Guidance on the use of Primary Care Model Clinical Trial Agreement (PC-mCTA)

December 2023

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Introduction

The first model clinical trial agreement ("mCTA") for pharmaceutical research in NHS[1] hospitals 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.

Since 2003, the suite of commercial site agreements has been refined and developed to take account of a changing regulatory regime and clinical trial environment.

The first version of the PC-mCTA was published in 2013, for research in independent contractors of NHS primary care services. PC-mCTA was updated in May 2022 to provide a UK-wide template, whilst aligning with UK guidance on the set up of research activity at NHS organisations (interventional research), A further revision was published in October 2023, to include a standard financial appendix and to align with the interactive Costing Tool national resource review.

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

Structure of the Guidance

This guidance is in three parts:

1. Section 1 provides an overview of how PC-mCTA should be used.

2. Section 2 is an overview of some of the provisions within PC-mCTA.

3. Section 3 provides background on the development of PC-mCTA, including a change history.

Section 1: Use of the PC-mCTA

1.1 **What is the PC-mCTA?**

The PC-mCTA is the standard form contract for use by industry Sponsors and NHS primary care independent contractor Trial Sites (but see 1.3 below for relationship between the PC-mCTAs and the Hub and Spoke Agreements) running contract clinical trials of investigational medicinal products (CTIMPs). NHS primary care independent contractors include general practice services, dental services, and community pharmacies. The PC-mCTA is not for use with primary care services that are legally part of NHS Trusts or Boards; in these circumstances, mCTA or CRO-mCTA should be used.

Two separate templates are provided, one bipartite and one tripartite. The bipartite PC-mCTA forms a contract between the research Sponsor and the NHS primary

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

care independent contractor Trial Site. The tripartite PC-mCTA adds the Principal Investigator as an additional Party to the Agreement.

In the context of PC-mCTA, contract CTIMPs are industry funded and sponsored CTIMPs in which NHS patients or healthy volunteers receive Investigational Medicinal Products ("IMPs") under the duty of care of NHS primary care independent contractors.

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

1.2 When should PC-mCTA be used?

The PC-mCTA is intended to be used:

a. for all phases of contract clinical trials, including Phase I trials in NHS patients or healthy volunteers under the duty of care of NHS primary care independent contractors.

b. with NHS primary care independent contractor 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 PC-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 PC-mCTA is not for use:

a. 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 primary care independent contractors in their NHS capacity. The Model Agreement for Non-Commercial Research in the Health Service (mNCA) or non-commercial Organisation Information Document (as appropriate) should be used for this purpose.

b. 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 PC-mCTA for a commercial CTIMP, the mNCA or Organisation Information Document, for non-commercially sponsored collaborative studies).

c. with any phase of contract Clinical Trial of advanced therapy investigational medicinal products (ATIMPs).

d. in any Contract Clinical Trials (Phases I to IV) performed by private institutions with patients recruited independently of their treatment within the NHS (i.e. PC-mCTA is for use in NHS primary care independent contractors only when acting in their NHS capacity).

e. 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.

1.3 Investigator Sites, Trial Sites and Hub and Spoke Agreements

The PC-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 now defined as the Trial Site.

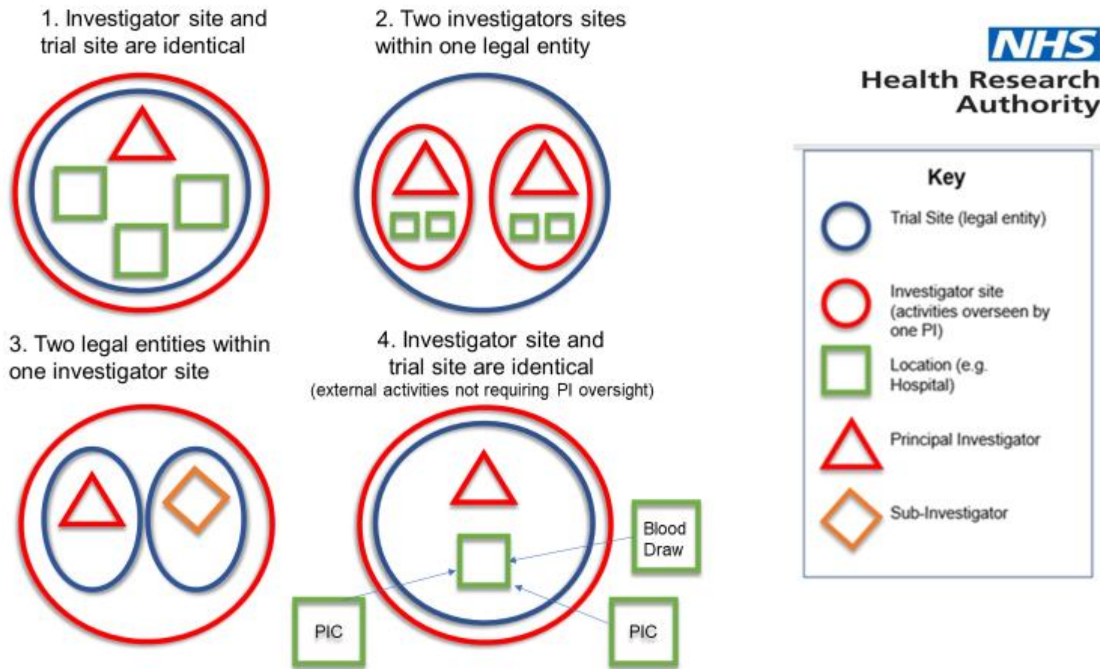
The above referenced set-up guidance defines a Trial Site as “a legal entity responsible for some element of an interventional research study for which PI oversight is required”. It also clarifies that one PI may oversee more than one trial site, or that one trial site may need more than one PI to ensure 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 study 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 PC-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 has been updated to facilitate this approach. The PC-mCTAs should not be modified 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 PC-mCTAs have been drafted to allow the Lead Trial Site (that which employs the PI) to contract with the Sponsor using the PC-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 PC-mCTA in such circumstances, allowing the Lead Trial Site to subcontract with Other Trial Sites in a consistent manner.

1.4 Modifications to the PC-mCTA

The PC-mCTAs have been developed through negotiation and discussion between a wide stakeholder group.

Prior to execution of a PC-mCTA, it is necessary for trial-specific information to be appended to, or options selected within, the PC-mCTA. The information required and options are identified on the front page of the PC-mCTAs (and throughout 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 PC-mCTAs should be used without modification. Any request by a sponsor to modify the PC-mCTA and / or to use any agreement to contract with an NHS primary care independent contractor other than the PC-mCTA, should be disclosed in the IRAS submission (a version of the template proposed for use, with tracked changes and detaied justification should be provided).

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

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

Section 2: Guidance on the Provisions in the PC-mCTA

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 clinicians practising in the NHS, all contract clinical trials must be governed by contracts between the Sponsor and NHS organisation, including independent providers of NHS commissioned primary care services (or, where appropriate, a subcontract between such organisations). This remains the case even when, for example, the investigator is employed by a university and holds an honorary contract with the Trial Site.

Where a Sponsor has legally delegated to a corporate affiliate of the Sponsor 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 PC-mCTA. 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.

Trial Sites have an obligation to inform medical academics’ substantive employers, which are usually universities, about clinical trials in which they are to take part.

The PC-mCTA should not be modified to form a tripartite agreement with an academic institution as a third party.

Except as may be the case with the tripartite PC-mCTA, Sponsors should not enter into a contract with an individual employee of either a Trial Site or a university in a personal capacity to undertake a clinical trial involving NHS patients or healthy volunteers under the duty of care of NHS primary care independent contractors. This prohibition applies to contracts governing the conduct of clinical trials (including the PC-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.

The tripartite PC-mCTA allows for the Principal Investigator to be one of the three Parties to the Agreement and may be used when this is considered acceptable to all three Parties. The participating NHS organisation (that is, the NHS primary care independent contractor) will always be one of the Parties to the Agreement.

2.2 Clause 2: Principal Investigator and Personnel

The Principal Investigator is not to be a signatory to the bipartite PC-mCTA. 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. In both the bipartite and tripartite PC-mCTAs, this obligation extends to procuring the services of Sub-Investigators and other personnel, including Sub-Investigators and other personnel at Other Trial Sites (in the tripartite PC-mCTA the obligation rests with both the Trial Site and the Principal Investigator). The PC-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 when using the bi-partite PC-mCTA that the Trial Site incorporates the obligations of the Principal Investigator and other investigators set out in the PC-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. Similar arrangements should be put in place for the tri-partite PC-mCTA for other investigators.

It is prudent for the clinical trial activities to be included in the work plans, or equivalent, of the Principal Investigator and any Sub-Investigators. The Trial Site may seek assurances from the Principal Investigator and any Sub-Investigators to satisfy the conditions of the PC-mCTA.

2.3 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. 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, provided that this is not overly burdensome for the Trial Site.

2.4 Clause 3.2 and 3.3: Governance

These Clauses set out the minimum compliance requirements for the conduct of clinical 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 notify Trial Sites (and Principal Investigators, where the PC-mCTA is tri-

partite) of specific requirements that relate to the performance of trials and that arise from such laws.

2.5 **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.

2.6 **Clause 3.6.1: Adverse Event Reporting**

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

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

To facilitate use of the PC-mCTAs for Phase I dose escalation trials in NHS patients or healthy volunteers under the duty of care of NHS primary care independent contractors, 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.

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

Modifications 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 in relation to their own compliance with foreign law.

2.9 **Clause 4.8: No Supply of Investigational Drugs by the Sponsor Prior to Approval**

Clause 4.8 requires Sponsors to delay supply of Investigational 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 Investigational Drugs for the purpose of the Clinical Trial, until all regulatory and ethics approvals have been obtained. 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.

2.10 **Clause 4.13**

Reflecting different types of clinical trial and differing Sponsor requirements, clause 4.13 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 study, 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.

2.11 Clause 4.14.2: Enrolment Targets

Clause 4.14.2 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.

2.12 Clause 4.16: Access, Research Misconduct and Regulatory Authorities

Reflecting the strict regulatory environment faced by Sponsors, 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.

Detailed provisions covering the Sponsor's access to the Trial Site and handling of possible misconduct are incorporated and these include various reporting requirements.

2.13 Clause 4.16.9: 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 assists the Trial Site to make alternative arrangements for archiving. Costs associated with archiving may be reimbursed by the Sponsor and should be charged to it by the Trial Site as a one-off cost at close-down of the study. Charges are not agreed at execution of the Agreement because it will not be known at this point how much archiving fees are likely to be; Trial Sites should calculate this at close-down. 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 after this point. This sub-clause also sets out the duration for archiving and procedures for destruction of Clinical Trial records.

2.14 Clause 4.16.10 and 4.16.11: Use of Material

The PC-mCTAs define "Material" as "…any clinical biological sample, or portion thereof, derived from Participants, including information related to such material, analysed by the Trial Site or Other Trial Site in accordance with the Protocol, or otherwise supplied under Appendix 6 to the Sponsor or its nominee." Clauses 4.16.10 and 4.16.11 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.

Clause 4.16.10 should be deleted where no analysis of material will take place at the Trial Site (or, as applicable, Other Trial Site(s)).

Clause 4.16.11 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) (and Principal Investigator, where tripartite), applicable to both (all) Parties and is applicable only where clause 4.16.11 applies. Otherwise, it should be deleted.

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 Principal Investigators, where tripartite) are strongly encouraged to review both the IRAS questions relating to use of Material and Participants in order to determine the feasibility (or otherwise) of use and / or participation in multiple Clinical Trials, as well as the accompanying notes which place restrictions on the use of Material.

2.15 mCTA Clause 4.18: 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).

2.16 Clause 5: Liabilities and Indemnities

It is essential that the respective Parties 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. NHS primary care independent contractors' 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 (and Principal Investigators, where tri-partite) to Sponsors 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 / or 11 (Intellectual Property), provides for the Trial Site's (and Principal Investigator's, where tripartite) liability to be limited to a maximum of twice the value of the Agreement. The Agreement value is the total payment due to be made by the Sponsor to the Trial Site, if the target number of patients is recruited. The second cap covers all other breaches of the agreement by the Trial Site (and / or Principal Investigator, if tripartite) and limits the Trial Site's / Principal Investigator'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 for their loss, it is considered that the risk of paying compensation on this basis provides an additional incentive for Trial Sites / Principal Investigators 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 the Sponsors' 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 are not required to take out clinical trials insurance, but Trial Sites / Principal Investigators 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.

2.17 Clause 6: Data Protection

The PC-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 modify 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 (and, where tri-partite, the Principal Investigator), as processor(s) 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 study 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. Modifications to the Clause to form an agreement for the export of personal data, or other modifications 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.

2.18 Clause 7: Freedom of Information

This Clause imposes obligations on Trial Sites (and Principal Investigators, where tri-partite) to take timely action to inform Sponsors 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.

2.19 Clause 10: Publications

The PC-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 Joint Position as defined in the PC-mCTAs.

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.

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

2.20 Clause 11: Intellectual Property (IP)

Four core principles underlie the PC-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 / or Principal Investigator under the tripartite agreement) and, depending on the inventor's employer (hospital or university, general practice, etc.), could be protected accordingly. Fourth, the Trial Site (and / or the Principal Investigator under the tripartite agreement) also has (have) the right to use know-how gained during the trial in its (their) 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 PC-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.

2.21 **Clause 16.1: Order of Precedence**

In most respects, the terms of the Protocol will prevail over the other terms of the PC-mCTAs. However, in respect of six important Clauses: 5 (Liabilities and Indemnities), 6 (Data Protection), 7 (Freedom of Information), 8 (Confidentiality), 10 (Publications), 11 (Intellectual Property) and 16 (Agreement and Modification), the terms set out in the PC-mCTAs will prevail.

2.22 **Clause 16.3: Changes to the Protocol**

The procedure to be followed when changes are made is set out in Clause 16.3 and if the change requires a revised financial schedule, this should be agreed, signed by the Parties and included in the Agreement. The implementation of

amendments requiring changes to the financial schedule should not be delayed until contract variation is completed. Instead, amendments should be implemented in a timely manner, whilst good faith negotiation between the parties continues to finalise and agree the variation.

2.23 **Clause 17: Force Majeure**

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

2.24 **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 modified, the parties should merely refrain from providing email addresses under Clause 18.2.

2.25 **Clause 19: Dispute resolution**

Under the PC-mCTAs, the parties are required, in the first instance, to attempt to resolve any dispute through discussion between authorised representatives which, if unsuccessful, may proceed to mediation. Unlike mCTA and CRO-mCTA, the PC-mCTAs do not include an escalation to senior managers, as it is considered that this is not meaningful given the flatter management structures in NHS primary care independent contractors. 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.

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

The Governing law of the PC-mCTAs is determined by reference to the nation of the UK within which the Trial Site is constituted.

2.27 **Clause 20.5: Counterparts and Signatures**

The signatories to the PC-mCTA will be the authorised representatives of the Sponsor and the Trial Site (and the Principal Investigator them self, where tripartite). The signatories must have legal authority to bind their respective organisations. In the case of the Trial Site, this is likely to be a partner or practice manager. In the case of the Sponsor, if the Sponsor has formally delegated authority to contractually bind it to a corporate affiliate of the Sponsor (or any other third party), this should be evidenced at Appendix 8.

The PC-mCTA allows for execution to be through use of an electronic signature and for execution to be via counterparts.

Sponsors and Trial Sites (and, where tripartite, Principal Investigators) are encouraged to discuss execution arrangements early in the contract negotiation, in order to determine the most appropriate arrangements for all Parties.

2.28 **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. 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.

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

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

2.30 **Appendix 4: Financial Arrangements**

The financial arrangements for the clinical trial should be appended as Appendix 4 of the PC-mCTA. Sponsors 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 include this as Clause 13 of the Financial Arrangements Appendix. Modifications 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 and a university that employs an investigator.

2.31 **Appendix 4: Clauses 1.2.1 and 1.2.2: National Contract Value Review (NCVR)**

NCVR requires Trial Sites to accept the outcome of the national resource review and the prices generated by the interactive Costing Tool. Independent contractors of primary care NHS services are not currently subject to the full requirements of NCVR. However, individual contractors may be members of a voluntary NCVR adherence scheme. The Parties should consult prior to Sponsor provision of this Agreement to the Trial Site, to determine whether these clauses should be retained or deleted.

2.32 **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 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 and Trial Sites should seek detailed guidance on VAT requirements from their local tax office as needed.

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

The mCTAs provide a payment term of forty-five (45) 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.

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

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

Appendix 4: Clause 6: Expenses

The definition of Expenses 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. It also includes "ethically-approved pass-through Participant costs", such as vouchers, compensation for inconvenience and time and payments for loss of earnings. This Clause details how payments for all of these Expenses are managed.

Where no Expenses will be reimbursed at an individual Trial Site, the amount entered into Clause 6.3 of this Appendix should be £0.00.

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

This Clause details the management of 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. Payment is to be made individually for each screen failure.

The Sponsor 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.

2.36 **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.

2.37 **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 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 **NCVR**, modification of the iCT-generated Finance Schedule is prohibited. The Sponsor changing the order of items within tables of the Finance Schedule for ease of reading is not a modification to the template. The Sponsor 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) is also not a modification and is permitted. 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.

Unmodified use of the Finance Schedule is recommended for studies which fall out of scope of the NCVR programme. In this case, the iCT (and therefore the Finance Schedule) is a guideline upon which to base discussions between the Sponsor and Trial Site. The Financial Appendix itself is however a part of the Agreement template and should be used without modification 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 should work with the Trial Site and, as necessary, any Other Trial Sites/PICs to ensure that the organisation-level 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 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.

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

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

2.39 **Appendix 6: Material Transfer Provisions**

Where no Material is to be supplied by the Trial Site to the Sponsor or their nominated representative, Appendix 6 should be deleted.

2.40 **Appendix 7: Equipment and Resources**

Where no Equipment or Resources are being provided Appendix 7 should be omitted from the final clinical trial agreement.

Appendix 7 includes tables where equipment and resources that are provided by Sponsors 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 Principal Investigator, where tripartite).

The Sponsor 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.

There is no option in the PC-mCTAs for a Master Indemnity Agreement (MIA) to be used. The PC-mCTAs differ from the other mCTAs in this regard – whilst an MIA may be relied upon in secondary / tertiary care in Scotland and Wales (but not in England or Northern Ireland), MIAs are not applicable to independent contractors of NHS primary care services anywhere in the UK.

2.41 **Appendix 8: Formal Delegation of Authority from Sponsor to a Corporate Affiliate 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 the corporate Affiliate of the Sponsor (or other third party), to sign this Agreement and thereby legal bind the Sponsor to its terms as a Party. Remove this Appendix if it is not applicable.

Contact Points for Advice and Assistance

For queries relating to the use of the PC-mCTAs for trials taking place in England: please contact the Health Research Authority, at alastair.nicholson@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.

Change History

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 4.16.9c 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 Participant 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 Expenses.

New definition added for Retention Period.

Clause 4

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 7

Addition of the EIRs throughout this Clause.

Clause 8

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

Clause 12

Old clauses 12.4 to 12.8 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.

Appendices

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

Summary of Key Changes in April 2023

General

References to Participating Organisation updated to Trial Site.

References to Clinical Trial Subject updated to Clinical Trial Participant.

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 Participants’ 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 may be’ removed, as the PC-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 5

Clarification of the term “fees payable” in clause 5.4.

Clarification of the term “value of the Agreement” in clause 5.5.

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 Participants 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 study 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.

Summary of Key Changes in January 2021

The January 2021 PC-mCTA is based upon the January 2021 mCTA and as such represents a significant development from the four nations specific 2013 PC-mCTAs. These developments include:

In place of one PC-mCTA for each of the four UK nations the PC-mCTA templates are now common for all UK nations. This follows the work undertaken for the 2018 mCTA and CRO-mCTA to create UK-wide agreement templates.

In place of one template per UK nation, each of which incorporated optional clauses to allow for the Agreement to be bipartite (between sponsor and NHS primary care independent contractor) or tripartite (between sponsor, NHS primary care independent contractor and Principal Investigator), there are now separate bipartite and tripartite UK-wide templates. Separating out the bipartite and tripartite templates allows the templates to meet accessibility requirements and should reduce drafting errors in localising templates for use.

PC-mCTA now takes account of GDPR/DPA 2018, as well as other changes in the regulatory and policy landscapes since 2013. In particular, PC-mCTA forms a GDPR Article 28(3)-compliant data processing agreement and takes account of the legal situation following from the UK’s exit from the EU.