific clinical trial, as to the indemnity and / or the adequacy of the Sponsor's clinical trials insurance.

2.26 **Clause 6: Data Protection**

The mCTAs include general provisions related to compliance with the relevant data protection laws and guidance. The definition of the term "Data Protection Laws and Guidance" includes "**legally enforceable** NHS requirements, Codes of Practice or Guidance issued by the Information Commissioner's Office, in each case in force from time to time in England, Northern Ireland, Scotland and / or Wales". Oversight of this compliance is provided through the clinical trials approval process, which includes a review of the mechanisms for protecting personal data.

Clause 6 is explicitly concerned with Personal Data as defined in the agreement, that is, only personal data of Participants, or potential Participants. The Personal Data of the Principal Investigator or Personnel are not dealt with in the template and requests to alter the template to change this will not be accepted. Sponsors are encouraged to fulfil their transparency obligations for processing the personal data of the PI and Personnel via their signature and delegation log, as per the example provided in IRAS.

Clause 6.2, when taken together with the clinical trial protocol, constitutes a GDPR Article 28(3) compliant data processing agreement between Sponsor, as controller of Personal Data processed for the purpose of the clinical trial, and the Trial Site, as processor of the Sponsor for this purpose.

Clause 6.2.5(a) explicitly references GDPR Article 28(1) and gives "obligations as an NHS organisation" as the guarantee that the sponsor should take in accordance with 28(1). NHS organisations are held to high standards of data protection in each of the four UK nations. Sponsors should therefore take assurance that the measures taken by the NHS are appropriate when relying upon existing NHS processes, systems, etc. for the processing of personal data (as opposed to when Clinical Trial specific provisions are required by the sponsor, such as Electronic Case Report Forms (eCRF), where the requirements of the sponsor should be clearly set out in, for example, the protocol, eCRF manual or other relevant document).

Clause 6.2.6 should set out the position of the Sponsor on the use of Participant Identification Centres (PICs) in the clinical trial and, where their use is permitted, whether the Trial Site may engage PICs under the general written authorisation of the agreement or only with specific written authorisation from, or on behalf of, the Sponsor.

Clause 6.3 provides for the sharing of Personal Data and or the pseudonymised data of data subjects. The drafting of Clause 6.3 is not intended to directly deal with sponsor responsibilities arising from the Data Protection Laws and Guidance, nor to provide the legal basis for the export of personal data to a country outside of the UK. Instead, the Clause is drafted to provide the Trial Site with assurances that NHS organisations are advised, in accordance with Caldicott and NHS policies and best practice, to obtain prior to releasing potentially identifiable confidential patient information to a third party. Alterations to the Clause to form an agreement for the export of personal data, or other alterations that fail to reflect the basis of the clause in Caldicott, NHS policy and best practice, should not be proposed and will not be accepted.

2.27 **Clause 7: Freedom of Information**

This Clause imposes obligations on Trial Sites to take timely action to inform Sponsors (and CROs, as applicable) about requests for information, consult fully with them about disclosure, and inform them, where reasonably practicable, in a timely way of any plans they may have to disclose information against the wishes of a Sponsor.

2.28 **Clause 8.5: Use of AI Tools**

Clause 8.5 specifies that any use of another Party's Confidential Information using AI Tools must receive consent from that Party before doing so. The exception to this is that Sponsor (or CRO) may use Trial Site's Confidential Information in the Sponsor's (or CRO's) Secure AI Tools, which by definition means the Confidential Information cannot be used to train the underlying AI model and must remain solely for Sponsor's (or CRO's) use. As with other uses of the Trial Site's Confidential Information by the Sponsor (or CRO), any use outside of the Secure AI Tool would require the Trial Site's consent.

2.29 **Clause 10: Publications**

The mCTAs recognise that Trial Sites have a responsibility to ensure appropriate publication and dissemination of clinical research for the benefit of patients and their peers. Publication should be done in an orderly way, usually in compliance with the publication policy set out in the Protocol, provided such policy is consistent with the requirements of the Medicines for Human Use (Clinical Trials) Regulations 2004 (as amended 2025).

This Clause sets out conditions governing the way that individual investigators should prepare any publications that they may intend to make, and the opportunities that they should allow Sponsors to comment on them. It also specifies the window of opportunity available to Sponsors in which they can protect proprietary information. It was drafted to ensure that publications based on limited and perhaps unrepresentative data from one site, or a limited number of sites, do not inadvertently misrepresent results, by requiring that the principal report(s) of each clinical trial is (are) published before articles based on subsets of the data.

Where the Principal Investigator or other Personnel contribute to the Sponsor's Multi-Centre Trial publication, Clause 10.6 obliges the Sponsor to give them

access to the Clinical Trial data from all sites involved in the Clinical Trial. This data should be the fully anonymised, aggregated trial data. In line with the data minimisation principles and requirements of GDPR, it is not expected that the Principal Investigator or Personnel will have access to the identifiable data of Participants who did not participate at the Trial Site.

The terms of the mCTAs allow publication of data derived from the Trial Site after the multi-centre publication and subject to the terms of Clause 10.

2.30 **Clause 11: Intellectual Property (IP)**

Four core principles underlie the mCTAs' IP Clauses. First, each party retains ownership of any pre-existing IP or Know-How owned by it or licensed to it. Second, any IP or Know-How generated at the Trial Site that relates to the clinical trial, the IMP or the Protocol (excluding any clinical procedure or related improvements) is the property of the Sponsor. Third, clinical procedures and related improvements are the property of the Trial Site and, depending on the inventor's employer (hospital or university), could be protected accordingly. Fourth, the Trial Site also has the right to use know-how gained during the trial in its normal activities, provided it does not result in disclosure of the Sponsor's confidential information. These provisions are designed to protect the Sponsor's IP and give it ownership of anything derived from it, while allowing the investigator's employer to protect and exploit clinical procedures and related improvements, and to use Know-How generated while the Clinical Trial is being undertaken.

Example 1
If an investigator, supplied with information in the investigator brochure about the characteristics of a new drug, identified a possible role for the drug in a different disease, or a potentially more effective combination with a second drug, the rights to that IP would lie with the Sponsor.

Example 2
If a Protocol specified that a certain type of CT scan should be taken, and while analysing the scan, an employee of the Trial Site developed a new method of analysing CT scans, the rights to that IP would lie with the Trial Site.

Example 3
A Sponsor supplies a case report form for use by an investigator for the Sponsor's clinical trial. In the course of carrying out the Sponsor's clinical trial, the investigator develops, for their own convenience and without being requested to or paid to by the Sponsor, a novel database on which to manage the Participant data. The rights to that IP would lie with the employer of the investigator.

The terms of the mCTAs do not give the Sponsor rights to all IP generated by employees of the Trial Site either in the course of the clinical trial or in the field of the clinical trial.

2.31 **Clause 16.1: Order of Precedence**

In most respects, the terms of the Protocol will prevail over the other terms of the mCTA. However, in respect of six (6) important Clauses: 5 (Liabilities and

Indemnities), 6 (Data Protection), 7 (Freedom of Information), 8 (Confidentiality), 10 (Publications), 11 (Intellectual Property) and 16 (Agreement and Variation), the terms set out in the mCTAs will prevail.

2.32 **Clause 16.3: Contract Variations and Protocol modifications**

The procedure to be followed when changes to the contract are made is set out in Clause 16.3. Where the contract variation involves a change to the Finance Schedule, the Sponsor is responsible for providing this to the Trial Site for its review. The Trial Site then has ten working days to review the revised Finance Schedule and respond to the Sponsor regarding the acceptability of the proposed changes. It is expected that wherever possible this response should be to accept the proposed changes. However, under exceptional circumstances it may be appropriate to request more information from the Sponsor, to propose alternative costs, or to reject the proposed changes. Where the Trial Site needs more time to form an opinion – for example, because the modification is very complex and has introduced a new trial arm – the Trial Site should still respond to the Sponsor within ten working days to request more time to review the acceptability of the changes. However, it is expected that requesting more time to review the proposed changes to the Finance Schedule will be the exception and not the norm.

The implementation of modifications requiring changes to the Finance Schedule should not be delayed until contract variation is completed. Instead, modifications should be implemented (including review and acceptance by the Principal Investigator, in line with Clause 4.7 (CRO-mCTA Clause 4.8)) in a timely manner, whilst good faith negotiation between the Parties continues to finalise and agree the financial aspects of the contract variation. This ensures that the Clinical Trial can be delivered as the Sponsor expects whilst the finer details of the contract variation are negotiated and agreed.

2.33 **Clause 17: Force Majeure**

The parties will agree a reasonable time limit after which delays due to an act of God et cetera, affecting one party's performance of their duties, allow the unaffected party to terminate the contract.

2.34 **Clause 18.1.1: Notices**

It is permitted to serve notice by e-mail, at the discretion of the Sponsor, as set out in this Clause. Where the Sponsor chooses not to allow for notices to be served by e-mail, the Clause should not be altered, the parties should merely refrain from providing email addresses under Clause 18.2.

2.35 **Clause 19: Dispute resolution**

Under the mCTAs, the Parties are required, in the first instance, to attempt to resolve any dispute through discussion between senior managers which, if unsuccessful, may proceed to mediation. An informal local procedure is specified, escalating, if necessary, through more formal processes. If mediation fails, the Parties can take the dispute to the courts of the jurisdiction in which the Trial Site is constituted.

2.36 **Clause 20.4: Governing Law and Jurisdiction**

The Governing law of the mCTA and CRO-mCTA is determined by reference to the nation of the UK within which the Trial Site is constituted.

2.37 **Clause 20.5: Counterparts and Signatures**

The signatories to the mCTA and CRO-mCTA will be the authorised representatives of the Sponsor and the Trial Site (and CRO, where applicable). In the case of the Trial Site, the signatory might be the Chief Executive, the Director of R&D, the Director of Finance, or another authorised person. For the Sponsor in the case of the mCTA, if the Sponsor has formally delegated authority to another party to contractually bind it, this should be evidenced at mCTA Appendix 8. In the case of CRO-mCTA, if the Sponsor has formally delegated authority to the CRO to sign the Agreement, and thereby bind the Sponsor as a Party to the Agreement, this should be evidenced in Appendix 8 and Appendix 9 of CRO-mCTA.

The mCTAs allow for execution to be through use of an electronic signature and for execution to be via counterparts. The mCTA does not specify the method of electronic signature, where this is used, and could be by software such as Adobe Acrobat or online tools such as DocuSign.

Sponsors, CROs (as applicable) and Trial Sites are encouraged to discuss execution arrangements early in the contract negotiation, in order to determine the most appropriate arrangements for all Parties, including the method of execution.

2.38 **Appendix 1: Timelines and Responsibilities of the Parties**

The milestones included in this Appendix are by way of example and the Parties may jointly amend the list as they see fit. It is noted that the target dates should be determined in relation to individual Trial Sites and not in relation to the relevant clinical trial as a whole. Timelines will require early negotiation involving the Principal Investigator and the Sponsor (and the CRO, where applicable). It will be particularly important that they are realistic with respect to the date that the protocol will be finalised, and should build in as footnotes, contingency plans for changes in the event that there is delay in, for example, regulatory or ethics committee approval. The shared responsibilities indicated on the table in Appendix 1 show that the timing of some events is dependent on good co-ordination between the Parties in, for example, scheduling the availabilities of the PI and all relevant Personnel for the initiation visit.

2.39 **Appendix 2: ABPI Clinical Trial Compensation Guidelines 2015 and Appendix 3: Form of Indemnity**

Both appendices are the current ABPI documents and no proposed alterations to either will be accepted.

2.40 **Appendix 4: Financial Arrangements**

The financial arrangements for the Clinical Trial between the Sponsor (and CRO, where applicable) and the Trial Site are included as Appendix 4 of the mCTAs.

Sponsors (and / or CROs, as applicable) should use the NIHR interactive Costing Tool (iCT) to create the Finance Schedule for the Trial Site, after the conclusion of the national resource review, and insert this as Clause 13 of the Financial Arrangements Appendix. Alterations to the Financial Arrangements Appendix outside of the yellow highlighted areas are not permitted.

The financial and other interests of universities that might employ the medical academics and sometimes the research fellows and research nurses involved in clinical trials should be recognised by Trial Sites. The notification arrangements noted above are designed to ensure that universities have the information needed for the protection of their interests. There should be formal agreement between Trial Sites and universities, covering their entire clinical trials portfolio, setting out processes for the identification of the university's direct and indirect costs and overheads, and the apportioning of research income between the institutions. This issue could be covered in the partnership agreements between Trial Sites and associated academic institutions that are negotiated in the process of implementing research governance arrangements.

There should not be separate financial arrangements between the Sponsor (or CRO, as applicable) and any Trial Site departments such as the pharmacy, nor with the university that employs an investigator.

2.41 **Appendix 4: Clause 2: Invoicing and VAT**

Sponsors and Trial Sites should work together to ensure that payments to the Trial Site are kept up to date. This is particularly important when considering the implementation of contract variations, and especially when updating the Finance Schedule to account for inflation, to ensure that any new prices do not apply to activities which have not yet been invoiced for and took place a long time ago.

It is the responsibility of the Trial Site to include VAT on invoices where needed, however, the Sponsor or CRO needs to provide information to support the Trial Site in identifying when VAT is applicable. HMRC's guidance VAT Health is available on their website. As a general rule, the following criteria apply:

- when invoicing a company at an address in the UK, VAT is chargeable;
- when invoicing a company at an address outside of the UK, zero-rated VAT should be added to invoices;
- when a Trial Site purchases equipment from a higher education institution, the purchase is exempt from VAT.

Sponsors, CROs and Trial Sites should seek detailed guidance on VAT requirements from their local tax office as needed.

2.42 **Appendix 4: Clause 2.3: Payment term**

The mCTAs provide a payment term of forty-five (45) calendar days. This payment term should not be revised with respect to any specific Clinical Trial. This payment term represents a balance between the financial processes of Trial Sites and those of Sponsors and CROs.

2.43 **Appendix 4: Clause 2.12: Longstop dates**

It is noted that the Sponsor (or CRO, as applicable) has a right to refuse payment of invoices which are not dated within sixty (60) calendar days of site close out (or within sixty (60) calendar days of the Sponsor providing final invoicing data if that data is requested within forty-five (45) calendar days of the site close out).

2.44 **Appendix 4: Clause 3: Pass-through Payments**

The Trial Site is responsible for making pass-through payments to any of its contractors or suppliers for prices which are included in the price specified in the Localised Online iCT Finance Schedule. The price includes localised market forces factor to support the local costs of various arrangements. Further information on what the market forces factor includes is available on the NIHR website.

2.45 **Appendix 4: Clause 6: Expenses and Other Pass-through Costs**

This Clause details how payment by the Sponsor (and / or CRO) to the Trial Site is managed for the following pass-through costs:

- Expenses, which includes reimbursement of costs incurred by Participants, others who may reasonably accompany them, and the Trial Site's Agents such as its staff, as a result of participation in or involvement with the Clinical Trial
- Ethically-Approved Participant Payments, such as vouchers, compensation for inconvenience and time and payments for loss of earnings for Participants and those who may reasonably accompany them which are agreed by the Research Ethics Committee
- payments for out of hours working which are not agreed through NCVR
- other pass-through costs which the Sponsor, CRO (where applicable) and Trial Site have identified as being required for the Clinical Trial and which are not already covered in the rest of this Clause or as part of NCVR overheads. The template agreements include suggestions for items, services and activities which could be pass-through costs.

2.46 **Appendix 4: Clause 6.5 (out of hours working)**

Clause 6.5 details pass-through costs for out of hours working where the Parties agree that this would be beneficial for the delivery of the Clinical Trial, but is not required by the Protocol or the Sponsor. Only the additional price for out of hours working should be included at the relevant hourly rate specified in the Localised Online iCT. Any out of hours working which is required by the Protocol or the Sponsor is already included in the Localised Online iCT and does not need to be detailed in this Clause. This Clause should not be used to include out of hours working which the Trial Site chooses to do but is not required by the Protocol or required by or agreed with the Sponsor – this type of out of hours working is covered by the market forces factor aspect of the price specified in the Localised Online iCT.

Example 1

The Protocol requires overnight monitoring of Participants after surgery to record data at set time points and any adverse events which occur. As this is required by the Protocol, the out of hours costs for research staff to monitor Participants is included as part of the National Contract Value Review (NCVR) and should therefore be included in the Localised Online iCT. This should not be added to Clause 6.5 as it will form part of the finance schedule at Appendix 4 Clause 13.

Example 2

The Protocol requires Participants to attend a clinic for blood tests. There is no requirement in the Protocol for this to happen out of hours and so it hasn't been included as part of NCVR, but the Trial Site knows that their Participants are more likely to attend appointments in the evening. Having evening appointments available could therefore increase retention at the Trial Site, or ensure that tests are done within the Protocol-required window. The Trial Site asks the Sponsor on this basis and in advance of contract execution if they can offer evening appointments to Participants and be reimbursed for this out of hours activity, and the Sponsor agrees. This is therefore an out of hours pass-through cost and should be added to this clause.

Example 3

The Trial Site sets up a day-time clinic for Participants to attend for Protocol-required blood tests. The appointments overrun and the research team stay late into the evening to ensure all appointments are completed, blood samples are sent off for testing and Clinical Trial records updated. Completing the activity out of hours is not required by the Protocol. This is not included as a specific cost in the Localised Online iCT, and should not be added to this clause as an out of hours pass-through cost on the off-chance that it could occur. The Trial Site is covered for these additional costs through the market forces factor in the staff time price specified in the Localised Online iCT.

2.47 **Appendix 4: Clause 6.8 (other pass-through costs)**

Any other pass-through costs which are not Expenses, Ethically-Approved Participant Payments, out of hours pass-through costs, or archiving should be added to this Clause. These pass-through costs are costs which:

- the Trial Site would not otherwise incur if it did not participate in the Clinical Trial and
- are specific to the Trial Site and
- are not included in the iCT and
- do not incur any overheads for the Trial Site and
- are needed to deliver the Clinical Trial locally.

The contract includes suggestions for pass-through costs which could be added here as agreed between the Sponsor and Trial Site.

- Interpreter services should be added where they are in addition to standard care and are provided by an external provider. Interpreter services provided

as part of standard care are paid for through the Trial Site's usual service provision.

- Any equipment which the Trial Site needs to purchase to deliver the Clinical Trial should be added here.
- Any Trial Drugs which are listed in Clause 4.12 (CRO-mCTA Clause 4.13) as being purchased by the Trial Site should be added here, with the cap specified as the BNF rate or equivalent spent by the Trial Site where no BNF rate exists.

Sponsors and Trial Sites should not add payment for NHS staff who are recruited specifically to support the delivery of the Clinical Trial. Where Sponsors choose to pay NHS organisations for staff time to specifically support the delivery of their studies (for example, a research nurse for one day per week) this should be managed through a separate agreement which is not specific to one Clinical Trial. Instead, there should be an overarching agreement in place regarding this to support the Sponsor's portfolio of research at the Trial Site.

Other pass-through costs could be added to the contract in line with the principles in this guidance.

2.48 **Appendix 4: Clause 8.1.1 (screen failures)**

This Clause details the management of screen failures with two options. Both options require payment to be made individually for each screen failure.

The first option is to be used when the Sponsor will pay for all Screen Failures so long as it was not clear to the Trial Site at the start of screening that the potential Participant would not be eligible to participate.

The second option is to be used for all other Screen Failures. An initial cap for payment to the Trial Site, based on a set number of screen failures specified by the Sponsor, is included in the first sentence. The Sponsor or CRO should indicate the number of screen failures it will pay for per number of Participants enrolled, dosed or randomised, if and when the cap is reached. Payment is to be made individually for each screen failure once the set number of Participants enrolled, dosed or randomised is met. If the Sponsor will not pay for any Screen Failures, "0" should be entered into every [X].

2.49 **Appendix 4: Clauses 8.1.2 (Screen Failure) and 9 (Unscheduled Visit) payments**

Clauses 8.1.2 and 9 require the Sponsor to be invoiced only for activities which are relevant to any screen failure or unscheduled visit, in line with the relevant individual task values set out in the Localised Online iCT. Individual activities are not listed in the contract so that Sponsors are not inadvertently invoiced for non-research, standard of care activity. Trial Sites are therefore required to use the information in the Localised Online iCT to determine what should be invoiced for. More information about how to use the iCT to create invoices is included in the guidance on Appendix 4: Clause 13: Finance Schedule (point 2.51 of this document).

2.50 **Appendix 4: Clause 12.3 (bank details)**

This clause provides bank details for payment to be made to the Trial Site. The Trial Site is responsible for ensuring that any payments received are disbursed appropriately internally, including to different hospitals within the same organisation, different departments, and to any Other Trial Sites within the Investigator Site and / or any PICs.

2.51 Appendix 4: Clause 13: Finance Schedule

The Finance Schedule is generated by the interactive Costing Tool (iCT), following completion of the iCT study resource review, release of iCT to the Sponsor and creation by the Sponsor of organisation-level Localised Online iCTs. The relevant Finance Schedule is to be inserted into the Finance Appendix when sharing the Agreement with the Trial Site; it does not need to be included in the version of the Agreement submitted for regulatory review.

For studies that fall within scope of the National Contract Value Review (NCVR) programme, alteration of the iCT-generated Finance Schedule is prohibited. The following actions are not considered to be alterations and are therefore permitted changes:

- Sponsor or CRO changing the order of items within tables of the Finance Schedule for ease of reading.
- Sponsor or CRO removing items from the Finance Schedule that are not relevant to that Trial Site (for example, removing items relevant only to an arm of the Clinical Trial not being conducted at that Trial Site, or removing nursing time which is covered through a separate agreement between Sponsor and Trial Site for the Sponsor's portfolio of studies at the Trial Site).
- adjustment of the decimal places to align the contract values with the financial management and invoicing system used at the Trial Site. Further information on the rationale for allowing this alteration is available in the Site Review section of the iCT Frequently Asked Questions.

In many cases, prior discussion with the Trial Site will be necessary to agree any items to be removed. Items may not be added by any Party outside of the NCVR national negotiation.

Unaltered use of the Finance Schedule is recommended for studies which fall out of scope of the NCVR programme. In this case, the Localised Online iCT (and therefore the Finance Schedule) is a guideline upon which to base discussions between the Sponsor or CRO and Trial Site. The Financial Appendix itself is however a part of the Agreement template and should be used without alteration for all studies, within or outside of the scope of NCVR.

Where the Trial Site will sub-contract with Other Trial Sites and / or with PICs, the Sponsor and / or CRO should work with the Trial Site and, as necessary, any Other Trial Sites / PICs to ensure that the Localised Online iCT (and therefore Finance Schedule) accurately reflects the activities and therefore the NCVR centrally negotiated prices for each relevant participating organisation.

The Financial Schedule is not designed to directly support invoicing or the internal disbursement of income. The Sponsor / CRO should provide the Trial Site with the

iCT Excel / csv export for that Trial Site, no later than Sponsor green-light for the Trial Site, to facilitate Trial Site invoicing and disbursement of funds.

The iCT is not designed as an invoicing system, though it does include appropriate data from which invoices can be created. The Excel export contains all the numerical data to create a budget or invoicing schedule which aligns with the mCTA. To create an itemised version of the activities to be invoiced for, the Sponsor / CRO should export the Localised Online iCT in the same financial year as the agreement of the contract so the data matches between contract and export. The Trial Site needs to do one of the following to the numerical data to itemise it for invoicing appropriately:

a. Divide the Totals column on the right hand side of the export by the number of occurrences of that activity during the Clinical Trial. Repeat this for each activity which needs to be invoiced for.
b. Upload the export to the local portfolio management system, which may have a programme to do the individual calculations for each activity.

Disbursement of funds within Trial Sites should align with the UKRD guidance on the NIHR's website on income distribution from RDN industry portfolio studies. Trial Sites in other UK nations should adhere to their own national guidance on disbursement of funds.

2.52 **Appendix 5: Conditions Applicable to the Principal Investigator**

It should be noted that there is an obligation on Trial Sites that are not members of the relevant risk pooling scheme, to ensure that the Principal Investigator carries professional liability insurance.

2.53 **Appendix 6: Material Transfer Provisions**

Where no Material is to be supplied by the Trial Site to the Sponsor or their nominated representative, tick the box to confirm that Appendix 6 does not apply.

2.54 **Appendix 7: Equipment and Resources**

Where no Equipment or Resources are being provided, tick the box to confirm that Appendix 7 does not apply.

Appendix 7 includes tables where equipment and resources that are provided by Sponsors (and / or CROs, as applicable) for the Clinical Trial should be listed. These tables include a column where the depreciated value of the equipment / resources can be detailed. It is noted that there is no standard method for determining depreciation and therefore, this must be discussed and agreed between Sponsor and Trial Site (and CRO, as applicable).

The Sponsor (or CRO, as applicable) should indicate whether alternative 1, 2 or 3 should be used with respect to disposition in Clause 4 of Appendix 7. The selection should be clearly indicated in the Agreement and the unused alternatives should be deleted from the Agreement.

The Sponsor (or CRO, as applicable) should indicate whether alternative 1 or 2 should be used with respect to liability in Clause 7.3 of Appendix 7. The selection

should be clearly indicated in the agreement and the unused alternative should be deleted from the Agreement.

Northern Ireland does not have any MIA arrangements and the MIA in England is not applicable to equipment loaned or gifted for the purpose of clinical trials. Alternative #1 must be used where the Trial Site is constituted in England or Northern Ireland.

2.55 **Appendix 8 (CRO-mCTA only): Sponsor's Clinical Trial Related Duties and Functions Under ICH-GCP to be Performed by CRO**

This Appendix should clearly set out which Sponsor responsibilities for site management will be performed by the CRO.

2.56 **Appendix 8 mCTA (Appendix 9 CRO-mCTA): Formal Delegation of Authority from Sponsor to Another Party to Contractually Bind the Sponsor as a Party to this Agreement**

Where applicable, attach here evidence of formal delegation of authority, from the Sponsor to another organisation, to sign this Agreement and thereby legally bind the Sponsor to its terms as a Party. The delegation of authority must explicitly state that the Sponsor allows the other organisation to sign agreements with sites on the Sponsor's behalf. Other activities such as negotiating contracts do not explicitly include entering into the agreement with the Trial Site on the Sponsor's behalf, and will not be accepted as sufficient evidence where they are present without this.

Where the Sponsor is not formally delegating authority to another organisation to contractually bind it as a Party to the Agreement, tick the box to confirm that this Appendix does not apply.

2.57 **Appendix 9 mCTA (Appendix 10 CRO-mCTA): Authority to Defer the Transparency Requirements for the Clinical Trial**

Where applicable, attach here email evidence from the Authority to defer the Transparency Requirements for the Clinical Trial.

Where the Authority has automatically issued a deferral, this will be included in the research ethics committee's favourable opinion letter and will therefore be shared with the Trial Site as evidence of the regulatory approval being in place.

Where there is no deferral in place to register the Clinical Trial, or where the deferral is provided within the research ethics committee's favourable opinion letter, tick the box to confirm that this Appendix does not apply.

Contact Points for Advice and Assistance

For queries relating to the use of the mCTAs for trials taking place in England: please contact the Health Research Authority, at research.agreements@hra.nhs.uk.

For queries relating to use in Wales:
please contact the Health and Care Research Wales Support and Delivery Centre at research-contracts@wales.nhs.uk.

For queries relating to use in Scotland:
please contact NHS Research Scotland at enquiries@nrs.org.uk.

For queries relating to use in Northern Ireland:
please contact ResearchContracts@innovations.hscni.net.

3. Background and Change History

Background

The mCTA was published by the Department of Health and the ABPI in 2003.

The mCTA was updated in 2006 to take into account the introduction of the EU clinical trials directive and the directive on good clinical practice in pharmaceutical research. Versions of the mCTA were also created for use in Northern Ireland, Scotland and Wales.

The first CRO-mCTA was published in 2007. Based on mCTA 2006, it allowed unaltered use of a template agreement in circumstances where a CRO undertook site management responsibilities and chose to become Party to the site agreement, allowing for the division of responsibilities between Sponsor and CRO to be set out.

A further update, to both the mCTA and CRO-mCTA, took place in 2011. Changes were made in two areas only: clarification that universities employing staff involved in contract clinical trials at Trial Sites are classed as agents of the Participating Organisation; and anti-bribery and corruption provisions were included.

The 2018 model was the fourth version of the mCTA, and the third version of the CRO-mCTA, and was influenced by the work of the Ministerial Industry Steering Group (MISG), a body which brings together government and the bio-pharmaceutical industry.

In 2016, the MISG Clinical Research Working Group (CRWG) recognised the need to enhance further the UK's position as a great place to do commercially funded research. Following feedback from NHS stakeholders and industry partners, it was decided to develop UK-wide mCTAs as well as bringing the mCTAs up to date with current practice and regulations.

The March 2020 mCTAs built upon the previous versions and reflected significant engagement with both NHS and commercial stakeholders. The most substantial changes took account of the introduction of the General Data Protection Regulation (GDPR) and the Data Protection Act 2018. From this version onwards, the mCTAs have formed GDPR Article 28(3) compliant data processing agreements, as well as incorporating provisions for the transfer of Personal Data and/or pseudonymised data.

The January 2021 mCTAs incorporate further industry feedback on the templates, as well as taking account of the legal situation at the end of the transition period for the UK leaving the EU.

The May 2022 versions take account of comments and suggestions received by users and align with the UK guidance on the set up of research activity at NHS organisations (interventional research), particularly in adaptations to allow for use, where required, as head agreements from which a ‘hub’ may subcontract to ‘spokes’.

The October 2023 versions of the mCTAs introduced the standardised Finance Appendix template as part of the government's response to the O'Shaughnessy Review of commercial clinical research in the UK.

The May 2025 versions of the mCTAs introduce further standardisation following on from feedback related to the changes introduced in October 2023.

The April 2026 versions of the mCTAs include changes related to the introduction of the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 and changes as a result of feedback received from industry, the NHS and MHRA.

It is anticipated that the mCTAs will be kept under ongoing review.

Change History

Summary of Key Changes in April 2026

General

Clarification that the Sponsor to be named in the Agreement is the organisation acting as Sponsor in the UK – which might be different to the organisation acting as Sponsor globally.

Changes to terminology throughout to reflect changes brought in by the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025:

- "Amendments" to describe updates to the Protocol and / or Clinical Trial changed to "modifications" to align with the regulations
- Contractual references to post-execution "modifications" in the Agreement changed to "variation" to prevent confusion with modifications under the regulations
- "Modifications" to the templated wording in the agreement updated to refer to "alterations" to prevent confusion with modifications under the regulations
- "Modifications" to legislation and guidance changed to "amended" to prevent confusion with modifications to the Clinical Trial under the regulations

Update to the name of Appendix 8 and associated recital to clarify that an organisation which is not the Sponsor or its Affiliate may be legally empowered to contractually bind the Sponsor.

Update to instructions.

Definitions

New definitions added to accommodate changes made as a result of the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025:

- Authority
- Public Registry
- Transparency Requirements

Definitions revised to accommodate changes made as a result of the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025:

- Clinical Trial Authorisation removed, and updated to Clinical Trial Approval (adding in the favourable opinion issued by the research ethics committee)
- Definition of Investigational Medicinal Product (IMP) updated to refer to that in the legislation
- Definition of Investigational Drugs removed, and updated to Trial Drugs to refer to the defined terms in the legislation
- Investigator Trial Master File updated to be Investigator Site File, and reference in ICH-GCP updated to refer to E6 R3
- Reference to requirements for what to store in the Sponsor Trial Master File updated to align with ICH-GCP E6 R3
- Definition of Sub-Investigator updated to align with ICH-GCP E6 R3

Clarification made in the definition of Confidential Information that it includes information which was previously shared under a confidentiality disclosure agreement which was superseded by the mCTA / CRO-mCTA being entered into.

Update to the legislation referred to in the Data Protection Laws and Guidance.

Clarification that the definition of Ethically-Approved Participant Payments includes payments made to parents, carers, or others accompanying Participants.

Clarification that the completion of all Protocol required activities at Investigator Site Trial Completion includes data collection and query resolution.

Definition of Joint Position deleted as the transparency requirements in the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 supersede those in the Joint Position.

The word “site” removed from the definition of Lead Trial Site to more accurately reflect the delivery model of the trial overall, not the particular site.

Update to the definition of Material based on options introduced to Clause 4.

Removal of the definition MHRA.

Addition of new definition Secure AI Tool.

Clarification that Trial Completion means the global conclusion of all Protocol required activities, including data collection and query resolution, for all Participants enrolled.

Clarification added that the Trial Monitor may be appointed on behalf of the Sponsor (for example, where the Trial Monitor is appointed by the global Sponsor on behalf of the UK Sponsor).

Removal of the reference to the version and date of the UK Policy Framework applicable to this Agreement; updates are managed through Clause 1.2.

Update to Clause 1.2 to clarify that the Declaration of Helsinki specified in the contract is the version which will be followed and will not be updated.

Clause 2

Clarification in Clause 2.3 regarding termination, in line with updates made to Clause 14.

Clause 3

Added email address to Clause 3.1 to modernise ways Trial Site and Principal Investigator can contact the Trial Monitor and report serious adverse events.

Added three options to Clause 3.3.4 for the Sponsor to specify which version of the Declaration of Helsinki it will follow.

Clause 4

Simplification in Clause 4.4.1 that the requirements are from the amended Medicines for Human Use (Clinical Trials) Regulations 2004.

Removal of Clauses 4.5 and 4.6 regarding registration and deferral of the Clinical Trial, and addition of replacement clauses in Clause 4.16.

Simplification of the new Clause 4.5 (previous Clause 4.7) in line with updates to the definitions.

Clarification in the new Clause 4.6 (previous Clause 4.8) that Trial Drugs not be used and the Clinical Trial shall not start until the Sponsor has received confirmation from the Public Registry that it has either been published or accepted onto the registry, in line with requirements of the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025.

Updates made to Clause 4.7 (previous Clause 4.9) to reflect the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 and MHRA expectations regarding implementation of modifications.

Clause 4.10 (previous Clause 4.12) updated to encompass Trial Drugs (that is, any drug mentioned in the Protocol) and to clarify that if the Trial Site has incurred VAT when purchasing Trial Drugs, the Sponsor will reimburse the Trial Site for the VAT incurred.

Addition of Clause 4.16, Transparency Requirements, to reflect requirements in the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025.

Clause 4.18.1 (previous Clause 4.19.1) updated to clarify MHRA expectations regarding management of restrictions on Principal Investigator and Personnel.

As per MHRA request, clarification in Clause 4.18.3 (previous Clause 4.19.3) that the Trial Site can, in certain circumstances, inform the Regulatory Authority that a Serious Breach has occurred.

Clause 4.18.9 (previous Clause 4.19.9) split into three separate sub-Clauses for clarity regarding archiving arrangements:

- Replacement of the reference in Clause 4.18.9 to the “MRC Principles and Guidelines for Good Research Practice” with the “MHRA’s Guidance on GxP data integrity” due to being more appropriate
- Addition of two further sub-Clauses to Clause 4.18.9 to clarify when the Retention Period needs to be legally extended

- Clarification in 4.18.11b that the costs of archiving are pass-through costs and therefore will not receive capacity build or market force factor costs
- Update to the electronic archiving fee to £1000 to more accurately reflect costs paid by NHS organisations

Addition of a new Clause 4.18.13 to clarify expectations regarding storage and destruction of Material where this is managed by the Trial Site.

Clause 4.19 (previous Clause 4.20) made mandatory for ease of use and to reflect Appendix 7 (Equipment and Resources) being included in all Agreements, even where not applicable.

Mechanism added to Clause 4.20 (previous Clause 4.21) to manage the addition of Other Trial Sites both prior to execution of the Agreement (addition of Clause 4.20.1) and after execution of the Agreement (contract variation).

New Clause 4.21 added and developed with MHRA as a result of feedback to accommodate scenarios where Sponsors contract with a home health care visit provider to perform home health care services for the Clinical Trial.

Clause 5

Clarification in Clause 5.6 at the request of the MHRA that Sponsor warrants that the insurance cover does not exclude Participants who are eligible to participate.

Clause 6

Addition of Clause 6.2.5.g to clarify that Trial Site must comply with GDPR Article 28(3)(h).

Clarification in Clause 6.2.6.a that where the Trial Site will contract with a PIC, it will do so using the unaltered model commercial participant identification centre agreement.

Clause 8

Clarification in Clause 8.1 that where the Parties use each other's Confidential Information outside of the Agreement, the prior written consent of the other Party shall not be unreasonably withheld or delayed.

Clarification in Clause 8.2.4 regarding the confidentiality of information received from another party which is not Party to the Agreement.

Clarification of the confidentiality requirements in Clause 8.4, and addition of the extension of confidentiality requirements where a deferral is in place.

Addition of a new Clause 8.5 to govern use of Confidential Information with artificial intelligence (AI).

Clause 10

Clause 10.1.1 amended to clarify that presentations and publications etc by the Trial Site, Other Trial Site and Principal Investigator shall be subject to any deferral issued by the Authority.

Deletion of Clause 10.4 (replaced by Transparency Requirements in Clause 4).

Clause 12

Clauses 12.6 and 12.7 added as a result of feedback to clarify that payments made to the Trial Site are not an inducement or bribe regarding the Sponsor's products or services.

Clause 12.8 added to clarify that Participants shall receive the IMPs and any devices used to administer IMP free of charge.

Clause 14

Termination clauses updated throughout to align more closely with the wording in the non-commercial agreements whilst retaining the underlying meaning and intent.

Clarifications made throughout as to when clauses apply to termination of the Agreement, early termination of the Agreement, or both.

Clarification added to Clause 14.2 about what happens if a Sub-Investigator becomes unavailable, with sub-Clauses 14.2.1 and 14.2.2 added to specify when impacts on the Investigator Site will be managed by termination.

Clarification in Clause 14.5 that where the Trial Site is in material or continuing breach of the Agreement, it has a responsibility to ensure that the Results it provides are reliable (so far as is reasonably possible).

Clarification in Clause 14.6 that the Trial Site shall ensure that unnecessary Clinical Trial-related activities are not undertaken once the Agreement is terminated early.

Clarification added to Clause 14.7 of what Trial Site activities shall be at termination of the Agreement, and that the activities shall be at the expense of the Sponsor.

Clause 15

Clarification in Clause 15.2 that sub-contracting includes the provision of equipment and resources from vendors.

Further clarification added to Clause 15.2 that any sub-contractors are bound by terms at least as stringent as those in the mCTA / CRO-mCTA.

Clause 16

Clarification of the procedure to manage contract variations, and in particular where the Finance Schedule is updated.

Clause 20

Addition of the Transparency Requirements to the Survival of Clauses.

Appendix 4

Restructure of Clause 6 (Expenses and Other Pass-through Costs) to bring payment method clauses together with their associated tables.

The guidance for Clause 6.5 updated to clarify when the out of hours clauses do not apply.

Addition of Clause 6.8 to clarify pass-through costs which the Sponsor expects to pay, with associated guidance added to the instruction pages.

Clause 8.1.1 split into two options for clarity of the scenarios which could apply.

Appendix 7

Checkboxes added to Clauses 3 and 4 to indicate if they do not apply.

Addition of Clause 7.2 to accommodate MHRA’s request for clarity on this point.

Appendix 9

Update to the name of this Appendix to reflect changes made due to the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025.

Summary of Key Changes in July 2025

General

Corrections of typos throughout.

Corrections of defined terms to the appropriate term throughout.

Definitions

Updated definition of Agent to clarify that this includes chief investigators contracted through a model commercial chief investigator agreement (mCCIA), enabling clauses within the mCTAs and mCCIAs to work together and allow the sharing of Confidential Information.

Updated definition of Confidential Information to clarify that this includes sharing information provided by the Sponsor's Agents, enabling clauses within the mCTAs and mCCIAs to work together and allow the sharing of Confidential Information.

Appendix 8

Clarification within the title of this Appendix that it can be used where a third party has been delegated authority to enter into the Agreement on behalf of the Sponsor.

Summary of Key Changes in May 2025

General

Timelines updated to reference "working days" throughout unless there is an underlying reason to use another way to measure timelines, such as legal or financial reasons.

Update to instructions.

Replacement of the defined term Research Governance Framework with UK Policy Framework.

Clarifications that this Agreement relates solely to the involvement of an individual as Principal Investigator, to provide clear separation of contractual terms where the same individual is also acting as Chief Investigator, which should be contracted separately.

Correction of the terms "cost", "fee" and "price" to be appropriate to the relevant usage throughout.

Definitions

Addition of the defined term Ethically-Approved Participant Payments.

Removal of ethically-approved pass-through Participant costs from the definition of Expenses.

Addition of the defined term Localised Online iCT.

Definition of Material is no longer optional.

Clause 1

Additional clause to confirm that references to the NHS throughout refer to the HSC where the Trial Site is constituted in Northern Ireland, and removal of recital E to reflect this.

Addition of clause 1.7 to include a provision that where any part of the Agreement is found to be illegal, invalid or unenforceable, the rest of the Agreement shall remain in full force and effect.

Clause 3.7

Minor adjustments to provide clarity that Prohibited Acts includes offences under the Bribery Act 2010.

Clause 4

Clarification in Clause 4.11 that this clause only applies where the Sponsor is providing Investigational Drugs to the Trial Site.

Addition of Clause 4.12 to confirm that the Sponsor will reimburse the Trial Site for the use of its own stock of Investigational Drug and / or rescue medication, and the price for reimbursement.

Addition of Clause 4.13 to confirm management of Investigational Drugs at termination or expiry of the Agreement.

Addition of Clause 4.14 to confirm how Investigational Drugs will be supplied and managed at the termination or expiry of the Agreement.

Amendment of Clause 4.19.9 to specify the price for archiving of physical or electronic records.

Removal of the requirement to add Other Trial Sites to the Agreement through a contract variation.

Clause 6

Clarification in Clause 6.2.1 that this relates to Personal Data Processed for the purpose of the Clinical Trial only.

Clarification in Clause 6.3.3 that Personal Data and Pseudonymised Data can be used outside of the Clinical Trial as long as it is as permitted in the approved consent form.

Addition of Clause 14.6, which was previously deleted in error. Addition of information to that Clause regarding automatically backed-up or archival copies of information. Addition of options to the same clause for management of Confidential Information at the end of the Clinical Trial – either return to Sponsor or destroy.

Appendix 4: Clause 6

Clarification that this clause related to pass-through costs more widely than Expenses.

Addition of a table in Clause 6.3 to specify caps for individual types of Expenses.

Addition of Clause 6.4 to set out of hours payments, where applicable.

Addition of Clause 6.5 to confirm Ethically-Approved Participant Payments.

Clarification within Clause 6.6 of how Expenses will be paid.

Addition of Clause 6.7 to confirm how Ethically-Approved Participant Payments will be paid.

Appendix 4: Clause 8

Addition of an option in Clause 8.1.1 for the Sponsor to pay for all Screen Failures.

Appendices 6-9

These Appendices are now mandatory to include so that referencing within the Agreement is retained. A box is included within each Appendix to indicate if it does not apply in the Agreement.

Summary of Key Changes in December 2023

General

Correction of typographical errors and inclusion of other omissions from the October 2023 templates.

Clause 4

Clarification of destruction of records when there is no response from the Sponsor in clause 4.16.9 (clause 4.17.9 CRO-mCTA)

Clause 4.16.9.c (Clause 4.17.9.c CRO-mCTA) is corrected and updated to clarify archiving fees

Clause 17

Removal of the in-clause definition of “A Delay” and associated update to the wording to ensure clarity

Appendix 4: Finance Appendix

Addition of Clause 1.4 in Appendix 4 (Financial Appendix) to ensure that Trial Sites can defer funds paid under the Agreement into future financial years to build future research capacity.

Summary of Key Changes in October 2023

General

References to Clinical Trial Subject updated to Participant.

References to contract variations simplified and clarified throughout.

Definitions

Clarification of the definition of Affiliate.

New definition added for Confidential Participant Information.

New definition added for Environmental Information Regulations (EIR).

New definition added for Expenses.

New definition added for Retention Period.

Clause 4

Addition of Clause 4.6 to clarify whether deferral of public registration has been requested.

Clause 4.15 added to include an obligation for Parties to ensure that their notice, contact and payment details are kept up to date and shared with the others until the Retention Period ends.

Clause 4.15 has been updated to include an obligation for the Sponsor to inform the Trial Site of any changes to the contact point for notices during the archiving period.

Clause 4.16.9 is modified to clarify that the Sponsor should not receive additional identifiable Confidential Participant Information if receiving Trial Site records after the Retention Period (in keeping with separation of Investigator Trial Master File and Sponsor Trial Master File). Arrangements added for ensuring the Trial Site is reimbursed for costs associated with archiving, in accordance with the Finance Appendix. A further addition is made to allow the Trial Site to destroy all Clinical Trial records after the Retention Period has ended, where the Trial Site has received no response from the Sponsor to its request to destroy the records.

Clause 5

Clarification on the meaning of “fees payable” added to Clause 5.4.

Clarification on the meaning of “value of the Agreement” added to Clause 5.5.

Clause 7

Addition of the EIRs throughout this Clause.

Clause 8

Addition of the EIRs to Clause 8.1.

Modification made to clarify that Clause 8 applies to Clinical Trial records during the Retention Period.

Clause 12

Clauses 12.4 to 12.8 in the May 2022 version either removed due to duplication or moved to Appendix 4.

Addition of new Clauses 12.3 and 12.4 to the October 2023 version to specify how payments will be managed to accommodate increases or decreases in recruitment and over- and under-recruitment.

Clause 20

Signature block at Clause 20.5 modified to clarify when the Sponsor signs the Agreement versus a third party signing the Agreement on behalf of the Sponsor.

Appendices

Addition of the template Finance Appendix in Appendix 4, including the use of the standardised Finance Schedule from the iCT export.

Addition of Appendix 9 (Appendix 10 CRO-mCTA).

Summary of Key Changes in May 2022

General

References to Participating Organisation updated to Trial Site.

Reference to non-applicability in Phase I trials with healthy volunteers removed, as the current template is considered suitable for use in such trials in the NHS.

Recitals

New recital G – for use when it is intended that the Trial Site will be a Lead Trial Site in a hub and spoke delivery model, subcontracting with Other Trial Sites.

Definitions

Revised definition for Data Protection Laws and Guidance (to reflect EU adequacy decision on UK data protection regime).

New definition added for Hub and Spoke Agreement.

New definition added for Investigator Site.

Definition of Site File changed to definition of Investigator Site File.

New definition added for Lead Trial Site.

Revised definition for Multi-Centre Trial, to specify that a Trial is Multi-Centre only if it has more than one Investigator Site (that is to say, more than one Principal Investigator).

New definition added for Other Trial Site.

New Definition added for Participant Identification Centre.

Definition of Site removed and references to Site throughout template updated (e.g. to Trial Site) or removed throughout.

Clause 3

Clause 3.6 removed as referenced to individual sites needing regulatory approval are outdated.

New optional clause 3.6.2 for use in dose escalation CTIMPs, introduced at the request of and drafted collaboratively with the MHRA GCP Inspectorate.

Clause 4

Clause 4.2 (and as applicable throughout the template) addition of reference to 'potential clinical trial subjects' added, to emphasise that the Parties responsibilities to respect principles of medical confidentiality and data protection are not limited only to enrolled participants but extend to persons who may be screened, etc. but not then enrolled.

Clause 4.6.1 'and as the case me be' removed, as the mCTA is intended for use only with CTIMPs.

New optional clause 4.14 for use when the Agreement is being used as a Head Agreement, from which the Lead Trial Site may subcontract to Other Trial Sites.

Clause 4.15.4 modified to clarify that monitoring may take place via remote means.

Clause 11

New clause 11.6 intended to provide additional assurance that Material will not be analysed so as to obtain privileged information relating to IMP to which clinical trial subjects may have been exposed in other research studies.

Clause 16

Clause 16.4 modified to allow there to be more than one Investigator Site contracted within the one Trial Site (i.e. for there to be multiple PIs for the Clinical Trial within the one NHS organisation) without the contract signed for the first PI being inadvertently superseded by contracts signed for subsequent PIs.

Appendices

Appendix 4 – additional instruction added to the note.

Appendix 7, clause 7.2 – note added to reiterate that only alternative 1 may be selected for Trial Sites in England or Northern Ireland (where Master Indemnity Agreement schemes do not operate to cover equipment used in research).

Summary of Key Changes in January 2021

Throughout, both mCTAs various minor modifications and errata corrections have been made which are not intended to modify the interpretation of the templates. In addition,

the following changes have been made specifically to account for the end of the transition period following the UK exiting the EU:

Recital F (CRO-mCTA Recital G)
Amended to refer to the sponsor not being established in the UK or another country listed under regulation 3 (11A) of The Medicines for Human Use (Clinical Trials) (Amendment) (EU Exit) Regulations 2019;

Definition of Data Protection Laws and Guidance
Amended to reference the UK GDPR and the requirements set out or referenced in Part Three, Title VII, Article 71(1) of the Withdrawal Agreement signed by the UK and the EU in December 2019;

Definition of GDPR
New definition added for UK GDPR;

Definition of GMP
Replacement of reference to “relevant European Union” regulations with reference to Schedule 2A (and regulation B17(1), if and when applicable) to The Human Medicines Regulations 2012 (for England, Scotland and Northern Ireland) and to any applicable EU standard (for Northern Ireland);

Definition of GVP
Replacement of reference to “relevant European Union” regulations with reference to UK regulations or standards on good pharmacovigilance practices and in the case of Northern Ireland any applicable EU requirement;

Definition of ICH-GCP
Replacement of reference to Directive 2001/20/EC, of the European Parliament, and related guidance with reference to such Good Clinical Practice requirements as may apply within the UK from time to time including the requirements of any regulations made under regulation 57 of The Medicines for Human Use (Clinical Trials) Regulations 2004/1031 (as amended by The Medicines for Human Use (Clinical Trials) (Amendment) (EU Exit) Regulations 2019) and any relevant guidance issued under those Regulations and, in the case of Northern Ireland, any applicable EU requirement;

Clause 3.2.1
Removal of clause referencing laws of the EU;

Clauses 3.2.8 and 3.2.9
New Clauses respectively referencing relevant law having effect by virtue of sections 2-4 of the European Union (Withdrawal) Act 2018 and (in Northern Ireland) laws of the European Union having effect as a result of the Protocol on Ireland/Northern Ireland;

Clause 4.7.1
Addition of reference to IMP marketing authorisation “within the relevant part of the UK” to reflect the position of Northern Ireland under the Protocol on Ireland/Northern Ireland;

Clause 6.2.9(b)
Clause modified to refer to “UK and the EEA”;

Clause 6.2.10
Clause modified to refer to “UK and the EEA”.

In addition to the above, the following modifications have been made following consideration by the UK Four Nations Contracting Leads of comments and requests from stakeholders:

Definition of Agreement
Amended to explicitly reference amendments to the Agreement;

Definition of Joint Position
Reference updated to latest published version;

Clause 2.7
New Clause added to further clarify the responsibilities of the Participating Organisation for the appropriate appointment of Personnel;

Clause 3.7.1
The Clause has been made optional, for inclusion only in agreements for Phase I clinical trials in NHS patients. The definition of SUSAR has been removed from the main definitions section and defined at its single occurrence, at 3.7.1(a);

Clause 6.1.2
Clause modified to clarify that the responsibility is for one Controller to notify the other Controller of any data breach only when the breach is of data of which both parties are at that time separate Controllers. For example, the Clause obliges the Participating Organisation to notify the Sponsor of a breach of medical records which contain data processed for the purpose of the Clinical Trial, as both Participating Organisation and Sponsor are separate Controllers of this data. It does not oblige the Sponsor to notify the Participating Organisation of breaches that may occur to data for which the Participating Organisation is no longer a Controller;

Clause 6.2.4
Clause modified to clarify responsibility of the Participating Organisation to notify the Controller of processing undertaken other than in accordance with the Sponsor instructions, BEFORE undertaking such processing, unless prohibited from doing so, but to emphasise that notification should take place after the processing as soon as possible after such prohibition is lifted, if it is lifted;

Clause 6.2.6
Clause modified to allow the Sponsor/CRO to propose a duration other than five (5) business days in this optional part of the Clause;

Clause 6.3.6
Clause modified to clarify that it is the responsibility of the Sponsor (and CRO) **TO TAKE REASONABLE STEPS** to proactively prevent Personal Data Breaches;

Clause 7.2
Scope of Clause broadened to apply not only to information that belongs to the Sponsor (CRO) or Affiliate but also to any information that relates to the agreement, to clarify that the Clause would apply to information not owned by the Sponsor but, for example, provided to the Sponsor by a Non-Affiliate third party;

Clause 8
Scope of Clause broadened again to clarify applicability to information provided by or on behalf of Affiliates or related persons;

Clause 10.4.1
Clause modified to be explicitly more permissive for the Sponsor (CRO) in determining

parties with whom it may share data to present or publish, in line with transparency expectations;

Clause 10.7
Clause modified so that it is not restricted to only the Sponsor protecting its proprietary information, thereby enabling the Clause to apply to circumstances when the Sponsor has brought the proprietary information of third parties to the clinical trial;

Clause 15.2
Modified to allow for the Sponsor (or CRO) to assign the Agreement, without prior consent, to a successor entity by virtue of merger, consolidation, sale, etc. whilst placing an obligation on the Sponsor (or CRO) to notify the participating organisation of such assignment/assignation in good time in writing;

Clause 16.3.2
Days, within which the participating organisation shall communicate with the Sponsor as to the impact of any proposed amendment, reduced to fourteen (14), to better align with the expectation that amendments are implemented no later than thirty-five (35) days after notification (although it should be noted that it is expected that amendment implementation is not delayed by contract negotiation, which should continue in good faith parallel and subsequent to amendment implementation);

Appendix 6, Section 4.3
Clarification made such that research ethics committee (REC) approval is needed only for use in research that itself requires a REC opinion;

Appendix 7
Modified to allow for applicable sections to be selected and enacted by check-box.