

# Governance review check guidelines,

V5.0, 21 November 2021

## Contents

Study wide governance criteria .....	2
Introduction .....	2
1. Application package.....	3
1.1 IRAS application completed correctly .....	3
2. Risk to participants	7
2.1 Participant information / consent documents and consent process .....	7
3. Risk to study .....	14
3.1 Protocol assessment.....	14
4. Risk to organisation .....	16
4.1 Allocation of responsibilities and rights are agreed and documented .....	16
4.2 Insurance / indemnity arrangements assessed.....	23
4.3 Financial arrangements assessed .....	28
5. Legal Compliance .....	30
5.1 Compliance with Data Protection law and data security issues assessed .....	30
5.2 CTIMPs – Arrangements for compliance with the Clinical Trials Regulations assessed.....	52
5.3 Compliance with national legislation regarding Adults unable to consent for themselves in a non-CTIMP.....	61
5.4 Compliance with national legislation regarding Human Tissue .....	70
5.5 Compliance with any other applicable laws or regulations .....	81
6. Approvals and authorisations.....	84
6.2 CTIMPs – Clinical Trial Authorisation (CTA) letter received.....	87
6.3 Devices – MHRA Notice of no objection received.....	89
6.4 Other regulatory approvals and authorisations received.....	91
Appendix A: Areas of review in HRA assessment which are additional to the UK study wide governance criteria.....	97
Human Resources Good Practice Resource Pack.....	97
Oversight Arrangements .....	97
Level of capacity and capability assessment expected of participating organisations .....	99
Appendix B Summary of Changes	112

# **Study wide governance criteria**

## **Introduction**

The Integrated Research Application System (IRAS) is the single system for applying for the permissions and approval for health and social care/ community research in the UK.

Study-wide review provides assurances to NHS/HSC organisations that information relating to a study is accurate and that the study, as described in the application document set, is compliant with legislation relating to the research. This is not an exhaustive list of checks, as individual studies may present their own questions. Where additional concerns are addressed for an individual study, this would usually be described in the study wide review made available to sites in Scotland and Northern Ireland and in the HRA and HCRW Approval letter in England and Wales. Study wide reviewers should review against their national requirements only but should highlight in the study wide review where nation specific differences apply. Where uncertainty exists, this should be escalated in line with Nation specific processes.

# 1. Application package

## 1.1 IRAS application completed correctly

### Introduction

The completion of the project filter/clinical dataset tailors the application information for the type of research study, by enabling only those questions and sections that are relevant to the study. The accurate completion of the IRAS project filter/clinical dataset is crucial to each study application. The integrated dataset for the study will be created from the answers given to the questions in the IRAS project filter/clinical dataset. The system will generate only those questions and sections that (a) apply to the study type and (b) are required by the bodies reviewing the study. In addition, certain questions are enabled in response to questions in the form itself.

Studies that meet the criteria for study-wide review but that have incorrectly completed project filters will be asked to submit a corrected IRAS form/project study information form if the error has a material effect on the content of the application. Studies that do not meet the criteria will be given appropriate advice on applying through alternative systems (e.g. research outside of the NHS/HSC or non-Research activities).

Particular care should be taken where studies involve:

### **Ionising radiation and, specifically, research exposures.**

Procedures involving ionising radiation include:

- Diagnostic X-rays, CT scans or DXA scans
- Radiotherapy (including brachytherapy and therapy using unsealed sources; or
- Radionuclide imaging (including diagnostic imaging and in vivo measurements)

Magnetic Resonance Imaging or ultrasound investigations do not involve ionising radiation

### **Human biological samples**

- New human biological samples are those where the research will involve collecting samples from participants primarily for research purposes.
- Existing human biological samples are those where the research will involve the use of residual material left over from routine clinical or diagnostic procedures, or existing stored samples from an archived collection or tissue bank. If the research team will conduct additional analysis on samples taken as per standard care, then they should indicate that they are making use of existing samples.

## **Participants who are children**

Research studies with participants who are under 16 years of age are considered to have children as participants. This also includes the use of samples or data from participants who are under 16 years of age.

## **Participants who are adults lacking capacity to consent for themselves**

This includes research studies (both CTIMP and non-CTIMP) where the research could **at any stage** include adults (aged 16 and over) who are unable to consent for themselves due to physical or mental incapacity (including temporary incapacity). Particular care should be given to the potential for the research study to include further research procedures on or in relation to such participants (including collection of new samples or data) following loss of capacity to consent during the study.

## **Students undertaking research as part of an educational qualification**

Student research means studies which are primarily for the purpose of obtaining an educational qualification. Studies where the main purpose is to undertake specific research - and the educational qualification is secondary - do not fall into this category. Group research (a programme of research designed by academic supervisor to support the attainment of a qualification for a group of students) is not subject to the student research eligibility criteria.

### **Student eligibility criteria**

**Undergraduate level:** Standalone research health and social care research cannot be carried out by undergraduate students.

**Masters' level:** Health and care professionals or trainees on health and care courses studying at health and care research active universities are able carry out research in NHS that requires a full REC review. Masters' students on health and care courses at health and care research active universities, who are **not** health and care professionals or trainees, can carry out research in the NHS, but only if it is suitable for Proportionate REC Review and/or non-REC applications (those requiring HRA and HCRW Approval and equivalent in Scotland and Northern Ireland only).

Students studying on other types of courses or where the university is not active in health and care research cannot carry out health and care research in the NHS.

**Doctorate level:** Doctorate students are eligible to complete standalone health and social care research.

If you have any questions on the eligibility of a specific study, please contact your line manager in the first instance for advice.

Students should not normally take the role of chief investigator at any level of study, as this function should be undertaken by supervisors or course leaders. Exception is made for an experienced care practitioner or manager undertaking an educational qualification for continuing professional development or a doctoral-level study while

employed by a health or social care provider or a university, or for a researcher undertaking a doctoral-level study in receipt of a fellowship.

In the case of a clinical trial of an investigational medicinal product, the Chief Investigator must be an authorised health care professional as defined in the Medicines for Human Use (Clinical Trials) Regulations 2004, as amended. This can be a doctor, a dentist a nurse or a pharmacist<sup>1</sup>; each role is defined in the regulations. For non-CTIMPs involving significant clinical risk, it may be inappropriate for the Chief Investigator to not be medically qualified.

Students conducting research in the NHS should have on-site supervision from NHS staff (which may include staff with honorary or clinical academic contracts). Universities and colleges should accept the role of sponsor for all educational research conducted by their own students for the purpose of fulfilling the academic requirements of the course. Sponsors of educational research should ensure that their supervisors can and do carry out the activities involved in fulfilling this role.

### **Identification of participating NHS organisations, nations and ‘site types’**

Participating nations should be selected in the IRAS project filter/clinical dataset where the research team expect research sites will be located. A research site is defined as the single organisation responsible for conducting the research at a particular locality. Study wide reviewers should note that the number and definition of site types may vary in different participating nations due to differences in how health services are structured.

The research site is not necessarily the location where research activities will actually take place. For example, in a research project by practice nurses from GP practices, interviews with participants may take place in the participant’s home, but the research site would be the GP practice, because the GP practice would be responsible for the research activity.

Organisations where clinicians or clinical units refer potential participants to the research team for assessment and possible recruitment are not considered to be research sites.

Different participating site types may arise in one of two different contexts.

1. Because of the involvement of different categories of participating organisations, e.g. some NHS organisations may participate as ‘Investigator Sites’ and others as ‘PICs’.
2. Where a study where different organisations conduct different activities, and are therefore of different types, but where each of these different groups meets the definition of an ‘Investigator site’.

---

<sup>1</sup> Where a PI on a CTIMP is not a medically qualified doctor (or, where appropriate, dentist) the PI must delegate certain activities (e.g. determination of causality of adverse events) to a research team member who is so qualified.

Where the study will involve Participant Identification Centres (PICs) the inclusion of PIC activity can be identified at the outset of a study even if no PICs have yet been identified but any PIC activities must be detailed.

Where NHS organisations are providing data as per routine practice only (e.g. routine monthly returns to the surveillance unit) they are not considered to be research sites. Where the central unit is an NHS organisation, we would expect this to come for governance review to provide assurances to that central organisation as a single centre study. Where NHS/HSC organisations need to undertake additional activities (e.g. provide data from notes, samples, approach patients etc.) to the routine monthly returns, then study wide reviewers should consider if that additional activity is significant enough to constitute a 'research' study, or just an extension of the standard surveillance programme.

## Study-wide considerations

Consider the study, using the study information provided by the applicant

- Is the project research? [The HRA decision tool](#) is available for sponsor organisations to inform their decision making process.
- Have the IRAS project filter/clinical dataset questions been answered correctly?
- Have the correct participating nations been identified, with one or more site(s) listed in Part C/Section G for each named nation and, where relevant, have nation specific documents been provided, for example to account for national legislative differences in relation to Adults Lacking Capacity and Minors?
- Have the researchers correctly identified the site 'types' that will participate in the research (and provided relevant documents for each site type).

## Notes / Resources

- [List of materials considered to be 'relevant material' under the Human Tissue Act 2004 | Human Tissue Authority](#)
- [The Medicines for Human Use \(Clinical Trials\) Regulations 2004](#)
- [Clinical trials for medicines: apply for authorisation in the UK - GOV.UK](#)
- [UK Policy Framework for Health and Social Care Research - Health Research Authority](#)
- [Defining research exposures - IRAS Help - Preparing & submitting applications - Radiation - defining research exposures](#)
- [Research involving children - Health Research Authority](#)
- [Student research - Health Research Authority](#)

## **2. Risk to participants**

NHS/HSC organisations should ensure that potential participants receive accurate information on any research that they may be approached to take part in. NHS/HSC organisations have a duty for ensuring that any legislation relating to that research is followed, thereby mitigating any risk to those participants.

### **2.1 Participant information / consent documents and consent process**

#### **Introduction**

Potential participants in most studies need information upon which to base their decision to take part or not (except, for example in the case of recruitment in emergency situations).

Consent should be given by a clear affirmative act such as by a written statement, including by electronic means or by an oral statement. This could include ticking a box when visiting an internet website or another statement or conduct which clearly indicates in this context the data subject's acceptance of the proposed activity, such as the return of a questionnaire. Silence, pre-ticked boxes or inactivity should not therefore constitute consent.

Study wide reviewers should ensure that the process of identifying potential study participants and taking consent complies with the common law duty of confidentiality. It should be noted that possession of a research passport, Honorary Research Contract or Letter of Access does not in itself provide a legal basis for researchers to access data for the purposes of identifying potential study participants. See section 5.1 for further details.

Participant information sheets and consent forms are only part of the information given to potential participants during the informed consent process. The process of seeking informed consent may also involve a discussion between members of the research team and the potential participant. Schedule 1 (GCP) of The Medicines for Human Use (Clinical Trials) Regulations 2004 require that the potential participant (i.e. the subject, under Part 3(1)), or the person with parental responsibility or the legal representative (Part 4(1) and Part 5(1)), has an interview 'in which they are given the opportunity to understand the objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted'. The potential participant may also have discussions with an independent person e.g. family member, or GP. It is not expected that the consent form has a clause for every activity, on the proviso that participant activity is clear in the PIS.

Where multiple information sheets have been provided for different participant groups, for example those participating in different arms of the study, then these should each be reviewed. Each PIS should include only information relevant to the group at which it is aimed. In studies under review by an NHS/HSC REC comment should be made by study wide reviewers on the sponsors decision to provide, or not to provide, different PIS documents for different study groups, as this is a judgement for the REC.

Where it is possible that criminal or other disclosures requiring action could occur during the study the sponsor should describe its process for managing this, including where disclosure to other care professionals (such as social services) or the police may be required. The fact that such disclosures may be required should be detailed in the PIS.

Where Participant Identification Centres are to be used, or where a participant will be under the care of more than one organisation during and for the purpose of the research project, the information provided to potential participants should clearly set out the responsibilities of the various organisations to the participant for specified elements of the study.

Research ethics committees consider the ethical implications of the information provided to potential participants, and of the consent process and the risk/benefit ratio of the trial, as it applies to participants, where relevant. NHS organisations need to be assured that potential participants receive accurate information on the research and that any legislation relating to that research is followed.

### **Potential ‘health-related findings’ (HRFs)**

During any study involving human participants, researchers may make a finding that has potential health or reproductive importance to an individual participant. Potential ‘health-related findings’ (HRFs) include incidental or unsolicited findings – a finding ‘which is discovered in the course of conducting research, but is beyond the aims of the study’, and pertinent findings that relate to the aims of the study. HRFs may result from many types of research involving human participants, such as imaging and genetic studies and studies involving physiological measurements or assays. Depending on the research context and the type of tests involved, HRFs will vary in both their nature and the frequency with which they arise. HRFs may arise in clinical trials, stand-alone studies, or in longitudinal studies that involve a range of tests conducted by different researchers over an extended period of time.

MRC and the Wellcome Trust have provided guidance on this topic<sup>2</sup> and consider that it is appropriate for researchers to feed back HRFs where the potential benefits of feedback to an individual clearly outweigh the potential harms and it is feasible to do so. However how best to handle these findings remains a topic of debate and will likely be guided, in any specific study, by the relevant research context. Since the position is legally untested, it is unclear whether, and if so to what extent, researchers owe a specific duty of care to participants under UK laws with respect to HRFs.

It is important to note that the lack of a clear legal position does not affect the ethical considerations. The sponsor should explain how they plan to handle any HRFs and justify the position to, or to not, inform participants of these. It is recommended that the sponsor seek advice from those with lived experience of the condition under study to develop their position.

---

<sup>2</sup> [Framework on the feedback of health-related findings in research – UKRI](#)

Study wide reviewers should ensure that the sponsors proposals in relation to HRFs are clearly expressed, and in England and Wales detailed in the Initial Information for REC form, to enable the REC to make a decision regarding the appropriateness of these proposals.

## Research involving Children

Consent can be given on behalf of the minor by a parent, or person with parental rights and responsibilities (Scotland) and assent obtained from the child. Information must be provided in an age appropriate manner so that the child is fully informed and involved in the consent/assent process in a manner that is appropriate to their age, understanding and the complexity of the study. There is not a legal basis for assent, however it is accepted as a documented record that the child or young person is not dissenting to participate. Young people over 16 are presumed to be capable of giving consent on their own behalf to participate in [Clinical Trials of Investigational Medicinal Products \(CTIMPs\)](#).

In research other than CTIMPs there is no statute in England, Wales or Northern Ireland governing a child's right to consent to research activity. Case law suggests that if a young person has sufficient understanding and intelligence to understand fully what is proposed and can use and weigh this information in reaching a decision (i.e. they are 'Gillick competent'), he or she can give consent to treatment. In the absence of law relating specifically to research, it is commonly assumed that the principle of 'Gillick competence' can be applied not only to consent for treatment, but also to consent for research. A child / young person's right to give consent is dependent upon their capacity to understand the specific circumstances and details of the research being proposed, which in turn will relate to the complexity of the research itself.

In Scotland The Age of Legal Capacity (Scotland) Act 1991 states that a 'A person under the age of 16 years shall have legal capacity to consent on his own behalf to any surgical, medical or dental procedure or treatment where, in the opinion of a qualified medical practitioner attending him, he is capable of understanding the nature and possible consequences of the procedure or treatment.' Under the Children (Scotland) Act 1995 children are presumed to have capacity to form a view from age of 12. However, capacity is a fluid concept and will depend on the complexity of the information and the research study and the understanding of the child, this must be assessed and documented by the person taking consent/assent. Although children with capacity have the right to give their consent, they also have the right to defer this responsibility to the person(s) with parental rights, to choose to assent and most importantly to dissent to their participation. Furthermore, for practical reasons it is not advised to consent a minor to participate in research without parental agreement, this should be documented in a parental consent/agreement form.

Where an individual is recruited to a study and, during the course of their involvement, will reach the age of majority the researchers should make arrangements to seek consent from that individual (where applicable), unless they have previously provided consent in their own right to participate. This does not need to be undertaken immediately, but should be sought as soon as reasonably practical, for example at the individuals next study visit.

It should also be noted that Data Protection legislation allows for consent to be relied upon as legal basis for children from 13 years of age. This does not mean that consent

SHOULD be relied upon and it is unlikely that it would be relied upon in research (see section 5.1).

## **Electronic Consent**

HRA and MHRA have published a joint statement on seeking and documenting consent using electronic methods. This is supported and endorsed by the UK health departments in Northern Ireland, Scotland and Wales and confirms that electronic methods may be used for seeking, confirming and documenting informed consent for participation in research and sets out joint expectations regarding the use of electronic signatures in CTIMPs. Electronic methods may therefore be used for seeking, confirming and documenting informed consent in research studies including CTIMPs. Information about the trial does not have to be in writing and can be provided to potential participants using electronic methods. Informed consent must be recorded ‘in writing’. However electronic methods for documenting consent can be considered to be in writing.

The UK eIDAS Regulations (SI 2016/696), defines an electronic signature as ‘data in electronic form which is attached to or logically associated with other electronic data and which is used by the signatory to sign’. The Medicines for Human Use (Clinical Trials) Regulations 2004 specifically allows for the use of electronic signatures as a method of signing documents referred to in the Regulations.

## **Study-wide considerations**

- Consider the proposed consent process to ensure that any legal implications presented by the study are addressed. Any specific requirements within the participant information sheet and consent process that may have local implications should be highlighted.
- The participant information sheet should clearly describe the study, including the arrangements for potential participants’ involvement, and be consistent with the other study documents (protocol, IRAS form/project study information form etc.).
- Where it is possible that criminal or other disclosures requiring action could occur during the study has the sponsor described its process for dealing with these and detailed the need for disclosure in such cases in the PIS.
- In Clinical Trials the PIS should include a short description of the drug, device or procedure being tested and describe the stage of its development. The potential side effects of these interventions should be clearly set out in the participant information sheet. Some pragmatic trials may compare two or more medications which are standard of care for patients with the condition being investigated, and participants (or centres) are randomised to receive one of the standard care medications. Where this is the case, it is acceptable for the participant information sheet to simply state that the side effects are described in the information leaflet which comes with the medicine (or similar).

- The participant information sheet should detail the procedures that participants will undertake during the trial, including all research exposures to ionizing radiation and if the study will involve the analysis of DNA/RNA. If different groups participants will undergo different procedures during the trial then this should be clear and, if these are significant, different PIS documents provided for each group.
- Where relevant, consider the accuracy of the information describing which organisation holds the duty of care to participants for the purposes of the study (for example when participants are recruited at PICs but the duty of care remains with the research site) at which times during the study, particularly if this will change during the course of the study.
- A description of the study insurance/indemnity and compensation should be provided in the PIS which is proportionate to the study type. This should always be provided in the case of clinical trials and other interventional studies. If a description of ABPI compliant compensation arrangements is given in the PIS it should not be limited to provision of costs for medical treatment. (See section 4.3 for detailed requirements)
- Consider the accuracy of any specific requirements relating to study treatment and a participant's care after their participation in the study. The arrangements for care after research should not lead to expectations by participants of care that cannot be guaranteed. Where specific arrangements for post-study care are described, the sponsor must specifically describe the arrangements for provision including how such provision will be funded. (See section 4.3 for detailed requirements)
- The full study title and IRAS reference should be present on both the participant information sheet/s and informed consent form/s, except in circumstances where inclusion of the full study title would not be appropriate. This is in order that participants have a single reference for a study.
- Has the sponsor detailed their arrangements for the collection, analysis, storage and disposal of Human Tissue in the PIS (see section 5.4 for detailed requirements).
- Has the sponsor detailed in the PIS their arrangements for the collection, use, sharing, security and integrity of patient data, including what will happen to it following the end of the study and have they included relevant information further to legislative requirements, such as in respect to GDPR transparency information? (see section 5.1 for detailed requirements).
- Where children are to be included as participants, arrangements for taking consent and, where appropriate, assent should be clear in the protocol and the different information, consent and (where applicable) assent documentation should be clearly labelled for use. It should be clear (where applicable) what arrangements will be in place for obtaining consent from participants assented as children upon attaining majority, should they do so whilst still participating in the research.

- Where Participant Identification Centres are to be used there should be a clear process for providing information to potential participants. It should be clear who is responsible for which aspects of the process.
- Has the sponsor explained their proposals for the management of Health-related findings and have they justified their decision to, or not to, provide these to participants. Where the sponsor does propose to provide these to participants is there a clear pathway by which they will do so.
- Where the sponsor proposes to utilize electronic consent, it should be clear
  - For all study types
    - How it will be possible to verify which version of the information sheet and consent form the electronic signature applies to?
    - What methods are in place to ensure that the person signing the electronic consent form is the person who will be participating in the research study?
  - For CTIMPs
    - How it will be ensured, for CTIMPs that the source consent documentation is available for inspection during and after the end of the trial according to the legally required retention period
    - How the site will retain control of the informed consent process and documentation so that personal identifiable data are not inappropriately disclosed beyond the site to either sponsors or third-party vendors?
    - Where a sponsor has commissioned a third party to provide an eConsent system, are the necessary information governance arrangements in place to ensure that participant confidentiality is protected with appropriate access and retention controls to the system? Where the sponsor is responsible for auditing, ensuring compliance, and maintaining access controls to the eConsent system they may provide the appropriate certifications to the site as needed.
    - How will a copy of the informed consent documentation (information sheet and signed consent form) be provided to the participant and retained in the investigator site file?
    - How the sponsor will enable MHRA Inspectors access the eConsent system in a readily available way during triggered, short notice or unannounced inspections?

- Where advanced or qualified electronic signatures have been used, whether an inextricable link be maintained between the metadata (the information in the electronic record that gives context, meaning, and security attributes to the data) and the document, thus demonstrating the electronic signature's authenticity for as long as applicable legislation requires, dependent on the type of trial?

## Notes/ Resources

- [Informing participants and seeking consent - Health Research Authority](#)
- [HRA and MHRA publish joint statement on seeking and documenting consent using electronic methods \(eConsent\) - Health Research Authority](#)
- [Generic Ionising Radiation Risk Statements v4](#)

## 3. Risk to study

The study sponsor is ultimately responsible for the study design. NHS/HSC organisations are however responsible for reviewing protocols to ensure that risks to the study are addressed through the local study management arrangements. Study-wide review provides assurance that the study documents describe the study clearly, consistently, and accurately.

### 3.1 Protocol assessment

#### Introduction

The protocol should describe the objectives, design, methodology, statistical considerations (or other methods of data analysis) and the management arrangements for of the study including the definition of the end of the study. In most cases this will be the date of the last visit of the last participant or the completion of any follow-up monitoring and data collection described in the protocol. For studies involving human tissue, the analysis of the samples should be undertaken as part of the data collection **before** the end of study is declared. It is recommended that a protocol describes the monitoring of the study and dissemination of the study findings. The content of a protocol may vary depending on study type, but all protocols should provide a clear description of the study activities, to ensure that the study may be conducted as intended in a consistent and repeatable fashion. A study must follow the protocol agreed by the study sponsor and approved by the relevant regulatory bodies. It is the Sponsor's responsibility to ensure that the study has scientific review that is proportionate to the study type.

Protocol templates for CTIMPs and qualitative research are available on the IRAS Help pages, whilst their use is not mandatory, they set out the organisation and detail expected from a protocol.

Study wide reviewers should note that, where information is not provided in the study protocol it may be acceptable for this to be provided in separate, supplementary information.

#### Study-wide considerations

- Confirm that the protocol clearly describes the activities to be undertaken at the NHS research site(s) and, as applicable, PICs and other participating NHS organisations. In particular, unless this information is (or the sponsor asserts will be), provided in other documents this should include
  - The arrangements for how study participants should be identified, approached and consented and what processes and activities participating NHS/HSC organisations will need to undertake to deliver this according to the sponsors requirements (including where this differs between different types of participating NHS/HSC organisations)

- The arrangements for the collection, use, storage, analysis and destruction of human tissue samples at participating NHS organisations
- The arrangements for the collection, use, sharing, security and integrity of participant data, including what will happen to it following the end of the study and what processes and activities participating NHS/HSC organisations will need to undertake to deliver this according to the sponsors requirements (including where this differs between different types of participating NHS/HSC organisations)
- Check that the protocol maintains consistency with other study documents to accurately and consistently describe the study.
- Check that the protocol includes a clear definition of the end of the study and that this is consistent with other study documents and national expectations.

#### **Notes / Resources**

- [IRAS Help - Preparing & submitting applications - Templates for supporting documents](#)

## **4. Risk to organisation**

A complex array of organisations and individuals may be involved in a study. There should be appropriate and clear agreement of the allocation of responsibilities and rights.

### **4.1 Allocation of responsibilities and rights are agreed and documented**

#### **Introduction**

The UK Policy Framework for Health and Social Care Research 2020 states that:

**'There should be clear designation of responsibility and accountability with clear lines of communication between all those involved in research. Communication pathways should be clear in terms of what, how, who, when and why, with documented roles and responsibilities. Dialogue and collaboration have a central role within a research project. Clear, upfront discussion of issues and agreement of principles and procedures for each project are essential to its effective conduct and success, as well as mitigating some risks.'**

Contracts between sponsor (and, where appropriate, CRO) and participating NHS organisation(s) play an important role in allowing all parties to meet the responsibilities set out in the policy framework. A suite of UK template contracts has been established (and is added to/maintained as needed) to ensure that the content of these agreements is appropriate and can be agreed study by study without lengthy negotiation.

The UK templates are tailored to meet specific needs (for example, commercial or non-commercial, interventional or non-interventional, etc.) and cover, as appropriate, matters such as insurance and indemnity, rights and responsibilities, financial arrangements and confidentiality. It is important that the template(s) included within the IRAS submission is (are) appropriate to the study type and the activities of the NHS organisations to be undertaken, as set out in the application, and that the level of detail provided in the template(s) is sufficient to assess accuracy and consistency with the overall application (for example, in terms of level of insurance cover). The contract also has a key role in the protection of the personal data of potential and actual research participants.

GDPR Article 28(3) requires that:

**'Processing by a processor shall be governed by a contract or other legal act [...], that is binding on the processor with regard to the controller and that sets out the subject-matter and duration of the processing, the nature and purpose of the processing, the type of personal data and categories of data subjects and the obligations and rights of the controller.'**

As the sponsor determines the data to be processed for the study, the purpose of this processing and the means of the processing, the sponsor is the controller of data processed for the purpose of the study. Where the site or PIC processes personal

data for the purpose of the study, the site or PIC is the processor of the sponsor and a GDPR Article 28(3) data processing agreement is required.

The UK templates each include clauses that (taken together with an appropriately drafted protocol, included within the contract by reference) form Article 28(3) compliant data processing agreements. The suite of agreements includes Participant Identification Centres (PIC) agreements, as well as site agreements.

Where no controller/processor relationship is established between the sponsor and an NHS organisation, GDPR does not require a legally binding agreement. This may be the case, for example, where a site is not itself processing personal data on behalf of the sponsor, because the research team is external to the site and the role of the site is restricted to NHS staff being interviewed or observed by the external team. It would also be the case where an NHS organisation is referring patients to another NHS organisation, for consideration for inclusion in an interventional research study, but is doing so primarily for clinical purposes and hence not in accordance with sponsor instruction.

In the latter instance, the NHS organisation has no formal role in the study and hence no agreement is needed. In the former instance, although no data processing agreement is needed, use of the appropriate template agreement is still appropriate because its other clauses, such as insurance and indemnity, rights and responsibilities, financial arrangements, and confidentiality, remain relevant. In all cases where an NHS organisation is participating in a study as a site or PIC, a formal agreement should be in place to document this.

Whilst each of the four UK nations has its own processes for negotiating and executing the contracts between sponsor and site(s)/PIC(s), there are common checks that should be undertaken by the lead nation as part of the UK Study Wide review.

Study wide reviewers, while not responsible for reviewing the content of the agreement per-se should still consider it in relation to other aspects of their study wide review to ensure general consistency between the agreement and other aspects of the study. Inconsistencies may arise either because of modifications to the model agreements or because of unusual study arrangements that are not reflected in the proposed model agreements.

In England and Wales the HRA/HCRW Initial Assessment and Approval Letters both clarify for the participating NHS organisations the form(s) that the agreement(s) will take for the NHS organisations participating in the study (for example, is the sponsor proposing use of an unmodified template agreement, will they be using the Organisation Information Document etc.) Study wide reviewers should detail the sponsors intentions in the SW review.

In Scotland and Northern Ireland equivalent information is provided in the SW review (and in some cases processes are in place to negotiate contracts centrally).

## **Commercial studies**

The suite of commercial template agreements is designed to be used without modification for commercial contract research in the NHS.

In England and Wales, NHS organisations (and, by extension, commercial sponsors and CROs) are required to use only the appropriate unmodified agreement for commercial contract research. In exceptional circumstances this requirement may be waived by the letter of HRA/HCRW Approval for the study. In some cases (CRO mCTA and mCTA), such waivers cannot be issued without prior UK agreement from the UK Four Nations Contracting Leads Group. Similarly, proposals for modifications to CRO-mCTA or mCTA for use with sites in Scotland or Northern Ireland will also be escalated to the UK Group. Requests for modifications to the other commercial agreements may be escalated to the contracting leads, as considered necessary (and it is likely that formal escalation will become the norm for all commercial agreements, as the full suite of templates embeds and matures). Sponsors and CROs are strongly advised to use only the appropriate unmodified model agreement, to avoid potentially significant delay.

It is expected that NHS/HSC organisations will accept unmodified mCTAs without further review of the standard template elements. In England, this expectation is a contractual requirement arising from NHS England's National Directive on Commercial Contract Research Studies. In Wales, the same expectation applies on a policy basis.

Where no appropriate model commercial UK template agreement exists for the type of study, the expectation that an unmodified template should be used does not apply. A bespoke agreement may be used. It is recommended that such agreements are based upon the most suitable existing national template. The UK contracting leads group is identifying gaps in the suite of agreements and working to fill these with new templates, agreed with relevant stakeholders.

## **Non-commercial studies**

For all non-commercially sponsored studies, unless there is a single participating NHS/HSC organisation and it is the same legal entity as the NHS/HSC Sponsor for the study, an Organisation Information Document(s), supplemented by an IRAS Schedule(s) of Events or SoECAT(s) should be provided in the IRAS submission. For studies that are not clinical trials, clinical investigations, or are otherwise interventional (in other words, for all non-interventional research), the Organisation Information Document should form the agreement between the sponsor and the participating NHS/HSC organisations. The Organisation Information Document forms a key component of the UK Local Information Pack for non-commercial research projects and should therefore still be submitted for interventional studies even when it is not to be enacted as the contract.

Some NHS organisations operate a joint research office (or similar arrangement) with the legally distinct entity that is the sponsor. Where this is true the data only Organisation Information Document may be used, at the discretion of the parties, to contractually manage only the data processing aspect of a non-interventional study. It should be clear in the sponsor cover letter for the submission where this is the case and evidence may be requested that the participating NHS site is content with this arrangement. In the same circumstance, where the study is interventional and hence governed by mNCA, no Organisation Information Document is needed.

In some studies, some NHS/HSC organisations will undertake different activities to others (for example, some sites may only be recruiting and following up participants, whilst other sites undertake the research procedures. In other cases, some sites may

be delivering one arm of the study and other sites another arm). In such scenarios the sponsor will need to create and submit an outline Organisation Information Document for each group of NHS/HSC organisation undertaking the same activities.

For non-commercial, interventional research, the model Non-Commercial Agreement (mNCA) should be used as the contract between sponsor and NHS/HSC site. This should be provided in the IRAS submission and Local Information Pack **in addition to** the appropriate Organisation Information Document(s) (in this scenario, the OID is used to provide supplementary information, whilst not itself forming the contract).

Whether the mNCA or Organisation Information Document is proposed as the agreement, it is strongly recommended that an unmodified template is used. The templates should be used as set out in their accompanying guidance. Where a template based on the model agreement is submitted but includes modification, the sponsor will be asked to explain the rationale for such modification. Where an agreement not based upon a model template is used, the sponsor will be asked to explain the rationale for not using a model agreement. Once justification is obtained, the UK SW reviewer should include this information in the SW review.

In England and Wales, the details of the proposed modifications and the rationale for each should be provided to participating NHS/HSC organisations in the HRA/HCRW Initial Assessment and Approval letters.

In Scotland the proposed agreement, including any proposed modifications, will be reviewed by the Study wide reviewer as part of the governance review and will need to be agreed before Research Permission is granted.

In Northern Ireland the study wide governance report should detail what agreement is being used so that this can be reviewed by participating HSC organisations.

### **Participant Identification Centres (PICs).**

PICs are NHS organisations that process personal data on behalf of the sponsor to identify potential research participants for another legal entity. Hence a controller (sponsor) / processor (NHS organisation) relationship is established between the sponsor and the PIC and a controller/processor agreement is required. PICs are not research sites and should not be treated in the same way as research sites. Both the commercial and non-commercial PIC agreements are drafted as sub-contracts, allowing the site to subcontract with the PIC as sub processor of the sponsor, although the sponsor remains responsible for overseeing such subcontracting.

Both the commercial and non-commercial PIC agreements pass through the data processing terms of their header agreements (mCTA and mNCA respectively) such that the PIC, as sub-processor of the participating NHS/HSC organisation, is bound to that organisation under the same terms as that organisation is bound to the sponsor (in line with GDPR). The m-C-PICA also includes a finance appendix such that costs associated with PIC activities may be passed through to the PIC from the participating NHS / HSC organisation (in line with the finance appendix of the mCTA in place between that organisation and the sponsor) and a description of the activities to be undertaken by the PIC.

Direct contracting from the sponsor to the PIC is acceptable, although no national template is provided for this. The inclusion of PIC activity can (and should) be included in the IRAS submission at the outset of a study even if no specific PICs have yet been identified.

An NHS/HSC organisation **is operating as a PIC** when it:

- Identifies potential research participants by processing personal data (e.g. through carrying out a search of patient records database to identify individuals that meet a study's eligibility criteria) for the purpose of a research study (as opposed to for clinical care purposes); and
- Is following the sponsor(s) instructions in identifying potential research participants; and
- Directs these potential participants elsewhere without undertaking any further research activity for that study (i.e. the research occurs at another legal entity).

Organisations are not considered PICs when

- A location within a single legal entity is undertaking PIC style activities from a separate physical location within the same legal entity (e.g. one hospital identifying potential participants to be referred to another hospital within the same NHS/HSC Trust/Board) the legal entity should be treated as an investigator site or other participating organisation and set up and contracted accordingly. Separate contracting is not required to cover the PIC style activities at different locations within the same legal entity
- They are referring to interventional studies potential participants identified in the course of normal activity (e.g. MDT, clinic, etc.) and for the purpose of clinical care. Such activity is not PIC activity, as the organisation undertaking it is an independent data controllers processing personal data for its own purpose (they are not processing data under the instructions of a sponsor, they are making normal clinical referrals for the purpose of patient care).
- They are only displaying posters, etc. to bring to the attention of their patients, or others, opportunities to participate in research projects.
- They are undertaking additional activities associated with the research that would make them a research site. Where this is the case it is not a PIC but an investigator site or other participating organisation and should be set-up and contracted accordingly.

A data processing agreement is a requirement for a PIC. The PIC agreement to be used in the study (where use of PICs is indicated) should be provided in the IRAS submission (or in the amendment to add PICs as a new approach to identifying potential participants, as applicable). Where the sponsor proposes a modified template, including where they propose to directly contract with PIC organisations, they should provide detailed justification for this in their IRAS submission and, where

the terms differ from those in the template, this may need to be escalated to the national contracting lead, or equivalent, within the lead nation.

Where Participant Identification Centres are to be used there should be a clear process for providing information to potential participants and this should be described in the IRAS application. It should be clear (both in the application and to the potential participants) who is responsible for which aspects of the process. This should include clarity for the potential participant on under whose care they would be for the purpose of the study (that they would be transferring from the duty of care of the PIC and into that of the research site, for the purpose of the research activity).

## Study-wide considerations

- Confirm the intentions of the sponsor (and CRO, as applicable) as to the agreement(s) it intends to propose to participant NHS/HSC organisations. Different agreements may be needed for different participating types of NHS/HSC organisations, for example where the study makes use of Investigator sites and PICs. These agreements should be selected in line with 4 nations expectations, for example is a commercial template proposed for a commercial study, is an interventional template proposed for interventional study, if the Organisation Information Document is being proposed as the agreement, consider whether this is appropriate to the circumstance etc.?
- Confirm if an unmodified template agreement is to be used for the study or whether any modifications in the template are being proposed and ensure that any modifications have been explained/justified by the applicant.
  - Where modifications are proposed to the mCTA or CRO mCTA, these must be escalated to the four nations contracting leads group. Modifications proposed to other agreements may also be so escalated but should first be considered in line with nation specific arrangements.
  - If a non-template agreement is being proposed, ensure that the reasons for this (e.g. that no appropriate template exists) have been described by the applicant. Only where it is agreed that no suitable national template exists will this usually be accepted. Escalation to national contracting lead (and, thereafter, to the four nations contracting leads group, as required) is likely to be appropriate where another rationale is provided.
  - Have the correct appendices been included in the template to be proposed to the site (for example, where material is being transferred, the material transfer clauses, where personal data is being transferred, the data transfer clauses (in the mNCA), where a party other than the sponsor is signing on behalf of the sponsor, the confirmation from the sponsor empowering this third party, etc.)?
  - Where an Organisational Information Document has been provided for a non-commercially sponsored study it should describe the study consistently with the other study documents provided.

- Has/have the templates provided been ‘localised’ to the study (localisation, to site level by, for example, adding the name of the site, site level finance information, etc. is not expected in IRAS submissions) in adequate detail and are the arrangements therefore described consistent with other elements of the study (for example, in relation to insurance and indemnity and the transfer of human biological materials, personal data, etc.)? An agreement would normally specify
  - The sponsor organisation for the study
  - The distribution of the key responsibilities
  - And, where appropriate
    - The arrangements for financial management (with reference to criteria 4.3)
    - The arrangements for monitoring of the study, pharmacovigilance or safety reporting (with reference to criteria 5.2)
    - Arrangements relating to insurance and indemnity including the level of compensation for negligent and non-negligent harm (with reference to criteria 4.2)
    - Any services contracted out to a third party (e.g. central laboratory services; centralised ECG interpretation; study monitoring and data collection).
    - The arrangements for the transfer of Human Biological Materials (with reference to criteria 5.4)
    - The arrangements for the handling and transfer of personal data (with reference to criteria 5.1)

## Notes / Resources

- [Model agreements](#)
- [Organisational Information Document and Schedule of Events](#)
- [Schedule of Events Cost Attribution Template \(SoECAT\)](#)

## **4.2 Insurance / indemnity arrangements assessed**

It is a sponsor's responsibility to ensure there is appropriate provision for compensation in the event of injury or death attributable to a study, and any insurance or indemnity to cover the liability of the investigator and sponsor(s)

### **Introduction**

The UK Policy Framework for Health and Social Care states that it is the responsibility of the sponsor to ensure that adequate insurance arrangements are in place to cover liabilities which may arise in relation to the design, management and conduct of the research project. The application should make clear the insurance and indemnity arrangements that are to be in place for the management, design and conduct of the study. The insurance arrangements should be relevant to the study and described appropriately for participants in the PIS, in a manner proportionate to the study type.

A copy of the insurance certificate is expected for all studies sponsored other than by NHS organisations. The insurance should cover the inclusion criteria of eligible participants. In some circumstances (e.g. research in conditions or with participants commonly excluded from insurance policies such as participants of childbearing potential and participants who are breast-feed) it is appropriate that this is accompanied by confirmation from the Sponsor that there are no applicable exclusions that would affect the insurance cover available for study participants. If the sponsor is unable to provide such confirmation (where it is considered appropriate to seek this), or it remains unclear whether there may be applicable exclusions to the policy, a copy/copies of the full insurance policy document/s may be requested.

A list of all insurance exclusions (or a statement from the sponsor that there are none) should be provided in the case of Phase I CTIMPs.

It is expected that NHS organisations do not request renewals of insurance certificates since it is the sponsor's responsibility to maintain insurance as set out to the REC. Any relevant change to the insurance arrangements would constitute a substantial amendment and hence be notified to REC for review.

It should be clear within the application whether the insurance limit is capped for the study as a whole or per patient. The sponsor of a clinical trial (which should be taken to include clinical investigations) not providing £5M of insurance cover should provide a justification for this. Study wide reviewers should provide this justification to participating NHS/HSC organisations to consider in their local review.

### **Negligent harm indemnity:**

Where the sponsor is not the NHS (where no evidence of insurance/indemnity is required) the sponsors insurance certificate (and, where relevant, the policy) shall usually specify Professional/ Employers liability and, where relevant, Clinical Trials Liability

### **Management of the study:**

The sponsor will normally hold insurance or provide indemnity to cover their liabilities as sponsor which would cover the overall management of the study. Where an NHS organisation is a sponsor, then cover is provided through NHS schemes. No proof of insurance is expected for NHS sponsored research. Where the sponsor is not the NHS (for example where it is a commercial company, or a higher education institution) insurance will be provided through an insurance scheme. A copy of the relevant certificate (and, where considered appropriate, the full policy) should be provided.

For studies limited to recruiting NHS staff and/or independent contractors as participants and not requiring REC review, proof of insurance/indemnity for the management of a study will not be requested.

### **Design of the study:**

As per the requirements of the UK Policy Framework for Health and Social Care the design of the study is the responsibility of the study sponsor. While the sponsor may take whatever advice it sees fit, or subcontract to a third party, it remains ultimately responsible for the study protocol and the design of the study expressed therein (and in other relevant documents). Where the sponsor proposes that liability for the design of the study be covered by another party a suitable justification should be provided for this.

Where an NHS organisation is a sponsor, then cover is provided through NHS schemes. No proof of insurance is expected for NHS sponsored research. Where the sponsor is not the NHS (for example where it is a commercial company, or a higher education institution) insurance will be provided through an insurance scheme. A copy of the relevant certificate (and, where considered appropriate, the full policy) should be provided.

For studies limited to recruiting NHS staff and/or independent contractors as participants and not requiring REC review, proof of insurance/indemnity for the design of a study will not be requested.

### **Conduct of the study:**

The conduct of the research refers to the study procedures, as described in the protocol, which are conducted by the research team with participants, data or human biological material. Employers of the research team are normally responsible for the actions of their staff who conduct research procedures as part of their employment. If an NHS member of staff performs research activities (in their capacity as an NHS member of staff – i.e. as part of their NHS job) in a non-NHS location, then NHS cover still applies.

Where the research involves NHS patients under the care of NHS organisations, cover for harm to participants resulting from clinical negligence is provided through NHS indemnity schemes. No proof of this cover is expected. Cover for the purposes of non-clinical negligence remains the responsibility of the employing organisation.

### **Primary care**

Independent contractors (e.g. GP practices, NHS dental practices) or the staff members they employ are covered by

- In England the Clinical Negligence Scheme for General Practice (CNSGP) and,
- In Wales, the General Medical Practice Indemnity (GMPI). These are state indemnity scheme covering NHS services provided by the GPs.
- Northern Ireland currently advise that GPs contact their insurer and let them know they are participating in a study providing any information requested by the insurers regarding the nature of the study and their particular role.
- In Scotland there is no State backed indemnity scheme for independent practices.

No evidence is required of the cover provided.

### **Non-negligent harm indemnity (also known as No Fault compensation):**

For **commercial studies** arrangements for no fault compensation should be provided in accordance with the Association of British Pharmaceutical Industry (ABPI) or Association of British Healthcare Industry (ABHI) schemes. The ABPI/ABHI compensation guidelines form part of the model agreement and may not be modified. Where a commercial sponsor proposes modification of the model agreement, or otherwise does not propose to provide ‘no fault compensation’ justification should be requested and escalated as per nation specific processes.

For **non-commercial studies**, arrangements for no fault compensation cannot be made in advance by the NHS or other public bodies (e.g. MRC). Such organisations, although not accepting liability, may consider making an ex gratia payment on a voluntary basis in the event of a claim. Some universities or higher education institutions may choose to provide no fault compensation for research involving their employees. If this is the case a copy of the policy should be provided. It is the role of RECs to decide whether or not a study can go ahead without a scheme of compensation for harm caused where there is no negligence.

### **Equipment indemnity**

Where equipment is under investigation and is the subject of the research proposal indemnity should be detailed, for commercial sponsors, in the study contract and evidence of insurance provided that appropriately covers the equipment being used – for example, products liability insurance. This may vary between participating nations (for Scottish purposes it may state that the Master Indemnity Agreement will apply whereas for participating organisations in England, Wales and Northern Ireland indemnity should be provided under the terms of the agreement)

In the case of non-commercial sponsors study wide assessors should clarify what the indemnity arrangements are in order to convey this information to participating NHS/HSC organisations with appropriate insurance and indemnity covered in the appropriate template agreement – with evidence of correct insurance in place.

Additionally, a research site might not have access to a piece of specific equipment to undertake the study, e.g. an ECG machine that transmits data directly to a central reading facility. In this case the Sponsor might make arrangements for the piece of equipment to be loaned or gifted to some or all research sites. Although such provision might be arranged by the Sponsor, the supplier may not be the Sponsor and hence the sponsor may be reluctant to itself indemnify that equipment. In a research study, the Sponsor must provide or arrange insurance, and should clarify the proposed insurance arrangements and explain whether it will directly indemnify participating organisations (with may be through the Master Indemnity Agreement (In Scotland) or through other means, (such as the study contract), or whether insurance will be provided by a third party such as the equipment manufacturer.

### **Study-wide considerations**

Before a study is initiated an agreement about compensation in the event of harm to participants should have been reached. If any organisation, or the sponsor themselves, offers compensation without proof of negligence, they should have made the appropriate arrangements.

Review the following aspects of the insurance/ indemnity arrangements:

- Assess whether there should be an insurance certificate (not expected for studies where NHS indemnity covers the liability that arises from the management, design or conduct of the study or for studies being undertaken in a Primary Care setting, e.g. GP Practises or NHS Dental Practises)
- Consider the level of insurance/ indemnity and whether it is appropriate to the study type and purpose taking into account any justifications provided by the sponsor for levels below £5M
- Are any specific exclusions to the cover detailed? (A full listing, or sponsor statement that there are no exclusions, should be provided for each Phase I CTIMP).
- For studies where study specific equipment is to be loaned or gifted to a research site confirm what equipment is to be loaned or gifted and whether this is equipment which is the subject of the research proposal or equipment being provided to facilitate the study at site SW review should clarify the planned arrangements for equipment that is to be loaned or gifted. This should be reflected in the options chosen in the model agreement and may well be nation specific (e.g. could rely on MIA in Scotland but not in England, Wales or Northern Ireland).
- A description of the study insurance/indemnity and compensation should be provided in the PIS which is proportionate to the study type. This should always be provided in the case of clinical trials and other interventional studies. If a description of ABPI compliant compensation arrangements is given in the PIS it should not be limited to provision of costs for medical treatment.

### **Notes / Resources**

[The Medicines for Human Use \(Clinical Trials\) Regulations 2004](#)

[The Medicines for Human Use \(Clinical Trials\) Amendment Regulations 2006](#)

[Responsibilities, liabilities and risk management in clinical trials of medicines](#)

[Arrangements for Clinical Negligence Claims in the NHS in England](#)

[Clinical trial compensation guidelines | ABPI](#)

[Insurance and compensation in the event of injury in Phase I clinical trials | ABPI](#)

[Association of British Healthcare Industries \(ABHI\) Indemnity Form](#)

## **Equipment Indemnity**

HRA Guidance [Use of Master Indemnity Agreement in research: updated DH guidance - Health Research Authority](#)

England: [Master indemnity agreement: approved suppliers - GOV.UK](#)

Scotland: [Health Facilities Scotland | National Services Scotland](#)

Wales: [NHS Wales Master Indemnity Agreement](#)

Ireland: [HSC Research and Development www.research.hscni.net | HSC Public Health Agency](#)

## **4.3 Financial arrangements assessed**

The way in which a study is financed is important to NHS organisations as they are legally accountable for use of public funds.

### **Introduction**

It is important that NHS/HSC organisations are aware of the activity involved in supporting a study and what it costs. NHS/HSC organisations should be aware of the planned expenditure and attribution of costs to ensure financial probity, compliance with the law and with the rules set out by HM Treasury regarding the use of public funds.

Where the study is funded through one or more programme grant(s), the IRAS application should reflect the amount or percentage of funding that is to be used for the study. This will give a clearer indication of the study funding than the value of the total programme grant.

For non-commercially sponsored studies, the Organisational Information Document is intended to contain a description of what funding (if any) is to be provided to each site type to cover research costs. It also requests that the sponsor specifies what support should be in place locally to deliver the study. The Schedule of Events/SoECAT is designed for sponsors to attribute the site costs of their research. Where a SoECAT has been completed, and the study team intend to apply for adoption on the portfolio, the SoECAT should be validated by a CRN AcoRD expert. One copy of the Schedule of Events/SoECAT should be provided for each participating NHS/HSC site type detailing the activities taking place at that site type.

For commercially sponsored studies in England and Wales an electronic interactive Costing Tool (iCT) should be completed and submitted through the NIHR Central Portfolio Management System (CPMS). No evidence of this submission is required.

In Scotland researchers should follow the relevant NRS guidance for Determining a Price for Commercial Research Studies across Scotland and the relevant process for non-commercial costings and detail in National Differences section of Study-Wide Governance Report if applicable.

### **Study-wide considerations**

#### **Non-commercial studies**

- Ensure the letter from funder is received (if applicable). N.B. This may be clearly described as a final award, or grant, or may include conditions. Either is acceptable.
- Consider whether the financial management arrangements have been appropriately described.
- Consider the appropriateness of arrangements to reimburse other parties.

- Ensure that the activities described in the IRAS Schedule of Events/SoECAT are consistent with other study documentation, e.g. protocol and participant information sheet (assurance may be taken on this from an AcoRD Specialist authorised SoECAT. N.B. SW reviewers should accept an authorised SoECAT as having been appropriately authorised, without further checks on the identity of the authorising party, as it is a locked document with the password available only to authorised AcoRD Specialists).

## **Commercial studies**

- In England and Wales, the NIHR interactive costing tool (iCT) should be completed and submitted to NIHR for all studies prior to IRAS submission, irrespective of whether the researchers wish to apply for adoption on the portfolio. No evidence of such submission is required.

## **Post study arrangements**

- Participants should not be given false or unrealistic expectations of post-study access to the study intervention. Where the application (particularly the participant information) suggests that post-study access to study therapies will be afforded to participants, the SW review will obtain from the sponsor evidence as to how this access will be funded and arranged.

## **In Scotland**

- Study wide reviewers should obtain assurance that the sponsor will follow the relevant NRS guidance for Determining a Price for Commercial Research Studies across Scotland and the relevant process for non-commercial costings and detail in National Differences section of Study-Wide Governance Report, if applicable.

## **Notes/ Resources**

- [Attributing the costs of health and social care research - GOV.UK](#)
- [Faster costing and contracting | NIHR](#)
- [Technical Assurance Payments Framework Guidance - Health Research Authority](#)

## **5.Legal Compliance**

### **5.1 Compliance with Data Protection law and data security issues assessed**

#### **Introduction**

Across the UK, the NHS treats the largest pool of patients in the world, with more than 1M patients and service users accessing services daily. The NHS is also one of the largest employers in the world, with more than 1.3M members of staff. The NHS is responsible for a vast repository of patient, service user and staff data.

The use and disclosure of this data is covered by a complex range of legal and professional obligations. NHS and HSC organisations, and persons working with and within them, are required by law:

- to protect the way that Personal Data is handled in accordance with The Data Protection Act 2018 (DPA), the UK General Data Protection Regulation (UK GDPR) and The Privacy and Electronic Communications Regulations 2003 (PECR);
- to ensure that privacy is respected, in accordance with the Human Rights Act 1998, and,
- to satisfy the obligation of confidentiality in common law.

In addition, NHS and HSC organisations, and persons working with and within them, are expected to:

- Handle confidential patient information in accordance with the Caldicott principles and the NHS codes of practice for confidentiality, and,
- Manage records securely in accordance with NHS record management and information security codes of practice.

These requirements and expectations are supplemented by an array of nation and profession specific codes and expectations.

It should be clear, to participating NHS/HSC organisations what data they will be required to collect or otherwise process. The flow of data, from collection (directly from study participants or otherwise from NHS records, or similar), through the processing within the NHS and thereafter to onward disclosure, should be clearly set-out, including clarity as to when the data should no longer be considered Personal Data or confidential information under common law, including the arrangements to render it so and the safeguards to maintain it as such. Where a study requires the installation of specific software on NHS systems, or the utilisation of hardware additional to standard NHS equipment, it should be clear what data security safeguards that the sponsor has enacted to ensure that this may be done lawfully and, where applicable, in compliance with NHS/HSC expectations, data protection and confidentiality policies.

UK study wide review provides assurance to NHS/HSC organisations involved in research activities, and persons working with and within them, that approved studies have been designed to be compliant with the law and to also adhere more generally to the applicable expectations. UK Study Wide review removes the need for individual NHS and HSC Organisations to review for themselves those areas set out as reviewed in this section, or otherwise specified as reviewed on a study basis, and supports the arrangements that they need to make in order to comply with their responsibilities as participating organisations.

## **UK GDPR and The Data Protection Act 2018**

UK GDPR and the DPA 2018 apply only to Personal Data.

Personal Data is defined as:

**'any information relating to an identified or identifiable natural person ('data subject'); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person.'**

The phrase 'natural person', means a living individual person. Data that may identify a person includes their name, address, NHS number, etc. In practice, this may also include all data which are or can be assigned to a person in any kind of way. For example, the telephone, credit card or personnel number of a person, account data, number plate, appearance, customer number or address may all be Personal Data. Whether or not something is Personal Data is often a complex and always a context dependent consideration.

The sponsor should ensure that it is clear what data will be collected and for how long this will remain Personal Data (i.e. what are the 'data-flows' – will any data leaving usual NHS systems, and leaving the NHS itself, still be Personal Data, or will it no longer be identifiable to the recipient?). A data flow diagram is an effective means of communicating this information, from sponsor to study wide reviewer and to sites, and it is good practice to include such a diagram in the IRAS submission documentation and local information pack provided to sites.

Once data can no longer be reasonably likely used to identify an individual living person, alone or in combination with other data reasonably likely to be in possession of the person or persons holding the data, then it is no longer Personal Data. For the avoidance of doubt, data which is coded, or 'linked anonymised,' is still considered Personal Data to the person or persons who hold the 'key' to re-identify the data (i.e. if the data and key are held within the same legal entity, the coded data remains Personal Data to the employees of that entity). If the de-identified data is sent to a separate legal entity, with which contractual safeguards are in place, such that they will not access the 'key' and will not attempt to re-identify the data, such de-identified data is unlikely to be Personal Data to that recipient.

## **Data Controller and Data Processor roles and responsibilities**

The Sponsor is the data Controller for data processing undertaken for the purposes of the research study, as it is the party that determines the purpose and means of the processing (as well as which data are to be processed), and the participating care organisation is the sponsor's data Processor. The care organisation is separately the Controller of data processing undertaken for its own purposes, outside of the research. This means that there may be two Controllers of the same data – each separately controlling the processing of that data for its own purposes. This is not Joint Controllership (the two parties are not jointly determining which data should be processed, in which ways, for which purposes).

Joint Data Controllership in research is possible. For example, in the case where a study is jointly sponsored, all sponsor responsibilities (including Controllership) will be joint. Co-sponsors may also agree to be Joint Controllers. It is also possible for non-sponsors to act jointly as Controllers with a research sponsor, such as when a Clinical Trials Unit advises a legally separate research sponsor and chooses to accept joint Controller status, without accepting joint or co-sponsorship status. In such a case, the joint data Controllers should document a clear division of responsibilities. It would not usually be necessary to present this agreement to the SW reviewer or to participating NHS organisations – but if joint-Controllership impacts on how the NHS should act (for example, from which organisation it should accept processing instructions) SW review should ensure that this has been made clear. These exceptions to the Sponsor being the only Controller for the Personal Data processed for the purpose of the study generally only apply to non-commercial research.

It is the responsibility of the sponsor, as data Controller to provide relevant information to participating NHS/HSC organisations to enable them to meet their obligations as data Processors. Specifically, it should be clear

- a. Whether and under what circumstances the participating NHS/HSC organisations are allowed to subcontract data processing, for example, to a Participant Identification Centre (this may be made clear by the sponsor via the contact proposed, or via other means) (GDPR Article 28(2)).
- b. How the participating NHS/HSC organisations will be provided with information to meet their GDPR Article 30(2) responsibilities without further review. Such information may be provided within, for example the IRAS dataset, protocol, contract, etc. (that information being):
  - (i) The 'category' of the processing to be undertaken, i.e. research.
  - (ii) The name and contact details of the Controller.
  - (iii) Where the sponsor is not established in the UK, the name and contact details of the sponsor's UK representative.
  - (iv) The name and contact details of the sponsor's Data Protection Officer (DPO), where applicable.
  - (v) Whether the Participating NHS/HSC organisation will be required to export Personal Data outside of the UK and, if so, to which countries/organisations and, where a GDPR Article 49(1) safeguard is relied upon, what this is (for example, explicit consent). N.B. It is generally expected that by the time of any

export of data, this would no longer be Personal Data (i.e. it would have been rendered no longer identifiable to the recipient). Furthermore, it is not usually the participating NHS/HSC organisation that is exporting the data, as the data processing is under the controllership of the sponsor and the NHS/HSC organisation would usually be providing this data to a party in the UK prior to export;

- (vi) Where the sponsor requires or allows for the NHS/HSC organisation to process Personal Data outside of its usual NHS/HSC systems and processes, a general description of the technical and organisational security measures that the sponsor will put in place/expect the NHS/HSC organisation to put in place. N.B. where no processing of Personal Data will take place outside of the usual NHS/HSC systems and processes, no such description is required.

### **Legal Basis for processing Personal Data and condition for processing special category Personal Data**

Data Protection legislation requires the Controller to have a legal basis (GDPR Article 6) for the processing (including by a Processor on its behalf) of Personal Data. It also requires that the Controller satisfy a condition (GDPR Article 9) for processing special category Personal Data, where applicable (Personal Data concerning health is always special category).

The UK health authorities, with ICO advice, expect that sponsors that are public bodies (e.g. NHS/HSC organisations, HEIs, research councils, etc.) rely upon task performed in the public interest as their legal basis (GDPR Article 6(1)(e)), with sponsors that are not public bodies (e.g. commercial companies, charities, etc.) relying upon legitimate interests (GDPR Article (6)(1)(f)). Both public and non-public bodies should rely upon processing being necessary for research purposes (9(2)(j)) as the condition.

Even when consent will be obtained from research participants, for ethical, common law and other purposes, (as in most cases it must or should be), consent (GDPR Article 6(1)( a)) and explicit consent (GDPR Article 9(2) (a)) **Should not be relied upon as GDPR legal basis or condition for data processing for the purposes of research.**

It is possible that the sponsor may choose to rely on consent for the purposes of the initial collection of study data, with all subsequent processing being on the bases described above, though this should be discouraged, not least because of the difficulty in adequately describing this arrangement to potential participants. If the sponsor wishes to rely upon consent and explicit consent under GDPR for the INITIAL COLLECTION of the Personal Data, this should be explicitly stated in the PIS and the following addressed.

- Why the sponsor is unable to rely upon a more appropriate legal basis (it is expected that consent would only be used where a legal basis more appropriate to research is not available – i.e. where the processing is not in the public interest/not a legitimate interest of the sponsor).

- How the sponsor will ensure that processing immediately ceases once consent (and hence the legal basis for further processing) is withdrawn and on what legal basis, with what transparency arrangements, this will occur (given that destruction, return, anonymisation, etc. are themselves forms of processing).
- How the sponsor has protected the scientific validity of the study, in the face of losing data once legal basis to process it has been withdrawn, without resort to over-recruitment and/or introducing bias to the study
- How the sponsor has addressed the imbalance of power question with regards to relying upon consent for data processing in a clinical setting

GDPR states that ‘Where a type of processing is likely to result in a high risk to the rights and freedoms of individuals, the Controller must, prior to the processing, carry out a data protection impact assessment.’<sup>3</sup>.

For Personal Data processed for the purpose of a healthcare research project, the sponsor of the project is the Controller and the participating NHS organisation is their Processor. DPIAs for the processing of Personal Data that is undertaken for the purpose of research are the responsibility of the sponsor. It is unlikely that the sponsor will be required to undertake DPIA at the individual study level, as a data protection by design approach should be followed, whereby systems, processes, templates, etc. are designed and risk assessed so as to give rise to compliant studies<sup>4</sup>. Study Wide reviewers may, only very exceptionally, request additional details from the sponsor relating to DPIA, such as in novel study designs, particularly those making use of novel information technology for the processing of Personal Data.

---

<sup>3</sup> General Data Protection Regulation (GDPR) Article 35(1); DPA 2018 Section 64(1)

<sup>4</sup> [Data Protection Impact Assessments - Health Research Authority \(hra.nhs.uk\)](https://www.hra.nhs.uk)

## Data Subject rights and appropriate additional safeguards

GDPR sets out the rights of data subjects. Some rights may be limited their full exercise may significantly achievement of the research purpose. The extent to which data subject rights may be limited depends on the Article 6 legal basis selected.

Article 6 basis	Right to be Informed (Art 13/14)	Right of Access (Art 15)	Right of Rectification (Art 16)	Right to Erasure (Art 17)	Right to Restriction (Art 18)	Right of Portability (Art 20)	Right to Object (Art 21)
6(1)(a) Consent N.B. Is available but leaves further processing without a legal basis if consent is withdrawn, see additional questions above for the sponsor. HRA would recommend against using this.	Yes (requirement to state consent can be w/d and processing before w/d remains lawful (Art 13(2)(c) + Art 14(2)(d))	Yes (there are no caveats in Art 15 depending on basis etc.)	Yes (there are no caveats in Art 16 depending on basis etc.)	Yes (if consent w/d and no other legal grounds) (Art 17(1)(b))	Yes (there are no caveats in Art 18 depending on basis etc.)	Yes (where provided, if automated) (Art 20(1))	No (not included in Art 21(1) - but consent can be w/d)
6(1)(c) Legal obligation N.B. This can be applicable only to CTIMPs.	Yes (there are no caveats in Art 13/14 depending on basis etc.)	Yes (there are no caveats in Art 15 depending on basis etc.)	Yes (there are no caveats in Art 16 depending on basis etc.)	No (Art 17(3)(b))	Yes (there are no caveats in Art 18 depending on basis etc.)	No (not included in Art 20(1))	No (not included in Art 21(1))
6(1)(e) Public task	Yes (there are no caveats in	Yes (there are no caveats in	Yes (there are no caveats in	No (Art 17(3)(b))	Yes (there are no caveats in	No (not included in Art 20(1))	Yes (Art 21(1)), unless for

N.B. Not available to non-public bodies	Art 13/14 depending on basis etc.)	Art 15 depending on basis etc.)	Art 16 depending on basis etc.)	Interacts with right to object (Art 21(1) – erase if objection upheld (Art 17(1)(c))	Art 18 depending on basis etc.). Interacts with right to object (Art 21(1) – restrict while objection considered (Art 18(1)(d))		research in public interest (Art 21(6)) – i.e. unless using condition 9(2)(j)
6(1)(f) Legitimate interests N.B. Not available to public bodies	Yes (requirement to specify the legitimate interests – (Art 13(1)(d) + Art 14(2)(b))	Yes (there are no caveats in Art 15 depending on basis etc.)	Yes (there are no caveats in Art 16 depending on basis etc.)	Yes, unless the LIs outweigh the rights. Interacts with right to object (Art 21(1)) – erase if objection upheld (Art 17(1)(c))	Yes (there are no caveats in Art 18 depending on basis etc.). Interacts with right to object (Art 21(1)) – restrict while objection considered (Art 18(1)(d))	No (not included in Art 20 1)	Yes (Art 21 1), unless for research in public interest (Art 21(6)) – i.e. unless using condition 9(2)(j)

Where special category personal information (e.g. relating to healthcare) is being processed, there must also be an article 9 condition, which has further interactions with the rights that flow from the Article 6 basis

<b>Article 9 special category condition</b>	<b>Right to be Informed (Art 13/14)</b>	<b>Right of Access (Art 15)</b>	<b>Right of Rectification (Art 16)</b>	<b>Right to Erasure (Art 17)</b>	<b>Right to Restriction (Art 18)</b>	<b>Right of Portability (Art 20)</b>	<b>Right to Object (Art 21)</b>
9(2)(a) Explicit consent N.B. Is available but leaves further processing without a legal basis if consent is withdrawn, see additional questions above for the sponsor. HRA would recommend against using this.	Yes (requirement to state consent can be w/d and processing before w/d remains lawful (Art 13(2)(c) + Art 14(2)(d))	Yes (there are no caveats in Art 15 depending on basis etc.)	Yes (there are no caveats in Art 16 depending on basis etc.)	Yes (if consent w/d and no other legal grounds) (Art 17(1)(b))	Yes (there are no caveats in Art 18 depending on basis etc.)	Yes (where provided, if automated) (Art 20(1))	No (not included in Art 21(1) - but consent can be w/d)
9(2)(j) Public interest – research (in accordance with Art 89 1)	Yes, but some information e.g. Art 15(2) derogated by DPA 2018, Sch 2, Part 6(27) (2)(a)	No – Art 15 (1) - (3) derogated by DPA 2018 Sch 2, Part 6(27)(2)(a)	No – Art 16 derogated by DPA 2018 Sch 2, Part 6(27)(2)(b)	No – if it will undermine the aims (Art 17(3)(d))	No – Art 18 1 derogated by DPA 2018 Sch 2, Part 6(27)(2)(c)	No (not included in Art 20(1))	No – Art 21 1 derogated by DPA 2018 Sch 2, Part 6(27)(2)(d)

It is important that potential participants are not led to believe that they have (legally enforceable) **RIGHTS** if they do not have them. Sponsors may choose to offer participants the ‘right’ to **REQUEST** to access data, etc. but these should not be expressed as unqualified **RIGHTS** where they are not (e.g. ‘you have the right to **REQUEST** access...’, etc. may be used but **NOT** ‘you have the **RIGHT TO** access’, etc.).

Data subject rights may be limited only where ‘Appropriate safeguards’ to the processing of Personal Data are in place. For health research these require the following:

- the research will not cause substantial damage or distress to the data subject (i.e. substantial physical harm, financial loss or psychological pain), (a condition that the REC will consider, as appropriate);
- medical research has approval from a research ethics committee (as defined in the DPA) if it involves processing data in order to do or decide something with respect to an individual person,
- the data Controller has technical and organisational safeguards in place that ensure respect for the principle of data minimisation and ensure that exemptions to data subjects’ rights are not exercised unless the rights are likely to render impossible or seriously impair the achievement of the purposes of the processing,
- if processing special category Personal Data, this must be in the public interest (demonstrated over and above using ‘task in the public interest’ as the legal basis)

## Transparency requirements

The sponsor (as Controller) obtains Personal Data **directly** from data subjects when the data is collected at the instruction of the sponsor and intended to be used for research purposes at the time it is collected. This includes, but is not limited to,

- Personal Data obtained on behalf of the sponsor by clinical staff at a site or a research laboratory,
- Personal data provided by the participant to employees or other agents of the sponsor (for example when tests are being undertaken for a person consented to a research study and the results of those tests are transcribed into a case report form).
- Personal data relating to study personnel from within the NHS/HSC, where this will be processed for the purposes of the research.

The sponsor (as Controller) obtains Personal Data **indirectly** when the Personal Data was collected under separate Controllership at the time it was provided by the data subject (for example when data is being collected from the medical records of a person consented to a research study for tests that were undertaken prior to their consent, such as may be the case when confirming eligibility).

Depending on whether data is obtained directly and/or indirectly, the sponsor should provide the transparency information detailed below. Exemptions to this provision of

transparency information may apply in specific cases where the Personal Data is obtained indirectly, such as in the case of respective case study research where consent is not obtained, when one of the following applies:

- Providing information to affected people is impossible or requires disproportionate effort, or;
- Providing information will seriously impair or render impossible the objective for which you are processing that Personal Data (i.e. researchers will not be able to deliver their research objectives).

Where such an exemption is relied upon the receiving sponsor should ensure that:

- Technical and organisational safeguards are in place that respect the principle of data minimisation, such as pseudonymisation, where possible, and;
- The reason for relying on an exemption is documented.

The HRA (on behalf of the four nations) has published recommended transparency wording for public sector (e.g. NHS/HSC organisations, HEIs, etc.) and non-public sector (e.g. commercial, charity, etc.) sponsors<sup>5</sup>. This information should be provided in a layered format, i.e. some information should be integrated into the PIS (and similar documents, e.g. pregnant partner information sheet) and other information will be provided in other places, for example on the sponsors website. Where the standard text is used as intended, no further review of transparency is required. A number of commercial and non-commercial sponsors have had their alternative proposed wording agreed by the HRA on behalf of the UK nations, at the sponsor level.

Study wide review should assess the data transparency information provided. Where the sponsor has not used the HRA's recommended wording, or other pre-approved wording, the study wide review will consider whether the information provided meets the requirements detailed below. It is not usually necessary to review the higher-level information used by the sponsor where information has been provided there in line with HRA recommendations. Where the sponsor has chosen to provide higher level information in the PIS this should be reviewed in line with the below.

---

<sup>5</sup> [Transparency wording for all sponsors - Health Research Authority](#)

<b>Transparency requirement</b>	<b>Personal Data obtained directly</b>	<b>Personal Data obtained indirectly</b>	<b>Location (based on UK recommendations)</b>	<b>Further details re: what to consider during study wide assessment</b>
Name of Controller and contact details (including of data protection officer and, where relevant, the UK representatives)	Yes	Yes	PIS for sponsor's name. Higher level (website) indicates sponsor is Controller. Higher level (website and supplement) include information about contacting DPO.	The PIS should state the name of the study sponsor. The sponsor should state that they are the data Controller and include contact information for their Data Protection Officer, where they have one (SW review will obtain justification in the case that a sponsor does not have a DPO). Such contact information may be generic (for example, a corporate DPO email address), rather than specific to a named individual. The sponsor may state that, in the first instance participants should contact their study doctor as contact with the sponsor will lead to unblinding.
Purposes of the processing, as well as the legal basis	Yes	Yes	PIS for purpose of specific study. Higher level (website and supplement) for general details on purpose of research. Higher level (supplement) for legal basis.	The sponsor should state the legal basis upon which they are relying. Although required to be clear on their legal basis, sponsors may choose to use less legalistic terminology in their study level information (relying upon web-based transparency information, etc. for the more formal language).
The legitimate interests of the Controller or third party, where applicable	Yes	Yes	Higher level (supplement).	If relying on legitimate interests the sponsor should state what these are.
The categories of Personal Data concerned	No	Yes	PIS. Technically it may not be needed (if data is obtained directly) but it is usually included anyway.	The sponsor should detail the categories of data that will be collected. Details of all specific data fields that will be collected are not necessary and more generic statements would be sufficient.

The recipients or categories of recipients of the Personal Data, if any	Yes	Yes	Higher level (supplement) states that data subject can ask who will look at records and where data will go.	<p>The sponsor needs to explain that</p> <ol style="list-style-type: none"> <li>1. Data will be sent to the sponsor. The sponsor should state whether this data will be sent in an identifiable, linked anonymised, or fully anonymised format. Usually this will be linked anonymised.</li> <li>2. Data may be shared with regulators, such as the MHRA and others in coded form. If there are any references to the REC receiving data in any form, then these should be deleted as this is not applicable in the UK.</li> <li>3. Data will be shared with sponsor representatives who may see data in an identifiable form for monitoring purposes. The HRA advise that sponsors do not commit to only either physical or remote monitoring but allow for either or both.</li> </ol>
The period for which the Personal Data will be stored	Yes	Yes	Higher level (supplement) states that data subject can ask how long data will be kept. Higher level (website) states that data may be kept indefinitely.	<p>The sponsor should state how long Personal Data will be retained for following the end of the study (usually 15 or 25 years) or, if this is unknown, state the conditions that will be used to determine this time period. It would be sufficient, when detailing these conditions to state, for example, that data will be retained as determined by legal obligations. GDPR does not override other requirements of the Data Protection Act. Data should be retained as long as it is necessary (as defined by the sponsor) to do so, and then deleted.</p> <p>Personal Data can be retained indefinitely for scientific research purposes. However, the sponsor should state an explicit reason for indefinite retention and should not retain data 'just in case'. It is for the sponsor to judge whether this</p>

				reason is sufficient. If data will be retained indefinitely then appropriate safeguards, as detailed above must be put in place
The data subject's rights under GDPR	Yes	Yes	PIS, higher level (website) and higher level (supplement) all indicate rights are limited.	<p>This should be consistent with the legal basis and special category condition chosen by the sponsor as per the table above.</p> <p>It is important that potential participants are not led to believe that they have (legally enforceable) rights if they do not have them. Sponsors may choose to offer participants the opportunity to access data, etc. but these should not be expressed as unqualified rights where they are not (e.g. 'you have the right to REQUEST access...', etc. may be used but NOT 'you have the right TO access', etc.). It is sufficient to tell participants that their data subject rights may be limited due to the purposes of the research and that any request to exercise data subject rights will be reviewed by the sponsors Data Protection Officer.</p> <p>A basic statement of rights, and that these may be limited, should be provided in the PIS. If the sponsor wishes to provide further information about specific rights, then this can be provided in higher level information.</p>
The right to lodge a complaint with the ICO	Yes	Yes	Higher level (both website and supplement).	The sponsor should state that participants have the right to complain to the Information Commissioner's Office if they are not happy with the sponsors response or believe the sponsor processing data in a way that is not right or lawful.
The source from which the Personal Data originate, and if applicable, whether it	No	Yes	PIS, Higher level (both website and supplement) for general information on sources. There may not	The sponsor should state where data has been obtained from and whether it has been obtained from a public source. This is only necessary for data that is obtained indirectly.

came from publicly accessible sources			be a PIS if data are being obtained indirectly.	The HRA recommend that this information be provided in the PIS. However, if data is being obtained indirectly there may not be a PIS, as consent may not be required. In this case information should be provided at a higher level, such as the sponsors website, for general information on sources.
Any automated decision-making, and, meaningful information about the logic involved, as well as the significance and the envisaged consequences of such processing for the data subject <sup>6</sup>	Yes	Yes	The HRA recommend that this information be provided in the PIS. If the sponsor is using the HRA recommended wording, then they will need to add their own wording to cover this aspect.	The sponsor should provide information regarding the significance and the envisaged consequences of such processing for the data subject.
How appropriate or suitable safeguards are achieved in relation to any Personal Data transferred out of Europe	Yes	Yes	Not included in HRA wording for PIS or higher level (website or supplement). If applicable, sponsor will need to address this in their own wording (e.g. in the PIS, if using HRA higher level wording).	<p>The sponsor should provide information regarding the safeguards that they are taking if Personal Data is being transferred out of the EEA.</p> <p>The HRA recommend that the sponsor detail, in the PIS, simply that appropriate safeguards are being taken. Further details on these safeguards can be provided at a higher level, for example the sponsors website.</p>

---

<sup>6</sup> In this context automated decision-making refers to use of Personal Data in machine learning or other technologies that will result in a decision about the individual, e.g. a diagnosis. Electronic randomisation technologies are not included.

## **Transfer of Personal Data**

### **Transfer of Personal data outside of NHS systems to other systems within the UK**

Ideally, personal data should only be processed, for the purposes of the research, within NHS systems (including electronic systems) with no data leaving these systems prior to being rendered no longer identifiable to the recipient (and hence no longer Personal Data). Where it is necessary for the purpose of the study for Personal Data to leave NHS systems, including where the Personal Data will be transferred outside of the NHS, the sponsor should explain how the security of data will be maintained outside of NHS systems, including following any transfer outside of the NHS..

### **Transfer of Personal data to a country or territory outside of the UK**

The international transfer of Personal Data, where this occurs for the purpose of the study, occurs under the Controllership of the sponsor. The data Processor will be responsible for transferring data to the sponsor, or to another data Processor acting under instructions of the sponsor. For example, where the site transposes data into an eCRF, the entity (which may not be the sponsor) managing the eCRF is operationally responsible for the further processing and transfer to the sponsor.

Where Personal Data are transferred out of the UK by the data Controller then Article 44 of the GDPR requires that such transfer of Personal Data to a third country (including for onward transfer to another third country) shall take place only if the conditions laid out in Chapter V are complied with by the Processor and Controller. The sponsor, as data Controller, is responsible for overseeing the international transfer of data and should have a legal mechanism in place to manage such transfer. GDPR Chapter V arrangements for export are therefore a matter for the sponsor as Controller. The NHS/HSC organisation is not usually the exporter and no attempt should be made to place upon the NHS/HSC GDPR Chapter V responsibilities for the export, including the use of GDPR Article 46 Standard Contract Clauses with the NHS/HSC as party.

The sponsor should explain whether Personal Data disclosed by participating organisations will leave the UK and, if so, under what Chapter V condition. The available conditions are

- Article 45, Transfers on the basis of an adequacy decision;

Pursuant to Article 45 of EU and UK GDPR, adequacy decisions are currently in place for Andorra, Argentina, Canada (commercial organisations), Faroe Islands, Guernsey, Israel, Isle of Man, Japan, Jersey, New Zealand, Switzerland and Uruguay as providing adequate protection. Adequacy talks are ongoing with South Korea.

The UK regards the EU and other EEA states and territories as adequate in terms of their data protection legislation (and the EU also regards the UK as adequate) so no further condition is necessary for the transfer of Personal Data from the UK to EEA/EU states (or from an EEA/EU state into the UK).

The European Union Court of Justice (CJEU) has invalidated the EU-US Privacy Shield in its decision in Facebook Ireland v. Schrems (Schrems II)<sup>7</sup>. The court determined that the Privacy Shield transfer mechanism does not provide the adequate protection required under EU law.

- Article 46, Transfers subject to appropriate safeguards.

Article 46 sets out safeguards that may be relied upon for transfers to third countries for which no adequacy decisions are in place:

- Legally binding and enforceable instrument (e.g. contract) between public authorities or bodies.
- Binding corporate rules in accordance with Article 47
- Standard data protection clauses adopted or approved by the Commission
- An approved code of conduct or certification mechanism, together with binding and enforceable commitments from the Controller/Processor in the third country

No relevant codes of conduct or certification mechanisms are yet in place. For public sector sponsored research Personal Data may be transferred to public authorities in third countries under appropriate contracts. Commercial or charitably sponsored research relying upon an article 46 safeguard for transfer would need to evidence that it is doing so under commission approved contract clauses or commission approved binding corporate rules:

- Article 49 Derogations for specific situations.

This is very likely to be Article 49 1 (a) '**the data subject has explicitly consented to the proposed transfer, after having been informed of the possible risks of such transfers for the data subject due to the absence of an adequacy decision and appropriate safeguards**'.

## Appointment of a UK Representative

Where the sponsor is a non-public body, is based outside of the UK and does not have a branch, office or other establishment in the UK then it should appoint a UK representative able to represent its obligations under UK GDPR. Details of this representative should be provided to study participants whose personal data is being processed for the purposes of the research.

---

<sup>7</sup> [EUR-Lex - 62018CJ0311 - EN - EUR-Lex](#)

## **Common Law duty of confidentiality**

In addition to compliance with the Data Protection Act and the GDPR, sponsors should ensure that privacy is respected in accordance with the Human Rights Act 1998 and that they satisfy, and direct their participating NHS/HSC organisations to satisfy the obligation of confidentiality in common law in relation to Confidential Patient Information and other confidential personal information (e.g. relating to research staff and/or non-patient research participants).

## **Definitions**

Confidential Patient Information is defined by section 251 of the NHS Act 2006 as follows

- 1) 'patient information' means
  - a. information (however recorded) which relates to the physical or mental health or condition of an individual, to the diagnosis of his condition or to his care or treatment, and
  - b. information (however recorded) which is to any extent derived, directly or indirectly, from such information, whether or not the identity of the individual in question is ascertainable from the information.
- 2) patient information is 'confidential patient information' where
  - a. the identity of the individual in question is ascertainable
    - i. from that information, or
    - ii. from that information and other information which is in the possession of, or is likely to come into the possession of, the person processing that information, and
  - b. that information was obtained or generated by a person who, in the circumstances, owed an obligation of confidence to that individual.

The 'Care team' is defined (in line with the National Data Guardian's 2013 Information Governance Review). This states that '**direct care is provided by health and social care staff working in 'care teams', which may include doctors, nurses and a wide range of staff on regulated professional registers, including social workers. Care teams may also contain members of staff, who are not registered with a regulatory authority, but who may need access to a proportion of someone's personal data to provide care safely**'. If the person accessing the requested information is not considered to fall within this definition, it is possible that without a legal basis to access identifiable information, disclosure could lead to a breach of confidentiality.

## Data confidentiality and security

The sponsor should clearly explain the flow of data. It should be clear who will access confidential personal information, what information they will be able to access and whether this is covered by clear legal bases under common law at all stages of the research. The sponsor should clarify when data is not, or is no longer, considered confidential patient information as, when it is not, compliance with the common law duty of confidentiality is no longer required.

Under common law, access to confidential patient information by person/s outside of the care team requires the express (explicit) consent of the person/s involved, or another legal basis. Sponsors may exercise this responsibility (for example) by setting out in the protocol, through staff training, or in another suitable place, the arrangements for how members of a usual care team only may access confidential patient information to identify potential participants. It should be made clear by the sponsor (in the protocol, or in another suitable document), what the legal basis is under common law for any access to confidential personal information prior to participants consenting to participate in the study, for example during initial identification of potential study participants.

If the research team will make use of patient or service user records, registries, etc. to identify potential participants then this can be done legally (that is, in line with common law) by fulfilling any of the following criteria

- The researcher gains the explicit consent of every patient with a record in the population pool being assessed
- The search is conducted by a health or social care professional who is a member of the care team , and there is no disclosure of identifiable information to the research team except to a member of the research team who also a member of the care team. (e.g. the care team send out the information and the participant contacts the researcher directly if they wish to receive further information about the research).
- The search makes use of ‘privacy enhancing technologies’ which ensure that there is no access to confidential patient information beyond the treating care team without consent
- Confidential patient information is accessed without consent in line with the requirements detailed below.

It should be noted that an assurance (however binding) of maintaining confidentiality by someone receiving confidential personal information/Personal Data does not provide a legal basis for access/processing, either under common law or Data Protection legislation. Although not itself a legal basis, it would likely be considered an appropriate safeguard. Research participant data needs to be maintained confidentially and securely. Particular consideration should be given to situations where there is a risk of access to sensitive health information (i.e. mental or sexual health) through access to full medical records or where there is a possibility of

identification due to a small dataset, for example because of the rarity of a given condition.

### **Use of confidential patient information without consent**

In certain circumstances, and with the necessary approvals, the common law duty of confidentiality may be set aside (other than in Northern Ireland, where no such mechanism exists), so that confidential patient information may be accessed outside of the care team without the consent of the data subjects or other legal basis (the support provides the legal basis). Common law consent is not required when using data that is not, or is no longer, confidential personal information. In England and Wales researchers may seek support from the Health Research Authority following advice from the Confidentiality Advisory Group (CAG). In Scotland researchers may seek approval from the Public Benefit and Privacy Panel (PBPP) for access to NHS Scotland originated data for research.

In Northern Ireland there is currently no equivalent to CAG or PBPP, therefore consent must be sought. researchers should refer to the Privacy Advisory Committee (Northern Ireland) Code of Practice and seek advice from HSC Trust Data Guardians.

Support from the HRA following CAG advice, PBPP approval or equivalent does not set aside the need to comply with UK GDPR, DPA 2018, or other legislation. There must still be a legal basis under the GDPR and transparency information should be made appropriately available and safeguards implemented.

### **Study-wide considerations**

- Is it clear what personal data participating NHS/HSC organisations will be required to collect, process and disclose during the research study. It is clear at what point data should no longer be considered Personal Data, including the arrangements to render it so and the safeguards to maintain it as such.
- Where the study requires the installation of specific software on NHS systems, or the utilization of hardware additional to standard NHS equipment is it clear what data security safeguards that the sponsor has enacted to ensure that this may be done lawfully and, where applicable, in compliance with NHS/HSC expectations, data protection and confidentiality policies.
- Has the sponsor confirmed that it will act as the data controller for the purposes of the research in line with study wide review expectations? Where the sponsor proposes joint data controllership arrangements are these appropriate considering the nature of the proposed study.
- Is it clear which GDPR Article 6 legal basis the sponsor, as data Controller, is relying on for the purposes of data processing for research purposes?

- Where applicable, is it clear which GDPR Article 9 additional condition the sponsor, as data Controller, is relying on, for the purposes of processing special category Personal Data for research purposes?
- Is it clear how the sponsor, as data controller, will fulfil its responsibilities to afford Data Subjects their rights, which may be limited in a research context, and to meet its own obligations for transparent processing, including providing a mechanism for their exercising of these rights, (for example, by the use of HRA recommended, or otherwise approved, transparency wording in its participant information provided to potential participants and otherwise made available in a layered approach)?
- Has the sponsor confirmed that Personal Data shall only be processed, for the purpose of the study, within usual NHS systems (including electronic systems), with no data leaving these systems prior to being rendered no longer identifiable to the recipient (and hence no longer Personal Data)? Where it is necessary for the purpose of the study for Personal Data to leave NHS systems, has the security and appropriateness of these arrangements for transfer been described and assured?
- Where Personal Data will leave the UK for research purposes has the sponsor explained the GDPR Chapter V basis for such transfer, ensuring that the Personal Data of NHS patients, service users and staff is afforded protections no less than within the UK? Where such protections cannot be guaranteed, the sponsor should ensure that explicit consent is obtained, following presentation to the Data Subject of the potential increased risks associated with the transfer.
- Where applicable has the sponsor appointed a UK representative for the purposes of GDPR able to represent its obligations and have data subjects been provided with contact details for this representative.
- Has the sponsor provided relevant information (for example in the IRAS form, protocol or study contract) to participating NHS/HSC organisations, to enable them to fulfil their responsibilities as data processors in pursuance to GDPR Article 28(2) and Article 30(2)?
- Is the sponsor proposing use of a GDPR Article 28(3) compliant data processing agreement (for example through use of an unmodified model agreement)? Where the sponsor is proposing use of a bespoke or otherwise modified agreement, does that agreement include appropriate contractual safeguards to ensure that Personal Data that is shared is treated in accordance with NHS/HSC expectations and/or that data that has been rendered non-identifiable has appropriate safeguards in place to protect it from re-identification?
- Are any messages to be communicated by electronic or other means, for the purpose of alerting potential participants to the opportunity to engage with the research, non-promotional in nature and hence not direct marketing for the purposes of PECR?

- Has the sponsor confirmed that it will meet its responsibility to ensure, and will instruct its sites so as to ensure (for example through appropriate contractual agreements and/or through the study protocol), that the study does not involve the unlawful disclosure of confidential information without consent at any stage of the research, unless an alternative legal mechanism is in place (for example, for confidential patient information, this might come from CAG support in England and/or Wales, or PBPP support in Scotland, or be provided by virtue of membership of the treating care team).
- Has the sponsor explained how it will ensure the confidentiality and security of personal data at all times during the study, including in publication, taking into account the context in which the data has been collected, for example the increased likelihood if identifiability in the case of rare conditions. Where confidentiality cannot be guaranteed is this explained in the PIS.
- Does the participant information sheet provide additional relevant information to participants, including?
  1. The purposes for which the data are to be processed
  2. What data are to be collected
  3. Who the information will be disclosed to?
  4. Whether any uses or disclosures are optional (in which case suitable clauses should be included in the study consent forms to enable these options to be exercised)
  5. The length of time data will be retained following the end of the study, or the criteria that will be used to determine such period.

#### **Notes/Resources:**

[General Data Protection Regulation](#)

[Data protection law - GOV.UK \(Keeling Schedule\)](#)

[Data Protection Act 2018](#)

#### **Confidentiality: NHS Code of Practice:**

England: [Confidentiality: NHS Code of Practice - GOV.UK](#)

[A Guide to Confidentiality in Health and Social Care - NHS Digital](#)

[A guide to confidentiality in health and social care references:](#)

Scotland: [NHS Code of Practice on Protecting Patient Confidentiality](#)

Wales: [Code of Practice for Health and Social Care in Wales](#)

Northern Ireland: [Code of Practice on Protecting the Confidentiality of Service User Information | Department of Health \(health-ni.gov.uk\)](#)

### **Information Security Management:**

England and Wales: [Information security management NHS code of practice - NHS Digital](#)

Scotland: [Information Governance](#)

Northern Ireland: [Digital Health and Care Northern Ireland - HSCB](#)

### **Records Management:**

[England, Wales and Northern Ireland NHS Code of Practice](#): and [England, Wales and Northern Ireland](#)

Scotland: [Records Management | National Records of Scotland](#)

Northern Ireland: [Good management, good records | Department of Health \(health-ni.gov.uk\)](#)

### **NHS Information Governance – Guidance on Legal and Professional Obligations**

England, Wales and Northern Ireland: [NHS Information Governance - Guidance on Legal and Professional Obligations - NHS Digital](#)

[England & Wales: Section 251 of NHS Act 2006 approval for the use of data without consent through the HRA Confidentiality Advisory Group](#)

Scotland: Approval is sought from the Public Benefit and Privacy Panel for access to NHS Scotland originated data for research: [Public Benefit and Privacy Panel for Health and Social Care](#)

Where access to locally held identifiable data is requested, Boards may expect that Caldicott Guardian approval is sought and obtained.

Northern Ireland:

[Digital Health and Care Northern Ireland - HSCB \(hscni.net\)](#)

[Privacy Advisory Committee \(Northern Ireland\) Code of Practice](#)

## 5.2 CTIMPs – Arrangements for compliance with the Clinical Trials Regulations assessed

### Introduction

The Medicines for Human Use (Clinical Trials) Regulations 2004, as amended, regulate the conduct of clinical trials of investigational medicinal products (CTIMPs) in the UK. The regulations include a number of provisions important to the protection of public health including

- **Good Clinical Practice** – The requirement to conduct all CTIMPs in accordance with the principles of good clinical practice (GCP) helps ensure that all CTIMPs conducted in the UK are to the appropriate high standard and the risks to participants are minimised.
- **Good Manufacturing Practice** – The requirement to manufacture all investigational medicinal products (IMPs) to good manufacturing practice (GMP) standards ensures participants do not receive poor quality or badly prepared medicines.
- **Inspections** – Inspections by the Medicines and Healthcare products Regulatory Agency (MHRA) to check the study follows the principles of GCP and GMP improves the overall quality of CTIMPs conducted in the UK and identifies areas of non-compliance.
- **Protection for incapacitated adults** – There are provisions for the additional protection of adults unable to give informed consent, who should be able to participate in a CTIMP and maybe benefit from an improved condition.
- **Protection for minors** – There are provisions for additional protection of minors (i.e. persons under the age of 16) who may take part in a CTIMP.
- **Pharmacovigilance arrangements** – Investigators and Sponsors together must record safety information and report, to the MHRA, serious unexpected adverse reactions they think the IMP causes.

When considering granting a Clinical Trial Authorisation (CTA), the MHRA assess the information and data relating to both the handling and safety of the IMP. The MHRA does not review the participant information sheet or review the arrangements for the monitoring or pharmacovigilance of the CTIMP (although they check for safety reporting provisions).

When considering giving a favourable opinion, the NHS Research Ethics Committee (REC) reviews the participant information sheet and the overall arrangements for monitoring safety during the study.

Under the regulations the Sponsor has specific responsibilities in relation to the initiation, management and financing (or arranging the financing) of a CTIMP. Study wide reviewers should ensure that the sponsor is clear how it will meet its

responsibilities. The Sponsor may delegate tasks within these responsibilities to third parties or to the research site.

### **Conduct of the CTIMP at participating NHS/HSC organisations**

The study protocol should clearly describe the conduct of the study at participating NHS/HSC organisations. It may be that the study will be conducted differently at different types of participating NHS/HSC organisations, in which case the arrangements of the conduct of the research at each of these 'site types' should be clearly explained. The study agreement should accurately reflect the study design as described in the protocol (and other relevant documents). If the study agreement describes something differently or in addition to the protocol, then clarification should be sought by Study Wide Reviewers from the sponsor.

The Medicines for Human Use (Clinical Trials) Regulations prohibit children under the age of 16 from giving consent to take part in a CTIMP. Young people over 16 are presumed to be capable of giving consent on their own behalf to participate in Clinical Trials of Investigational Medicinal Products (CTIMPs). The study should clearly describe what arrangements will be in place for obtaining consent from participants assented as children upon attaining majority, should they do so whilst still participating in the research.

### **Management of the CTIMP at participating NHS/HSC organisations**

It should be clear to participating NHS/HSC organisations how the study will be managed. This should include details regarding how the study will be monitored, processes for source data verification (including verification of the consent process and participant's consent to take part in the CTIMP), the arrangements for the handling of the IMP and its storage, preparation and dispensing and processes for storage and archiving of trial materials such as documents and samples in a secure manner. Where these arrangements will be different at some NHS/HSC participating organisations as opposed to others this should be clearly stated.

The sponsor should confirm that, in the case of Phase 1 dose escalation studies, 100% source document verification will be used to support the dose escalation decisions. In the event that alternative arrangements are proposed the sponsor should provide a justification of this.

### **Delegation of activities**

The sponsor should clearly state whether any activities described in the protocol will be delegated, either to the participating NHS/HSC organisations or to a third party. These might include central laboratory testing, out-of-hours medical cover for safety issues and/or the specific use of sponsor provided equipment to carry out procedures

### **Witnessed consent**

There is no requirement under The Medicines for Human Use (Clinical Trials) Regulations 2004 for informed consent to be routinely witnessed as the decision whether an individual has been appropriately informed, and is therefore capable of giving informed consent is one that only the individual in question can make. However, the Regulations do make provision for ‘if the person is unable to sign or to mark a document so as to indicate his consent, is given orally in the presence of at least one witness and recorded in writing’. There is no requirement that this witness be impartial, and it may therefore, for example, be a member of the research team (though it should be a different individual to the one actually taking informed consent from the study participant). Witnessed consent can be seen as an important means of increasing inclusivity in clinical trials by enabling those unable to write, but otherwise fully capable of deciding to participate, to take part.

### **Protection for incapacitated adults**

The recruitment of Adults<sup>8</sup> that lack capacity to consent for themselves is governed by the requirements of the Medicines for Human Use (Clinical Trials) Regulations 2004. This is applicable UK wide and supersedes the relevant nation specific legislation applicable in non-CTIMPs.

Phase 1 trials must not include adults unable to consent for themselves, as one of the requirements of Part 5 of Schedule 1 to the Regulations is that there are grounds for expecting that administering the investigational medicinal product will produce a benefit to the subject outweighing the risks or produce no risk at all. (This is considered incompatible with the definition of a Phase 1 trial under the Regulations.)

### **REC Favourable Opinion**

REC favourable opinion should be sought from a REC recognised by UKECA to review CTIMPs of the relevant type. The REC does not also need to be flagged to review studies involving adults lacking capacity/adults with incapacity but is required by Regulation 15(7) of the Clinical Trials Regulations to obtain advice before giving its opinion on any trial involving adults unable to consent for themselves.

Where the trial is to be conducted at one or more sites in Scotland, and the Chief Investigator is professionally based in Scotland (Scotland A REC), it should be allocated to ‘the Ethics Committee’ constituted by Scottish Ministers under the Adults with Incapacity (Scotland) Act 2000 (Scotland A REC).

Only a single ethical opinion is required to cover the whole of the UK (including where this review is undertaken by Scotland A REC).

### **Appointment of Legal Representatives**

---

<sup>8</sup> For the purposes of the Medicines for Human Use (Clinical Trials) Regulations 2004 ‘Adults’ are defined as those aged 18 and over.

A legal representative can be asked to give consent on behalf of an adult who lacks the capacity to do so themselves. The sponsor should explain how they will appoint and provide information to legal representatives. The process for identification of legal representatives should be clearly explained by the sponsor who should ensure that this complies with the requirements of the common law duty of confidentiality.

The legal representative must be

- Told that they are being asked to give consent on behalf of the incapacitated adult,
- Told that they are free to decide whether they wish to make this decision or not, and
- Told that they are being asked to consider what the adult would want, and to set aside their own personal views when making this decision.
- Given sufficient information, in an understandable form, about the trial to ensure that they can make an informed decision.

Those who are able to act as a legal representative in Clinical Trials of Investigational Medicinal Products (CTIMPs), in England, Wales and Northern Ireland are:

- 1) Personal legal representative i.e. a person not connected with the conduct of the trial who is suitable to act as the legal representative by virtue of their relationship with the adult and is available and willing to do so.
- 2) If a personal legal representative is not available then a Professional legal representative i.e. a doctor responsible for the medical treatment of the adult if they are independent of the study, or a person nominated by the healthcare provider may be utilised.

Those who are able to act as a legal representative in Clinical Trials of Investigational Medicinal Products (CTIMPs), in Scotland are:

- 1) Personal legal representative i.e. Adult's Welfare Guardian or Welfare Attorney, or if not appointed: The adult's nearest relative<sup>9</sup>.
- 2) If neither are reasonably contactable the researchers may approach a Professional legal representative i.e. a doctor responsible for the medical treatment of the adult if they are independent of the study, or a person nominated by the healthcare provider.

### **Provision of Information to participants who lack capacity**

---

<sup>9</sup> The term 'nearest relative' is defined in the Mental Health (Scotland) Act 1984. The act provides a hierarchy of relationships. In decreasing order of closeness, these are: Spouse, Child, Father or mother, Brother or sister, Grandparent, Grandchild, Uncle or aunt, nephew, or niece.

Even if they are unable to consent for themselves participants should be provided with information about the study, its risks, and benefits, according to their capacity of understanding. If, at any time the participant expresses a view, in any way (which may not necessarily be verbally) that they do not wish to take part in the research, this view must be acted upon.

## **Emergency Research**

In the UK the law allows adults not able to consent for themselves to be recruited into Clinical Trials of Investigational Medicinal Products (CTIMPs) without prior consent in emergency situations if (in addition to the other requirements of the Medicines for Human Use (Clinical Trials) Regulations:

- 1) Treatment needs to be given urgently, and
- 2) It is also necessary to take urgent action to administer the drug (IMP) for the purposes of the trial, and
- 3) It is not reasonably practicable to obtain consent from a legal representative, and
- 4) The procedure is approved by an NHS Research Ethics Committee, and
- 5) Consent is sought from a legal representative as soon as possible

Should an individual recruited in such a manner die before consent can be sought from a legal representative the sponsor should consider its position in relation to the Common Law duty of Confidentiality. If the research, in an emergency setting, can be considered as only one option (among several) by which care can be provided then the processing of identifiable patient data for the purpose of delivering that care is covered by the legal basis of necessity. The sponsor should consider whether, further processing for research purposes, for example completion of CRF's requires the processing of personal identifiable data, or whether such processing can be conducted using data which is only identifiable to the care team (and otherwise anonymised such that the Common Law duty of Confidentiality no longer applies). Where this is not possible the sponsor should explain what alternative legal basis will be relied upon.

## **Arrangements for compliance with the further requirements of the Medicines for Human Use (Clinical Trials) Regulations 2004 in relation to adults that lack capacity to consent for themselves**

The sponsor should

- 1) State what clinical condition the participants in the trial will have, explain how the proposed trial relates directly to this condition and explain why the trial could not be carried out as effectively if confined to adults capable of giving consent
- 2) Detail the grounds for expecting that administering the medicinal product to be tested in the trial will produce a benefit to the subject outweighing the risks or produce no risk at all.

- 3) Detail the risk threshold and explain how the degree of distress will be defined and constantly monitored.
- 4) Refrain from offering any incentives or financial inducement to the participant or their legal representative, except provision for compensation in the event of injury or loss.

## Protection for minors

The Medicines for Human Use (Clinical Trials) Regulations prohibit children under the age of 16 from giving consent to take part in a CTIMP. The sponsor should be clear what arrangements will be put in place to seek appropriate consent to include individuals under the age of 16 in the trial, where appropriate. Where individuals will reach the age of 16 during the trial the sponsor should explain what arrangements are in place to take consent from these individuals at this time and provide appropriate documentation for this purpose.

## Study-wide considerations

- Has the sponsor explained how the study will be conducted and managed at different participating NHS/HSC organisations, taking into account differences between the activities undertaken at these organisations and the different ‘site types’ participating in the research?
- Has the sponsor explained how the study will be monitored, including whether this will be remote or in person, including details regarding source document verification (which should be 100% in Phase 1 escalation studies), the arrangements for the handling of the IMP and its storage, preparation and dispensing and processes for storage and archiving of trial materials such as documents and samples in a secure manner.
- Has the appropriate study agreement been selected based on the design of the study and does the proposed agreement accurately reflect the study arrangements? If the study agreement describes something differently or in addition to the protocol, then clarification should be provided by the sponsor.
- Where the study proposes to recruit children has the sponsor put appropriate arrangements in place to take consent from the appropriate legal parties (such as parent or legal representative). Where children will reach 16 during the course of the research what arrangements has the sponsor made to obtain consent (if they will still be involved in the study).
- Has the sponsor stated whether any activities will be delegated and are these reflected in the proposed contract arrangements (where applicable)?
- Has the sponsor made appropriate arrangements for witnessed consent (where applicable)? If they have the sponsor should provide an

explanation regarding why this is considered necessary and detail the relevant practical arrangements, including how the impartial witness will be identified (including if this will have any resource implications for participating NHS/HSC organisations) and how will it be known that the potential participant gives their informed consent for the purposes of audit and monitoring purposes.

- In relation to Adults that lack capacity to consent for themselves
  - Has the sponsor made provision for appropriate ethical review (including where review by Scotland A REC is required)? Has the sponsor provided relevant information to facilitate this review, including:
    - Whether the trial be carried out equally effectively if confined to adults capable of giving consent?
    - Whether the trial relates directly to the clinical condition of the participants.
    - What benefit is provision of the IMP is expected to have for the study participants and does the trial involve any foreseeable risk or burden for these participants, or interfere in any way with their freedom of action or privacy?
  - Does the process for the identification of legal representatives comply with the common law duty of confidentiality?
  - Has the sponsor made appropriate arrangements for the provision of information to legal representatives and has appropriate documentation been provided for this purpose?
  - Has the sponsor explained what information will be provided to participants, according to their capacity of understanding? Where the sponsor does not propose to provide any such information an appropriate justification should be provided.
  - Where the sponsor proposes to recruit in an emergency setting has the sponsor
    - Explained why this is necessary
    - Made appropriate arrangements to seek consent from Legal Representatives, or the study participant themselves, as soon as possible.
    - Explained how data will be processed in accordance with the common law duty of confidentiality, particularly in circumstances where the participant dies before consent from a Legal Representative can be obtained.
    - Obtained favourable opinion for the proposed procedures from a recognised REC.

- Has the sponsor made arrangements to offer any incentives or financial inducement to the participant or their legal representative? If so, except in the case of provision for compensation in the event of injury or loss, study wide reviewers should challenge this as such payments are prohibited by the Regulations.
- Does the protocol (or other relevant document) appropriate processes in place for who will make the decision on whether participants have capacity to consent for themselves.

## **Pharmacy Assurance**

Although not required for regulatory purposes HRA Pharmacy assurance is in place to provide a central technical pharmacy review. This is a process to support identified NHS/HSC sites' pharmacy departments to assess whether they can participate in the research by providing information to sites to support their assessment of Capacity and Capability/NHS/HSC permission therefore supporting study set up.

The review is completed by the lead nation. In Scotland and Northern Ireland, the review is completed as part of national SW processes, though in England and Wales it is optional. The aim in England, Northern Ireland and Wales is for the review to start prior to the IRAS submission and for it to be completed by the point of the HRA/HCRW Initial Assessment letter being sent to the applicant, though sometimes the review can still be ongoing after this point. In Scotland the coordinated pharmacy review process is started after the IRAS submission is made.

Reviewers in all nations should record in their UK SW review whether the study is in receipt of a nationally coordinated Pharmacy Assurance or whether it is still going through the process. Pharmacy Assurance does not need to be in place before the SW review is complete.

It is important for SW reviewers to ascertain whether the study is being or has been processed through Pharmacy Assurance so that confirmation of this can be included in the relevant correspondence. In England and Wales this confirmation should be provided to the REC in the Initial Assessment for REC form, as well as to participating NHS organisations in the HRA/HCRW Initial Assessment and Approval letters.

A Pharmacy Assurance flag will be visible in HARP if the study has been or is going through Pharmacy Assurance, and the confirmation of Pharmacy Assurance email will also be uploaded to the study documents. SW reviewers should be aware that it may take up to a day after import of the application into HARP for the Pharmacy Assurance flag and confirmation email to be made available as this is done manually.

Any queries regarding the Pharmacy Assurance can be addressed to the lead nation:

Scotland - [gram.nrspcc@nhs.scot](mailto:gram.nrspcc@nhs.scot)

Northern Ireland - [pharmacytechnicalassurance@hscni.net](mailto:pharmacytechnicalassurance@hscni.net)

England or Wales - [pharmacy.assurance@hra.nhs.uk](mailto:pharmacy.assurance@hra.nhs.uk)

As Pharmacy Assurance is optional in England and Wales, no action needs to be taken if the applicant has not submitted through this route.

## **Notes / Resources**

[The Medicines for Human Use \(Clinical Trials\) Regulations 2004, as amended](#)

[EudraLex - Volume 4 - Good Manufacturing Practice \(GMP\) guidelines | Public Health](#)

[EudraLex - Volume 10 - Clinical trials guidelines | Public Health](#)

[Medicines, medical devices and blood regulation and safety: Clinical trials and investigations - detailed information - GOV.UK](#)

[ICH Topic E 6 \(R2\), Guideline for Good Clinical Practice Section 5.18 - Monitoring](#)

[Consent and Participant information sheet preparation guidance.](#)

[ICH Topic E 6 \(R2\), Guideline for Good Clinical Practice Section 5.14 - Supplying and Handling Investigational Product\(s\)](#)

[Archiving of Documents](#)

[IRAS Help - Preparing & submitting applications - Pharmacy Assurance](#)

[Applying for Pharmacy Assurance - Health Research Authority](#)

## **5.3 Compliance with national legislation regarding Adults unable to consent for themselves in a non-CTIMP**

### **Introduction**

Different national legislation applies across the UK in relation to the inclusion of Adults unable to consent for themselves in research. The main relevant differences in legislation across the UK are detailed below:

<b>England</b>	<b>Scotland</b>	<b>Wales</b>	<b>Northern Ireland</b>
The Mental Capacity Act 2005 applies	The Adults with Incapacity (Scotland) Act 2000 applies	The Mental Capacity Act 2005 applies	The Mental Capacity Act (Northern Ireland) 2016 applies

The Mental Capacity Act 2005 (MCA) provides a comprehensive framework (in England and Wales) for decision making on behalf of adults aged 16 and over who are unable to make decisions for themselves, i.e. they lack capacity. The Act applies to (amongst other things) any intrusive research within England and Wales, wherever it takes place, except for clinical trials of investigational medicinal products.

Different regulatory provisions apply in Scotland and Northern Ireland. In Scotland, the inclusion of adults lacking capacity in research is governed by the provisions of Section 51 of the Adults with Incapacity (Scotland) Act 2000. In Northern Ireland, the inclusion of adults lacking capacity in research is governed by the Section 132 provisions of the Mental Capacity Act (Northern Ireland) 2016. As the acts that apply in Northern Ireland, England and Wales are closely aligned, a scheme of mutual recognition of NHS/HSC research ethics committee (REC) review for research involving adults lacking capacity to consent has been agreed between these three nations.

The study-wide reviewer will be responsible for considering the study according to the national legislation of their nation alone. However, the study-wide reviewer must highlight to the other participating UK nations where there are differences in legislation that will need to be considered.

### **REC Favourable Opinion**

In England, Wales and Northern Ireland approval must be sought from an 'Appropriate body'. To be considered as 'Appropriate body' a REC must be recognised as such by either the Mental Capacity (Research) (Amendment) Regulations (Northern Ireland) 2020 or the Health Research Authority.

In October 2019, the Mental Capacity Act (Northern Ireland) 2016 came into operation. This act is closely aligned with Mental Capacity Act 2005, which applies in England and Wales. This means that a scheme of mutual recognition of NHS/HSC research ethics committee (REC) review for research involving adults lacking capacity to consent has been agreed between these three nations. This means that

for a research project involving adults lacking capacity to consent and with sites in England/Wales and Northern Ireland only requires one NHS/HSC REC review.

In Scotland approval under the Adults with Incapacity (Scotland) Act must be sought from the Scotland A REC.

In the case of studies taking place at participating NHS/HSC organisations in both Scotland and another UK nation an application must be made to both Scotland A REC and another REC recognised for the purpose in either England, Wales or Northern Ireland. The study may commence (assuming all other relevant approvals are in place) once favourable opinion is given by the REC in the relevant jurisdiction (for example the study may commence in Scotland once favourable opinion has been granted by Scotland A REC without waiting for favourable opinion from the other reviewing REC). It should be noted that where a study proposes to recruit Adults Lacking Capacity only in Scotland (or only in England/Wales/Northern Ireland) then only a single REC application is required, which should be made in either Scotland, or England/Wales/Northern Ireland, based on where Adults Lacking Capacity will be recruited.

The Sponsor should provide the following relevant to enable the reviewing REC to consider:

- 1) Whether the research is connected with an impairing condition affecting research participants who are unable to consent, or with the treatment of the condition. An impairing condition means a condition which is attributable to (or causes or contributes to) an impairment or disturbance in the functioning of the mind or brain.
- 2) Whether or not the research could be carried out as effectively if it was confined to research participants able to give consent, i.e. is it necessary to include research participants lacking capacity in order to meet the research objectives?
- 3) The proposed arrangements to identify, consult and provide information to consultees and/or legally appropriate representatives.
- 4) (In the event of recruitment in an emergency setting in England, Wales and Northern Ireland), whether this is justified in the circumstances and whether the research team have appropriate procedures in place to seek consent from a capable research participant (if recovered) or to consult a consultee as soon as practicable after urgent treatment has been provided.
- 5) Whether the research is of potential benefit to research participants lacking capacity without imposing a disproportionate burden, OR, whether the research is intended to provide knowledge of the causes or the treatment or care of the condition affecting participants lacking capacity or of a similar condition, and additionally:

- a. The risk to participants is likely to be negligible<sup>10</sup>
  - b. The research will not significantly interfere with their freedom of action or privacy
  - c. The research will not be unduly invasive or restrictive.
- 6) Whether they are satisfied that arrangements are in place to ensure that
- a. Nothing will be done:
    - i. to which research participants lacking capacity appear to object (unless it is to protect them from harm or reduce/prevent pain or discomfort)
    - ii. which would be contrary to any known advance decision or statement they have made
  - b. If research participants indicate in any way that they wish to be withdrawn from the project, they must be withdrawn without delay, except where this involves stopping treatment and there could be a significant risk to their health.
  - c. The interests of research participants will be assumed to outweigh those of science and society.

### **Provision of advice/consent from consultees/Legal representatives**

The process for identification of, and provision of information to, consultees (in England, Wales and Northern Ireland) and/or Legal representatives (in Scotland) should be clearly explained by the sponsor who should ensure that this complies with the requirements of the common law duty of confidentiality.

The MRC ethics guide ‘Medical research involving adults who cannot consent’ (2007) notes that, whilst incentives or financial inducements should not be used, MRC policy is that, as in other research, payment of legitimate expenses of participants or representatives directly related to participation in the trial is generally considered acceptable.

#### **In England, Wales and Northern Ireland.**

In England, Wales and Northern Ireland advice should be sought from consultees regarding whether an adult lacking capacity to consent would wish to be included in the proposed study. The Mental Capacity Act does not specify a hierarchy. It is a matter of judgment for the researcher, in consultation with the participant’s care team, to identify the most appropriate person. This will normally be the participant’s

---

<sup>10</sup> Minimal risk has been defined by the Council of Europe as a risk that ‘will result, at the most, in a very slight and temporary negative impact on the health of the person concerned’. The Council defines minimal burden on participants as that where it is ‘to be expected that the discomfort will be, at the most, temporary and very slight for the person concerned. ‘Negligible’ is interpreted as equivalent to ‘minimal’. - **MRC ETHICS GUIDE 2007, Medical research involving adults who cannot consent**

usual carer, or another person closely concerned with their welfare. This may or may not be the nearest relative.

Consultees are not asked to give consent on behalf of the adult, but rather to provide an opinion on the views and feelings of the potential participant. The term assent or consent must therefore not be used in any study paperwork in the context of seeking advice from consultees. A consultee may be either a personal consultee (i.e. a person who cares for the adult lacking capacity or is interested in that person's welfare, but is not doing so for remuneration or acting in a professional capacity) or, if no personal consultee is available, a nominated consultee may be approached (i.e. a professional who is independent of the study).

While there is no statutory requirement for the consultee to sign a form, but it is strongly recommended that the researcher uses a Consultee Declaration Form to confirm that the consultee has received the information, has had the opportunity to ask questions and has advised they have no objection to the participation of the person lacking capacity. Where carers will also be recruited as research participants in their own right, the information sheet should distinguish clearly between the two roles and the carer should sign a consent form separate from the consultee declaration sheet.

Where the study is happening in Northern Ireland, England and/or Wales both Acts should be referenced in the study paperwork and 'For use in England, Wales and Northern Ireland' should be made clear in relevant study paperwork, e.g. protocol, Consultee information sheet, Consultee Declaration form, etc. Where the study is happening in Northern Ireland only, the Mental Capacity Act (Northern Ireland) 2016 should be referenced in the study paper work and 'For use in Northern Ireland' should be made clear in relevant study paperwork, e.g. protocol, Consultee information sheet, Consultee Declaration form, etc.

Where the sponsor significantly amends the study protocol, or otherwise plans to obtain further consent from participants then advice must be sought from consultees on behalf of any adults who have lost capacity.

Consultees must be

- Told that they are being asked to advise on the views and feelings they believe the adult would have towards participation in the research.
- Told that they are free to decide whether they wish to provide this advice or not.
- Given sufficient information, in an understandable form, about the research to ensure that they can provide informed advice.

## In Scotland

In Scotland a legal representative must asked to give consent on behalf of an adult who lacks the capacity to do so themselves. Those who are able to act as a legal representative in research other than Clinical Trials of Investigational Medicinal Products (i.e. non-CTIMPs), in Scotland are

- Adult's Welfare Guardian or Welfare Attorney,
- The adult's nearest relative (as defined by the Adults with Incapacity (Scotland) Act)<sup>11</sup> (if an Adult's Welfare Guardian or Welfare Attorney has not been appointed)

The legal representative must be

- Told that they are being asked to give consent on behalf of the incapacitated adult,
- Told that they are free to decide whether they wish to make this decision or not, and
- Told that they are being asked to consider what the adult would want, and to set aside their own personal views when making this decision.
- Given sufficient information, in an understandable form, about the trial to ensure that they can make an informed decision.

### **Provision of Information to participants who lack capacity**

Even if they are unable to consent for themselves participants should be provided with information about the study, its risks, and benefits, according to their capacity of understanding. Nothing may be done to which a participant appears to object (whether by showing signs of resistance or otherwise) except where what is being done is intended to protect him from harm or to reduce or prevent pain or discomfort. If, at any time the participant expresses a view, in any way (which may not necessarily be verbally) that they do not wish to take part in the research, this view must be acted upon.

### **Participants regaining capacity during the study**

If it is considered likely that adult participants might regain capacity during the course of the research the sponsor should plan for how they will be involved in the ongoing consent process. In most cases it will be most appropriate to provide information on what has happened while they lacked capacity and to ask them to consent to their continued participation in the research (including giving them the option to withdraw themselves and their previously collected data from the research). The research team should

- Inform the legal representative (in Scotland) or consultee in (England/Wales and Northern Ireland) of this possibility at the outset and

---

<sup>11</sup> The Adults with Incapacity (Scotland) Act uses the hierarchy of relationships defined in the Mental Health (Scotland) Act 1984 as the definition of nearest relative. In decreasing order of closeness, these are: Spouse, Child, Father or mother, Brother or sister, Grandparent, Grandchild, Uncle or aunt, Nephew or niece.

explain what processes you will follow in the event of a participant regaining the capacity to consent.

- Provide an appropriate Participant Information Sheet and consent form for participants that explains what has happened to date and what consent is now sought for
- Plan for how a situation where a participant withdraws consent will be handled.

## **Participants that lose capacity during participation in research**

### **In England and Wales**

A core principle of the Mental Capacity Act 2005 is that capacity should be assumed unless established otherwise. If a participant has consented to take part, it may generally be assumed that capacity remains in place, but the researcher should be alert to any changes suggesting that capacity has been lost. Where it is considered likely that consent will be lost during the course of the research the sponsor should explain what monitoring arrangements they will put in place.

Where consent is established to have been lost, and it is the intention of the research team that the participant would remain in the study and would be required by the protocol to undergo further interventions and procedures that constitute 'intrusive research' then approval by a recognised REC should be sought and advice should from consultees obtained (following the processes detailed above).

Where consent has been obtained prior to loss of capacity and the participant gave specific consent to use previously collected samples and data following loss of capacity, these may be retained in identifiable form if this is necessary for the research.

In situations where the potential for losing capacity was discussed as part of the original consent then advice from consultees is still required when considering whether to continue to involve the relevant participating in the study. The original consent given by participants should not automatically be considered absolute (though consultees would be expected to give regard to it) and the current circumstances of the participant must be considered.

### **In Scotland**

Legally there is no specific provision for adults who lose capacity while taking part in non-CTIMPs in Scotland. Therefore, in most circumstances the original consent should be respected. However, a request by a legal representative to withdraw someone from a study after they have lost capacity, should be considered carefully to ensure that it reflects the wishes of the person before they lost capacity, and that their current situation is fully considered, including possible benefits and harms that might arise as a consequence of their continued participation.

Where the sponsor significantly amends the study protocol, or otherwise plans to obtain further consent from participants then advice must be sought from consultees on behalf of any adults who have lost capacity.

## In Northern Ireland

In Northern Ireland consent taken prior to loss of capacity remains legally valid after loss of capacity provided the research protocol has not changed significantly. Where loss of capacity during the study is considered a significant risk, and the researchers plan to continue to involve participants in the study this should be considered during the initial consent discussions and options for the future provided to participants.

## Emergency Research

### In England, Wales and Northern Ireland

In England, Wales and Northern Ireland the law allows adults not able to consent for themselves to be recruited without prior advice from a consultee if:

1. Treatment needs to be given urgently, and
2. It is not reasonably practicable to seek advice from a consultee, and
3. The procedure is approved by a recognised REC, and
4. A consultee is consulted as soon as possible to seek advice on the participant's likely views and feelings.

If adults recruited in such a manner regain their capacity to consent, then the provisions provided above should be followed. Should an individual recruited in such a manner die before advice can be sought from a consultee the sponsor should consider its position in relation to the Common Law duty of Confidentiality. If the research, in an emergency setting, can be considered as only option (among several) by which care can be provided then the processing of identifiable patient data for the purpose of delivering that care is covered by the legal basis of necessity. The sponsor should consider whether, further processing for research purposes, for example completion of CRF's requires the processing of personal identifiable data, or whether such processing can be conducted using data which is only identifiable to the care team (and otherwise anonymised such that the Common Law duty of Confidentiality no longer applies). Where this is not possible the sponsor should explain what alternative legal basis will be relied upon.

## In Scotland

In Scotland the law does not provide any 'exemptions' or alternatives for the involvement of adults not able to consent for themselves in non-CTIMP research, even in emergency situations. Therefore, appropriate consent must be sought, as detailed above, before an adult can be involved in the research.

## **Assessment of capacity**

Study wide review should ascertain that protocol has appropriate processes in place for who will make the decision on whether participants have capacity to consent for themselves. The protocol should detail whether the PI will themselves make this assessment or whether this will be delegated to members of their research team. In England and Wales The Mental Capacity Act Code of Practice<sup>12</sup> states that ‘The person who assesses an individual’s capacity to make a decision will usually be the person who is directly concerned with the individual at the time the decision needs to be made’. the assessor ‘must have a ‘reasonable belief’ that the person lacks capacity to agree to the action or decision to be taken’ but there are no specific requirements that assessor be trained or qualified in any specific respect. Rather, when making their assessment, the assessor should take account of the Code of Practice suggestions regarding the factors that should be taken into account, and how these factors might be considered.

## **Study wide considerations**

- Has the sponsor made provision for appropriate ethical review, considering the UK nations in which the study will take place?
- Has relevant information been provided by the sponsor to enable the REC to effectively and appropriately review the study?
- Does the process for the identification of legal representatives and/or consultees comply with the common law duty of confidentiality?
- Has the sponsor made appropriate arrangements for the provision of information to consultees (in England, Wales and Northern Ireland), and/or legal representatives (in Scotland) and has appropriate documentation been provided for this purpose?
- Has the sponsor explained what information will be provided to participants, according to their capacity of understanding? Where the sponsor does not propose to provide any such information an appropriate justification should be provided.
- Has the sponsor made arrangements to offer any incentives or financial inducement to the participant or their legal representative? If so, except in the case of provision for compensation in the event of injury or loss. study wide reviewers should challenge this as such payments are discouraged, except where explicitly approved by the REC.

---

<sup>12</sup> [Mental Capacity Act Code of Practice - GOV.UK](#)

- Has the sponsor made appropriate arrangements for how a situation where an adult participant regains capacity will be handled (if applicable)?
- Where applicable has the sponsor made appropriate, nation specific, arrangements for how they will address a situation where a participant, who previously provided consent to participate in the research, loses capacity to consent for themselves, including with respect to the provision of relevant documentation.
- Has the sponsor made arrangements if they plan to obtain further consent from participants, to seek further advice from consultees (in England, Wales and Northern Ireland) or Legal representatives (in Scotland) on behalf of any adults who have lost capacity?
- Where the sponsor proposes to recruit in an emergency setting
  - (in England, Wales and Northern Ireland) has the sponsor
    - Explained why this is necessary
    - Sought review from a REC recognised as an 'Appropriate Body'.
    - Made appropriate arrangements to seek advice from consultees as soon as possible following the emergency.
    - Explained how data will be processed in accordance with the common law duty of confidentiality, particularly in circumstances where the participant dies before consultee advice can be obtained.
  - In Scotland has the sponsor explained how consent will be sought from legal representatives before commencing research procedures.

## Notes/Resources

- [Mental Capacity Act 2005](#)
- [Mental Capacity Act Code of Practice - GOV.UK](#)
- [Adults with Incapacity \(Scotland\) Act 2000](#)

## 5.4 Compliance with national legislation regarding Human Tissue

### Introduction

Different national legislation applies across the UK in relation to the arrangements for the use of Human Tissue in research. The main relevant differences in legislation across the UK are detailed below:

England	Scotland	Wales	Northern Ireland
The Human Tissue Act 2004 applies	The Human Tissue (Scotland) Act 2006 applies to tissue from the deceased. The HTA's remit in relation to research does not extend to Scotland except in the case of DNA	The Human Tissue Act 2004 applies	The Human Tissue Act 2004 applies

The Human Tissue Act 2004 sets out a legal framework for regulating the storage and use of human tissue from the living, and removal, storage and use of human tissue from the deceased, for purposes including 'research in connection with disorders, or the functioning, of the human body'. Where biological material is to be rendered acellular (and is thereby no longer considered to be relevant material for the purposes of the Human Tissue Act), it should be clear when and where this will occur.

The Human Tissue (Scotland) Act 2006 sets out provisions for the removal, retention and use of 'organs, tissue and tissue samples' from the deceased, i.e. body parts or bodily fluids (including any derivative of skin) removed post mortem, and subsequently used for research. It does not regulate the use of tissue from the living for research.

The study-wide reviewer will be responsible for considering the study according to the national legislation of their nation alone. However, the study-wide reviewer must highlight to the other participating UK nations where there are differences in legislation that will need to be considered. Study wide reviewers should be clear, when considering the arrangements for collection and use of human tissue, how information governance requirements and expectations will be met (e.g. how and when will biological material be pseudonymised or anonymised?) (see section 5.1 for further details).

### Consent

Consent (or Authorisation) is a fundamental principle of both the Human Tissue Act 2004 and the Human Tissue (Scotland) Act 2006. Please see sections 2.1 and 5.1 for further details regarding the requirements for the purposes of obtaining this.

Consent can be specific to the project itself, or more generic to include storage and future use. If the sponsor is seeking generic consent then they should consider how much information should be provided to potential participants to help them understand the scope of future use and what this might mean for them balancing the need to

ensure informed consent with the uncertainty of what research requirements may arise in the future.

It should be made clear at the outset, when consent, or authorisation is being sought, that it can be withdrawn at any time. The practical implications of withdrawing consent should be discussed to help participants, or their representatives, understand what is realistic in terms of withdrawal and to manage expectations.

### In England, Wales and Northern Ireland

Consent is always required under common law to remove biological material from a human and is legally required to store and use ‘relevant material’ from the living or deceased for a ‘scheduled purpose’ such as research (unless one of the exemptions below applies). Relevant material is defined as ‘material, other than gametes, which consists of or includes human cells’ and a full list of the materials considered to be ‘relevant’ is provided by the HTA<sup>13</sup>.

In relation to the living consent should be obtained from the person concerned, assuming they have the capacity to consent for themselves. Where they do not then, where tissues are being used as part of a clinical trial of an investigational medicinal product (CTIMP), the UK Medicines for Human Use (Clinical Trials) Regulations 2004 apply (see section 5.2 for details). Where the tissue will be used in non-CTIMP research, in England and Wales, the Mental Capacity Act 2005 applies and in Northern Ireland the Mental Capacity Act (Northern Ireland) 2016 applies (see section 5.3 for details).

In relation to children, if a child is considered competent, then consent should be sought from the child. If a child is not competent, or not willing to make a decision, consent should be obtained from a person with parental responsibility. Even when a child is competent to consent, it is good practice to consult those with parental responsibility and involve them in the process of the child making the decision. Where tissues are being used as part of a CTIMP a child (under 16) cannot legally provide consent for themselves and consent should be sought from a person with parental responsibility.

‘Appropriate consent’ is required to obtain relevant material from the deceased (unless the person died more than 100 years ago). Appropriate consent means

- The consent of the deceased person given before death,
- If there was no prior consent by the deceased person, the consent of a nominated representative,

---

<sup>13</sup> [Relevant material under the Human Tissue Act 2004 | Human Tissue Authority](#)

- If no representative was appointed, a person in a ‘qualifying relationship’<sup>14</sup>
- For a deceased child, the person who had parental responsibility immediately prior to the child’s death or another person in a qualifying relationship

## In Scotland

In terms of research, the Human Tissue (Scotland) Act 2006 does not regulate the use of tissue from the living for research. Instead this is governed by the requirements of the common law, NHS Research Scotland Human Tissue Accreditation Scheme, and other related legislation (such as the Adults with Incapacity Act 2000). Informed consent is legally required for research if the tissue is from a living person and the samples are identifiable (or are anonymised but there is no approval from a Research Ethics Committee).

The Human Tissue (Scotland) Act 2006 does set out provisions for the removal, retention and use of ‘organs, tissue and tissue samples’ from the deceased, i.e. body parts or bodily fluids (including any derivative of skin) removed post mortem, and subsequently used for research. Authorisation is legally required for research if the issue is collected after 01 September 2006 (for both anonymous and identifiable samples). Authorisation can be provided by individuals themselves before death, a ‘nominee’<sup>15</sup> or ‘nearest relative’ (in order of priority)<sup>16</sup>. It should be noted that a Welfare Attorney or Welfare Guardian cannot give authorisation on behalf of an incapacitated adult for activities post-mortem unless they are a ‘nominee’ or a ‘nearest relative’ of the deceased.

In relation to the collection of tissue from children after death authorisation should be provided by

- For a child 12 years of age and over
  - Themselves before death if deemed competent or, if not deemed competent, a person with parental rights and responsibilities.
  - After death a ‘nominee’ or person with parental responsibility
- For a child under 12 years of age
  - A person with parental rights and responsibilities only

---

<sup>14</sup> Please see HTA Code of Practise A for details, at [Public guides to the HTA Codes of Practice | Human Tissue Authority](#)

<sup>15</sup> A person (aged 12 and over) can, before death, nominate a person or persons to represent them after their death. Nominees can authorise post-mortem examination and the removal/retention of organs or tissues for research.

<sup>16</sup> Further information on the order of priority can be found at [Regulatory Support Centre Summary Of Legal Requirements For Research With Human Tissues In Scotland](#)

Material is exempted from the requirements of the Act and can legally be used for research without Authorisation if it is an existing sample, obtained before 01 September 2006, (including any identifiable or anonymous material from the living or deceased).

#### Collection of Human Tissue from Adults unable to Consent for themselves

Where the study will involve the collection of tissue samples from adults that are unable to consent for themselves the sponsor should ensure that arrangements are in place to follow the provisions the relevant, nation specific legislation.

#### In CTIMPs

In CTIMPs, in accordance with the Medicines for Human Use Act 2004, which apply UK wide, a Legal Representative should be appointed who will be asked to provide consent on behalf of the individual be recruited. This consent fulfils the consent requirements of the nation specific Human Tissue legislation. Please see section 5.2 for further details.

#### In non-CTIMPs

In Scotland, the Adults with Incapacity (Scotland) Act 2000 allows legal representative to give consent on behalf of an adult who lacks the capacity to do so. This consent fulfils the consent requirements of the nation specific Human Tissue legislation.

In England, Wales and Northern Ireland, The Human Tissue Act 2004 (Persons who Lack Capacity to Consent and Transplants) Regulations 2006, provides for this situation. This Regulation provides that where activities which fall under the Human Tissue Act 2004 are being undertaken with adults lack the capacity to consent, the Mental Capacity Act 2005, and therefore advice should be sought from consultees.

Please see section 5.3 for further details.

#### Consent exemptions

Consent is required to use and store relevant material for research, unless one of the following legal exemptions applies

- The relevant material is classed as an existing holding i.e. held prior to 1st September 2006.
- The relevant material is imported
- The relevant material has been taken from a living person AND the researcher is not able to identify the person AND the research project is ethically approved by an NHS REC
- The relevant material is to be received from an HTA-licensed RTB with generic ethical approval from recognised REC and the biological samples are **non-identifiable** to the researcher

- The relevant material is from a person who died more than 100 years ago.

The sponsor should state whether they intend to obtain consent for the use of relevant material for research purposes and, where they do not, provide a justification explaining why this is not required. It should be noted that the HTA code of practice on research confirms that Although there are legal exemptions from the need for consent under the HT Act ('consent exceptions'), it is good practice to obtain consent wherever it is practical to do so, considering ethical issues such as the feasibility of identifying and re contacting tissue donors, any distress that may be caused through reminding donors/relatives of serious illness or injury and any potential health related findings that the research may uncover for the donor. For existing holdings, it is good practice to consider the ethical issues involved in their potential use, balancing this against the issues involved in obtaining new samples. For imported tissues it is good practice to get assurance that samples have been obtained with valid consent in the country of origin.

## DNA Analysis

Under Section 45 of the Human Tissue Act it is an offence to hold 'bodily material' with the intent to analyse its DNA and use the results for research without 'qualifying consent.' This guidance also applies to RNA analysis when used to provide information about DNA for research). There are some exceptions when obtaining consent is not practicable. Unlike the rest of the Human Tissue Act, Section 45 applies across the whole of the UK, including in Scotland.

The term 'qualifying consent' is only used within Section 45 of the HT Act. In practice, obtaining qualifying consent is fundamentally the same as obtaining any other consent for research except that

- In relation to deceased adults if the deceased has appointed a 'nominated representative' then their consent will only be valid for DNA analysis if that person was also in a 'qualifying relationship' with the deceased (as there is no provision for consent provided by a nominated representative under Section 45 of the HT Act).

The HTA Code of practice on Research states that if consent for research has previously been obtained and it is later decided to include DNA analysis in the research, as long as the consent does not rule-out DNA analysis, then the original consent will suffice as 'qualifying' consent for use in England, Wales and Northern Ireland. However, where the sponsor knows, when seeking consent, that they intend to conduct DNA analysis, then the HTA expects this to be made clear to donors during the consent process.

## Licencing requirements

### In England, Wales, and Northern Ireland

Under the Human Tissue Act 2004, a license is required to store 'relevant material' for research in connection with disorders, or the functioning of, the human body

(unless an exemption applies). The HTA additionally license premises, such as Research Tissue Banks, which store tissue from the living and deceased for research. The HTA expects licensed establishments to meet the HTA's Research Standards<sup>17</sup>. The HT Act requires that removal of tissue from the deceased for research within the scope of the HT Act must always take place under the authority of an HTA license. In other words, the specific removal premises must be licensed and a Designated Individual (DI) will be responsible for the removal activity.

A list of licensed research establishments is given on the HTA's website; [Find an establishment | Human Tissue Authority](#)

A license is required to store relevant material from the living or deceased for research in connection with disorders or the functioning of the human body unless:

- It is for a specific project approved, or pending approval, by a Research Ethics Committee or where storage after a specific project is deemed essential as a record of the completed research project, for example to verify or quality check the research data. Storage for this purpose without an HTA License should be for a defined period as set out in the protocol and should be for no longer than 12 months. For studies involving human tissue, the analysis of the samples should be undertaken as part of the data collection before the end of study is declared.
- Storage is incidental to transportation
- It is stored with the intent to render the sample acellular
- It is obtained from an HTA-licensed research tissue bank
- (in relation to the deceased) It is from a person who died prior to 01 September 2006 and at least 100 years have elapsed since their death

The sponsor should be clear on its arrangements for obtaining relevant licenses (where applicable). For studies involving human tissue, the analysis of the samples should be undertaken as part of the data collection before the end of study is declared. If researchers wish to store tissue for other purposes, for example for future research, or for longer than 12 months the tissue should be transferred to an existing licensed research establishment.

## In Scotland

The storage of tissue within Scotland does not require licencing. On behalf of the Chief Scientist Office, NHS Research Scotland carry out the Scottish Human Tissue Accreditation Scheme for the collection and storage of tissue under the guardianship of NHS Scotland Research Tissue Banks / Biorepositories based on criteria that are

---

<sup>17</sup> [Research and the Human Tissue Act 2004 Licensing](#)

equivalent to the standards expected within the UK. Sponsor & NHS REC delegate approval to their nodal biorepositories so that at the end of a study if there is surplus tissue this will either be stored within the NRS Biorepository or can registered with the nodal biorepository who will ensure that this tissue meets accreditation standards.

## **Import and export of human tissue**

### **In England, Wales and Northern Ireland**

The Human Tissue Act 2004 covers the import and export of relevant material to and from England, Wales and Northern Ireland. When ‘relevant material’ is coming into England, Wales or Northern Ireland from Scotland it is considered an import and vice versa an export.

Although consent is a fundamental principle of the HT Act, the consent provisions do not apply to imported material. However it is good practice to gain assurance that consent has been obtained in the source country and, where it has not been, the sponsor should provide a justification for this including (where applicable) assurance that appropriate ethical approval, or equivalent, has been obtained in the host country which will judge ethical acceptance of the research in line with local customs and traditions. MRC provides guidance on the considerations for low and middle income countries<sup>18</sup> and the UK REC may wish to take a view when reviewing the study before issuing a favourable opinion for the research to be conducted in the UK.

Relevant material must not be imported and exported solely to avoid the consent requirements.

Where relevant material will be imported then the sponsor should put in place a Material Transfer Agreement to provide assurances to the importer that this tissue has been collected in line with local legal requirements.

Following the withdrawal of the UK from the European Union the implementation of the Northern Ireland Protocol has had an impact on the import and export of Human Tissue to and from Northern Ireland. If the sponsor anticipates that this will be required as a part of the research protocol, then they should seek advice from the Human Tissue Authority<sup>19</sup> and the Northern Ireland Coordinating Centre.

### **In Scotland**

Similar standards are expected for the import and export of human tissue into/out of Scotland. Where this is anticipated advice should be sought from the Scottish National Coordinating Centre and/or the relevant Biorepository. An NHS National

---

<sup>18</sup> [Management of global health trials: MRC guidelines – UKRI](#)

<sup>19</sup> Guidance from the Human Tissue Authority can be found at [UK Transition guidance | Human Tissue Authority](#).

Research Scotland Material Transfer Agreement should be in place for all tissue involving a designated Biorepository. There are three available material transfer agreements. These are for

1. Material only,
2. Consented tissue and associated data
3. Unconsented tissue and associated data

The sponsor should ensure that they execute the correct agreement depending on their proposed study arrangements. Study wide reviewers should be clear on the proposed arrangements and should seek clarification from the sponsor if required.

### **Analysis of samples**

The sponsor should be clear what arrangements have been made for the analysis of samples and clarify how this information will be provided to participating NHS/HSC organisations to enable them to understand their responsibilities (usually in the study protocol or another related document, such as a laboratory manual). It should be noted that there is no requirement that a laboratory manual be provided for the purposes of study wide review as, at that time, it may not have been written

The main analysis of the samples for the purposes of answering the research question should be undertaken as part of the data collection before the end of study is declared. Study wide reviewers should ensure that relevant information will be provided to participating NHS/HSC organisations to enable them to understand their responsibilities. Such information should include

1. If samples will be analysed locally then the sponsor should explain to participating NHS/HSC organisations whether, and if so in what respects, this differs from standard of care arrangements.
2. If samples will be transferred to a central lab then the sponsor should explain the arrangements for such transfer including whether the sponsor or the participating NHS/HSC organisation will be responsible for arranging the courier to transport the samples and whether a separate Material Transfer Agreement is required.

Where the sponsor considers that the analysis of samples may produce potential health related findings the provisions in section 2.1 should be referred to and relevant information provided.

### **Storage arrangements for samples (where applicable)**

The sponsor should be clear whether any samples will be stored during or after the research study and whether such storage will take place locally at the participating NHS/HSC organisation or at a central facility. It should be clear how long samples will be stored for, whether they will be stored in an identifiable or anonymised format, for what purposes they will be stored, and what will happen to the samples at the end of this time. Study wide reviewers should ensure that it is clear how this information will be provided to participating NHS/HSC organisations to enable them

to understand their responsibilities and confirm that relevant information regarding retention is included in the Participant Information Sheet(s).

### **Disposal arrangements for samples**

The sponsor should explain their arrangements for the handling of Human Tissue following the end of the study.

Before disposing of human tissue, the sponsor should consider options for maximising use, in line with donors' expectations. Where the sponsor proposed to destroy samples, rather than retain them for use in future research a justification should be provided, particularly in the case of rare or potentially valuable samples or samples obtained from pre-existing collections, such as pathology departments.

Where biological material has been transported outside of the participating organisation, it should be clear whether and how the biological material will be returned, retained or destroyed and the agreement/arrangements (e.g. model agreement material transfer clauses) for this.

There will be times when disposal is the most appropriate option i.e. following the terms of consent or where samples are no longer fit for purpose. In this case study wide reviewers should ensure that the sponsor has explained the arrangements for sample destruction, including when and how the samples will be destroyed and how this destruction will be recorded in line with the HTA codes of practise and MRC guidance<sup>20</sup>, including how samples will be handled for destruction in a sensitive and respectful manner (particularly in relation to the destruction of samples from the deceased). Within Scotland the NRS Biorepositories can help to support researchers and sponsors in the disposal of tissue whilst providing relevant policies and documentation.

The sponsor should explain how they will manage a situation where a donor revokes consent for use of their samples (may be some/all) for research and requests destruction including how the sponsor/central facilities will be made aware of this request if the samples have already been shipped and when this will not be possible (i.e. if samples have been fully anonymised).

### **Study-wide considerations**

- It should be clear what Human Biological materials the study will make use of and whether any collection or analysis of such material is optional.
- It should be clear, of the Human Biological materials to be collected, what is 'relevant material' and what is not. In relation to relevant material

---

<sup>20</sup> [Research and the Human Tissue Act 2004 - Disposal](#)

it should be clear at what point that will be rendered a-cellular (if applicable).

- Has the sponsor explained, and detailed in the PIS, how information governance requirements and expectations will be met in relation to any data associated with human tissue samples (e.g. if, and if so how and when biological material will be pseudonymised or anonymised?)
- Has the sponsor described, and detailed in the PIS, their arrangements for ensuring informed consent is in place for the purposes of the collection, storage and use of new, or existing, Human Tissue samples from the living, as appropriate, and do these comply with the relevant national legislative requirements?
- Has the sponsor described, and detailed in the PIS, their arrangements for ensuring informed consent (or Authorisation) is in place, as appropriate, for the purposes of the collection, storage and use, of new, or existing, tissue samples from the deceased as appropriate, and do these comply with the relevant national legislative requirements.
- Has the sponsor explained how they will manage a situation where a donor revokes consent for use of their samples (may be some/all) for research and requests destruction including how the sponsor/central facilities will be made aware of this request if the samples have already been shipped and when this will not be possible (i.e. if samples have been fully anonymised). Has relevant information been provided in the PIS regarding the participants right to withdraw their consent and samples from the study (including where any limitations may apply to this)?
- Where the sponsor is seeking generic consent for future storage and use of samples have they provided appropriate information in the PIS to potential participants to help them understand the scope of future use and what this might mean for them balancing the need to ensure informed consent with the uncertainty of what research requirements may arise in the future.
- Has the sponsor made arrangements to comply with the relevant licencing requirements of the Human Tissue Act, and/or, in Scotland, made arrangements to transfer any surplus tissue to an NHS Scotland Research Tissue Banks / Biorepositories at the end of the study?
- Where tissue will be imported and exported (including between Scotland and the rest of the UK)
  - Has the sponsor clarified whether consent will be sought in the source country and, where it not be, has the sponsor provided an appropriate justification for this?
  - Has the sponsor put in place appropriate contractual arrangements will be in place to cover this activity?

- Where the study will involve DNA analysis (RNA analysis when used to provide information about DNA for research) has the sponsor made arrangements to obtain appropriate 'qualifying consent' and has this intended analysis been detailed in the PIS.
- Has the sponsor confirmed what arrangements have been made for the analysis of samples and clarified how this information will be provided to participating NHS/HSC organisations to enable them to understand their responsibilities?
- Has the sponsor confirmed, and detailed in the PIS, what arrangements have been made for the storage of samples following the end of the study and clarified how relevant information will be provided to participating NHS/HSC organisations to enable them to understand their responsibilities?
- Has the sponsor confirmed, and detailed in the PIS, what arrangements have been made for the handling of Human Tissue following the end of the study in relation to, as applicable, retention for use in future research, return of material to the original holders and disposal in accordance with the HTA code of practise.

## Notes/Resources

[Human tissue - Research - Medical Research Council](#)

[Use of human tissue in research - Health Research Authority](#)

[Research tissue banks and research databases - Health Research Authority](#)

[Human Tissue Act 2004](#)

[Human Tissue \(Scotland\) Act 2006](#)

[The Human Tissue Act 2004 \(Persons who Lack Capacity to Consent and Transplants\) Regulations 2006](#)

## **5.5 Compliance with any other applicable laws or regulations**

### **Introduction**

There are other legislative requirements to which research must adhere and some key differences in research related legislation across the UK.

The study-wide reviewer will be responsible for considering the study according to the national legislation of their nation alone. However, the study-wide reviewer must highlight to the other participating UK nations where there are differences in legislation that will need to be considered.

### **The Ionising Radiation (Medical Exposure) Regulations 2017 and the Ionising Radiation (Medical Exposure) Regulations (Northern Ireland) 2018 (both referred to as IRMER)**

The regulations state that 'A person must not carry out an exposure unless [...] in the case of an exposure taking place in the course of a research programme under regulation 3(c), that programme has been approved by an ethics committee' (IRMER 11, 1 (d)). There is guidance in the IRAS website which describes when an exposure is considered a [research exposure](#) under the legislation and therefore requires REC review.

To support review by REC of research studies involving research exposures (see '1.1 IRAS Application Completed Correctly') the IRAS form includes a review by MPE(s) and CRE(s) (when the project filter is completed correctly). The information in the IRAS MPE and CRE review also supports site capacity and capability.

There is a UK-wide policy expectation that MPE and CRE review is completed in the IRAS form where a study involves research exposures. Radiation Assurance is a UK-wide process for studies taking place in the NHS/HSC which supports consistent and reliable MPE and CRE reviews being provided to the relevant regulatory bodies and sites (the assurance includes assessing that the risk statements given in the PIS are appropriate). It is expected that applicants of studies taking place in the NHS/HSC seek MPE and CRE review through Radiation Assurance to support regulatory reviews and site activities.

The regulations also give further requirements for regulatory review for research programmes involving the administration of radioactive substances (see section 6.4).

- Has the sponsor correctly identified that the study involves radiation exposures and, if it does, have they sought appropriate review from MPE(s) and CRE(s) and has this been recorded in the IRAS application form? It is the sponsor's responsibility to decide whether a study involves research exposures, taking into consideration the legislation and guidance available by study wide review functions may seek justification from the sponsor of their decisions where this is unclear.

- Where MPE(s) and CRE(s) review has been obtained through the radiation Assurance process SW review functions should undertake the following. Where Radiation Assurance has not been provided but MPE and CRE review is available in the IRAS form, no further action needs to be taken.
  - Ensure that this is accurately recorded in HARP (a yellow flag with a black border and black text will be enabled)
  - State, in the SW review that MPE and CRE review was provided through Radiation Assurance and (in England and Wales) detail this in the initial assessment for REC and HRA/HCRW Initial Assessment and Approval letters.

### **Compliance with the Provisions of the Welsh Language Act 1993 (Studies with participating NHS organisations in Wales only)**

If the study team anticipate in advance that study participants will require information in Welsh or any other language, they should make provision for translation as part of the initial arrangements for study set up. They should also be prepared for potential research participants to request patient facing documentation in Welsh and English and make the necessary arrangements to support the request. Therefore, all necessary measures should be taken to provide the translation of written information and interpretation of patient information on request from a patient or carer.

It is highly recommended that researchers seek advice from their local NHS R&D office(s) about the language requirements of the local population and the Welsh language policies in place at the site.

### **Study-wide considerations**

- Has the sponsor correctly identified that the study involves radiation exposures and, if it does, have they sought appropriate review from MPE(s) and CRE(s) and has this been recorded in the IRAS application form? It is the sponsor's responsibility to decide whether a study involves research exposures, taking into consideration the legislation and guidance available by study wide review functions may seek justification from the sponsor of their decisions where this is unclear.
- Where MPE(s) and CRE(s) review has been obtained through the radiation Assurance process SW review functions should undertake the following. Where Radiation Assurance has not been provided but MPE and CRE review is available in the IRAS form, no further action needs to be taken.
  - Ensure that this is accurately recorded in HARP (a yellow flag with a black border and black text will be enabled)
  - State, in the SW review that MPE and CRE review was provided through Radiation Assurance and (in England and Wales) detail this

in the initial assessment for REC and HRA/HCRW Initial Assessment and Approval letters.

### **In relation to the provisions of the Welsh Language Act 1993**

- The sponsor should explain what arrangements they have made to comply with the provisions of the Welsh Language Act 1993.

### **Notes/Resources**

[Welsh Language Act 1993](#)

## 6.Approvals and authorisations

### 6.1 NHS Research Ethics Committee favourable opinion received for applicable studies

#### Introduction

The UK has a hybrid system of research ethics committees (RECs). There are two main categories of committee:

- NHS RECs, and
- Non-NHS RECs (e.g. institution-based higher education RECs).

Working in a centrally administered system, NHS RECs can consider and give an opinion on research anywhere in the UK. NHS RECs review research applications to give an opinion about whether the research is ethical. They are entirely independent of research sponsors, funders and investigators.

The UK policy document ‘Governance Arrangements for Research Ethics Committees’ document describes what a REC should be like and when their review is needed.

NHS RECs are:

- ‘Recognised’ (i.e. legally recognised by UKECA) to give an opinion on CTIMPs.
- ‘Authorised’, meaning they are set up under GAfREC (**Governance Arrangements for Research Ethics Committees**), but not recognised by UKECA to consider CTIMPs.

NHS RECs may have expertise in a particular area, e.g. medical devices, adults lacking capacity, prisoners, US DHHS funded research. These RECs will be flagged for particular expertise.

NHS RECs should reach one decision when considering research applications:

- **Final opinion**, i.e. favourable with standard conditions; favourable with additional conditions; or unfavourable.
- **Provisional opinion with request for further information**
- **Provisional opinion pending consultation with referee**

Note: The Ministry of Defence Research Ethics Committee (MoDREC) is set up by the MoD and recognised by UKECA to consider clinical trials. MoDREC approved research that continues in the NHS or adult social care sectors in the UK after participants move into their care, does not need to be considered by an NHS REC.

The only exception to this is research that needs to be considered under the Adults with Incapacity (Scotland) Act 2000.

### **Study-wide considerations**

#### **Does the study require NHS Research Ethics Committee (REC) favourable opinion?**

Confirm if the study needs NHS REC opinion.

Use the Health Research Authority (HRA) decision tool '[Do I need NHS Ethics approval?](#)' to decide if the research needs NHS REC favourable opinion.

In some circumstances nation specific REC review is required.

- Where the study proposed to recruit adults lacking capacity in Scotland then review by Scotland A REC is required. Where the study proposes to recruit adults lacking capacity in Scotland and in other UK nations then ethical review is required both by Scotland A REC and also by a REC in another UK nation.
- Where the study involves persons or information about persons under the care of an organisation covered by the Nursing Homes Regulations (Northern Ireland) 2005, the Residential Care Homes Regulations (Northern Ireland) 2005, the Independent Health Care Regulations (Northern Ireland) 2005 or otherwise intends to take place in a Social Care setting in Northern Ireland then it must have review by a Health and Social Care REC in Northern Ireland. Where such a study additionally proposes to recruit participants in other UK nations then this favourable opinion granted by the REC in Northern Ireland will be applicable to the other UK nations and no additional review is required.

#### **Has the NHS REC favourable opinion letter and all relevant correspondence been received?**

Confirm receipt of the NHS REC favourable opinion letter and all relevant correspondence.

It is important that the favourable opinion letter and all relevant correspondence is collated and made available/ distributed to all participating nations to ensure that:

- Any queries raised and addressed as part of the REC review are not re-examined unnecessarily.
- The applicant is unable to revise a study document leaving out information already asked for by the REC.

#### **Have the conditions of NHS REC favourable opinion been met?**

Confirm the applicant has met any conditions identified as part of the NHS REC favourable opinion.

In giving a favourable opinion, the NHS REC may specify conditions the applicant has to meet before to the start of the study (or the start at each site). These will be clearly set out in the NHS REC favourable opinion letter.

The applicant writes to the NHS REC to tell them they have met the conditions. If necessary, they must also include copies of final documents for reference purposes.

The NHS REC will confirm receipt using an 'Acknowledgement of documentation provided following favourable opinion with conditions' letter. This will give a complete list of the final documents approved for the study.

### **Have the documents needed for UK study wide review been received?**

For non-CTIMPs study wide reviewers should confirm receipt of all the correct documents (i.e. correctly labelled, version numbered and dated) needed to carry out UK study wide review.

When carrying out the UK study wide review, it is not necessary to receive or to review all documents sent to the NHS REC or listed in NHS REC favourable opinion letters.

These documents are not required to carry out the UK study wide review and should not be requested:

- Letter from statistician
- Summary CV of Chief Investigator (CI)
- Referee's report or other scientific critique report
- Summary, synopsis or diagram (flowchart) of protocol in non-technical language
- Details of Data Monitoring Committee
- Summary of product characteristics (SmPC)
- Covering letter on headed paper
- Letter from Sponsor
- Confirmation of EudraCT number
- Manufacturer Authorisation
- Certificate of analysis
- Outline of active trials
- List of competent authorities

- GMP documents
- GLP documents
- IMPD
- EUDRACTPDF/XML

Note: If there are any new or updated documents because of NHS REC review, it is necessary to get the new or updated documents.

Any errors or omissions in the NHS REC favourable opinion letter, is the responsibility of the Sponsor, or delegate, to liaise with the NHS REC to have corrections made.

### **Notes/Resources**

#### [Governance arrangements for Research Ethics Committees - Health Research Authority](#)

Certain conditions detailed within REC favourable opinion letters are standard and should not be considered to be additional conditions. These include obtaining additional regulatory approvals where applicable.

## **6.2 CTIMPs – Clinical Trial Authorisation (CTA) letter received**

### **Introduction**

No clinical trial of an investigational medicinal product (CTIMP) in the UK can be started or carried out, recruit participants or advertise to recruit participants until the Medicines and Healthcare products Regulatory Agency (MHRA) authorises it.

The MHRA also provides a proportionate notification scheme for lower-risk trials, defined as ‘Type A’ trials. In ‘Type A’ trials, the Sponsor considers that the risk to participants from the IMP is no greater than that of standard care.

The Sponsor is responsible for determining if the research is a CTIMP requiring a Clinical Trial Authorisation. All trials whether ‘full’ applications or applications under the notification scheme, require a Clinical Trial Authorisation. The authorisation may be in different formats depending on proportionality.

The Sponsor or delegate makes an application (or notification) for authorisation using the standard EudraCT (or IRAS) application form with accompanying documents.

The MHRA can carry out the review of an application in parallel to the review by the participating NHS/ HSC organisation. An NHS/ HSC organisation should not delay beginning its review until the MHRA grants an authorisation.

There is no requirement for the Sponsor to supply a copy of the application, submitted to the MHRA, to the NHS organisation for review as well.

The participating NHS/ HSC organisation should not initiate a CTIMP until the MHRA grants that CTIMP a Clinical Trial Authorisation (or equivalent under the Clinical Trial Notification Scheme).

## **Study-wide considerations**

### **Does the study require a Clinical Trial Authorisation?**

Confirm if the study needs authorisation from the MHRA.

Use the MHRA's online algorithm '[Clinical trials for medicines: apply for authorisation in the UK - GOV.UK](#)' to decide if the research needs authorisation. If in doubt, the Study Wide reviewer may request that the applicant obtain clarification from the MHRA (by completing the relevant form and sending it with the protocol to [clinicaltrialhelpline@mhra.gov.uk](mailto:clinicaltrialhelpline@mhra.gov.uk)), or may themselves seek clarification (via the same email address, with a copy of the protocol but without the form).

### **Has the MHRA Clinical Trial Authorisation and relevant correspondence been received?**

Confirm receipt of the MHRA Clinical Trial Authorisation (including acknowledgement where accepted under the Notifications scheme) and all relevant correspondence.

It is important that the authorisation (or acknowledgement where accepted under the Notification scheme) and relevant correspondence is collated and made available/distributed to all participating nations to make sure that:

- Any queries raised and addressed as part of the assessment are not re-examined unnecessarily
- The applicant is unable to revise a study document leaving out information already asked for by the MHRA.

### **Does the authorisation have any conditions to meet?**

Identify and highlight any conditions the authorisation specifies the Sponsor needs to meet during the study.

The MHRA will normally only issue conditions that do not require a response, or that will require a substantial amendment sometime during the study.

## **Notes/Resources**

For eligibility for the MHRA Notification Scheme:

[Clinical trials for medicines: apply for authorisation in the UK - GOV.UK](#)

[Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products](#)

## 6.3 Devices – MHRA Notice of no objection received

### Introduction

The sponsor is responsible for determining whether a study involving a medical device is an investigation that requires a notice of no objection from the Medicines and Healthcare products Regulatory Agency (MHRA).

A Notice of No Objection must be obtained from MHRA Devices for a clinical investigation of a medical device undertaken by the manufacturer for UKCA/CE/CE UKNI marking purposes. This will be either an investigation of a non-CE marked product, or an investigation of a CE marked product that has been modified or is to be used outside its intended purpose. Further, sponsors of a ‘Proof of Concept’ / prototype clinical study must obtain from the MHRA a No Objection letter confirming the study does not require a formal clinical investigation’

MHRA approval is not always required in the case of:

- Medical devices manufactured ‘in-house’ in a healthcare establishment
- Clinician led off-label use of a medical device.

The MHRA review of an application for Medical Device applications can be carried out in parallel to the review for the NHS and REC. There is no requirement for the Sponsor to supply a copy of the Medical Device application, submitted to the MHRA, to the NHS for review as well.

The NHS organisation should not allow the study to start until the Medical Device application has been granted a Notice of no objection.

For studies requiring an MHRA notice of no objection, UK Study Wide review will not be completed (and, in England and Wales, HRA/HCRW Approval will not be issued) before the MHRA notice of no objection has been issued and the sponsor has confirmed in writing that any conditions on the notice have been met, including evidencing this where requested.

In England and Wales there is no expectation that the applicant send their MHRA notice of no objection to the HRA/HCRW, as these will be communicated directly, although the HRA/HCRW may choose to contact the applicant to confirm that any applicable conditions have been met.

### Study-wide considerations

Where required confirm the Medical Device application has been granted a Notice of no objection by the MHRA.

## **Has the MHRA Notice of no objection letter for the medical device application been received?**

When reviewing if the MHRA Notice of no objection has been received, consideration should be given to the following. A MHRA Notice of no objection does not exempt an NHS/HSC organisation from adhering to the MHRA's guidance and an NHS/HSC internal guidance on managing medical devices, to ensure that all devices are safe before use.

### **Notice of no objection without conditions**

A MHRA Notice of no objection letter without conditions should be accepted as received.

### **Notice of no objection with conditions**

A MHRA Notice of no objection letter may be received indicating conditions as part of the authorisation.

- Confirm that there is evidence that the conditions of the Notice of no objection have been met.
- If appropriate, correspondence between the Sponsor and the MHRA related to addressing any conditions should have been received.

### **Clarifications made in the medical device application submitted to the MHRA**

During their review of a Medical Device application the MHRA may request clarifications in relation to the application.

- If correspondence is received relating to any clarifications made in Medical Device application submitted to the MHRA, the clarifications should be highlighted to the research site.
- In some cases, it may not be appropriate to view all correspondence between the Sponsor and the MHRA, as the correspondence may be commercially confidential, not relevant to the NHS.

### **Amendments**

Confirm that any substantial amendments requiring review by the MHRA for continued Notice of no objection have been supplied to the MHRA.

## 6.4 Other regulatory approvals and authorisations received

### Introduction

Some studies will require approvals from bodies other than REC and MHRA. The study-wide reviewer should assess which approvals are required and whether such approvals should be in place before the study may start. Where an approval is required before the study may start in any UK nation, UK SW review should not be concluded until it is in place. There are instances where such approval/s is/are required but the study may start in one or more UK nation before they are in place (e.g. an outstanding HMPPS approval, required for England and Wales, should not delay a study starting in Scotland and/or Northern Ireland). In such instances, UK SW review should be concluded even where the approval/s is/are not in place, but the reviewer should emphasise the outstanding approval/s required in their SW review document.

### Administration of radioactive substances

The Ionising Radiation (Medical Exposure) Regulations 2017 and the Ionising Radiation (Medical Exposure) Regulations (Northern Ireland) 2018 (both referred to as IRMER) place requirements on the authorisation and conduct of research projects involving the administration of radioactive medicinal products to humans.

Central ARSAC research approval must be obtained for all research projects that:

- require the administration of radioactive substances, and/or.
- specify the frequency, activity or processing for an administration that would otherwise be considered standard care

Central ARSAC research approval is not required for projects where:

- the protocol does not specify any administrations of radioactive substances, and/or.
- the only administration of a radioactive substance mentioned in the protocol is an inclusion criterion that would be received by all participants as part of standard care - for example, a trial where all participants must have received a radioiodine therapy to be considered eligible

There is further guidance on the IRAS website about which exposures are considered [research exposures](#) and therefore whether ARSAC approval may be required.

Central ARSAC Research Approval is applied for via IRAS. The SW reviewer should assess whether a study requires ARSAC research approval before it may commence and, where it does, should not complete their SW review until this approval is in place.

For research studies involving the administration of radioactive materials which are additional to normal care at a site, the site itself and a relevant nuclear medicine professional at that site require an ARSAC licence covering the exposures (as research exposures). SW review does not assess which sites might need to be covered in this way, nor are any SW checks necessary that any sites are covered. These are local concerns.

Procedures involving the administration of radioactive materials include:

- PET-CT
- Nuclear Medicine Bone Scans
- MUGA

Diagnostic X-rays, CT scans and DXA do not involve the administration of radioactive materials.

### **Accessing patient information without consent**

#### **In England and Wales**

[The Health Research Authority's \(HRA\) Confidentiality Advisory Group \(CAG\)](#), has been established for the purposes of section 251 of the NHS Act 2006, and the COPI regulations 2002, to provide independent expert advice to the HRA on whether applications to access confidential patient information without consent for research should or should not be supported. Supported applications allow the controller(s) of the relevant data sources, if they wish, to provide specified information to the recipient for the purposes of the relevant activity without being in breach of the common law duty of confidence. Support provides a lawful basis to allow the information to be processed by the relevant parties for the specified purposes without incurring a breach of the common law duty of confidence.

The role of CAG is to review applications and advise whether there is sufficient justification to process requested confidential patient information for the purposes described in the application. Applications to the CAG are required for access by persons outside of the care team to:

- Identifiable patient information relating to people living in, or receiving healthcare in England and/or Wales without explicit consent, prior to the disclosure of confidential information, or
- Human Fertilisation and Embryology Authority (HFEA) Register Data

The Health Research Authority Confidentiality Advisory Group should also be notified of **all** amendments to the information provided in the original application to CAG. This is because support to process confidential patient information without consent is based on the precise details originally provided to CAG and so any change will **not** be covered by the existing support until a formal amendment is made **and** the amendment is supported. Amendments should be submitted using the

CAG specific amendment form available [here](#). The amendment will be considered in accordance with the CAG SOPS, and a formal letter issued that will confirm whether or not it has been approved or if further information is required. All amendments must be listed in the annual review that the applicant should submit to the CAG.

## In Scotland

If your project seeks access to NHS Scotland data including unconsented or consented administrative data from national or multiple NHS Scotland Boards then approval is required from the [NHS Public Benefit and Privacy Panel for Health and Social Care](#)

For projects seeking access to data from a single Scottish site Caldicott Guardian approval may also be required from the relevant Scottish Health Board.

## In Northern Ireland

There is no equivalent legislation in place that enables confidential personal information to be shared without consent for research.

## Human Fertilisation and Embryology Authority (HFEA)

A licence from HFEA is required for:

- Research involving human embryos and gametes
- Disclosure of protected information from the HFEA Register

## Human Tissue Authority (HTA, England, Wales and Northern Ireland)

The HTA does not approve individual projects or license activity itself but organisations that store human tissue for research ('establishments'), including the following activities:

- Removal of relevant material from the deceased for the scheduled purpose of research
- Storage of relevant material (from both the living and the deceased) for the scheduled purpose of research

A licence is not required for storage in connection with a specific research project with approval from a REC.

Organisations where clinicians or clinical units collect and supply biological samples or data to a research tissue bank or research database are not considered to be research sites. For example, a hospital may provide biological samples surplus to diagnostic use to a research tissue bank. If the biological sample or data is not collected specifically for the purposes of a particular research project, then the organisation is a Tissue Collection Centre (TCC).

## **Study-wide considerations**

### **ARSAC**

Local ARSAC licenses are issued at a site and individual level and there is no requirement for local ARSAC licenses to be issued prior to completing the study-wide review.

### **Accessing patient information without consent**

Confirm the study has received the appropriate approvals to access patient information without the patient's consent (or another legal basis is in place, as applicable and appropriate). Each nation considers the request to access patient information without consent differently. The study-wide reviewer should also highlight that the approval to access patient information without consent may not be applicable to another nation, and that the reviewers in those other nations should consider this before satisfying the check.

### **Accessing criminal offenders**

Confirm the study has received the appropriate approvals to access criminal offenders. Each nation considers the access to criminal offenders for research studies differently. The study-wide reviewer should also highlight that the approval to access criminal offenders may not be applicable to another nation, and that the reviewers in those other nations should consider this before satisfying the check.

#### **In England and Wales**

In England and Wales approval should be obtained from Her Majesty's Prison and Probation Service (HMPPS) for any research project which requires access across HMPPS (including headquarters), including any community-based/custodial provider in England or Wales, e.g. Community Rehabilitation Companies (CRCs) and their subcontractors, Contracted Prisons and Young Offenders' Institutions (YOIs) and Secure Training Centres (STCs).

#### **In Scotland**

After obtaining clearance from the Scottish Prison Service Research Access and Ethics Committee (RAEC) applications for research proceed as per standard processes via IRAS. Further guidance can be found at [Permissions | NHS Research Scotland | NHS Research Scotland](#).

#### **In Northern Ireland**

HMPPS is not applicable to Northern Ireland. Advice on health and social care research involving prisoners in Northern Ireland, can be obtained from [research.development@setrust.hscni.net](mailto:research.development@setrust.hscni.net)

## **Studies funded by the US Department of Health and Human Services (DHHS)**

Confirm that the study has been reviewed by an appropriate Research Ethics Committee (REC), i.e. a REC that has been flagged ‘IRB Registered.’

As well as being flagged to review research studies funded by the DHHS they must also be able to review the type of study being supported. For example, a clinical trial of an investigational medicinal product (CTIMP) with funding support from the DHHS must be reviewed by a committee that is both recognised to review the relevant type of CTIMP and registered with the OHRP. Details of the committees that are registered with the US Office for Human Research Protections (OHRP) can be obtained from the National Research Ethics Service (NRES) Central Allocation System (CAS).

## **HFEA**

Confirm that an HFEA licence has been issued.

## **HTA (England, Wales and Northern Ireland)**

Where the application refers to a licensed research tissue bank, confirm that an HTA licence has been issued.

Where the research involves collection of tissue from sites for a licensed research tissue bank, highlight that the sites are Tissue Collection Centres.

## **Genetically Modified Organisms (GMOs)**

There are two broad categories of use of Genetically Modified Organisms (GMOs), each with their own legislative framework and supervisory authorities:

- Contained Use, overseen by the Health and Safety Executive (HSE) which has a UK wide remit. Contained Use activities are further divided into risked-based classes. Authorisation from the HSE is for a Contained Use within a specific class at registered premises. A new application is not required to undertake any further activities in the same class at the same premises.
- Deliberate Release, which is overseen by DEFRA in England and equivalent authorities in Scotland, Wales and Northern Ireland. Authorisation is for certain premises to release GMOs.

As the authorisations for GMOs are issued for premises and cover a type of activity rather a specific research study, there is no requirement for GMO authorisations to be issued prior to completing the study-wide review. Where a research study involves the use of GMOs, this should be noted in the study-wide review. It is not expected that the study-wide review will determine the type of activity (Contained Use or Deliberate Release), or a class of activity within these types. The output of the study-wide review for NHS/HSC organisations should flag that the research study involves the use of GMOs and that the organisations should consider whether

they have existing authorisation for this type of activity at their premises, or if they will require a new authorisation from the relevant supervisory authority for the use of GMOs required for the study.

### **Notes/ Resources**

Managing Medical Devices - [Safeguarding public health \(publishing.service.gov.uk\)](https://www.publishing.service.gov.uk)

[How to Notify the MHRA about a clinical investigation for a medical device - GOV.UK](https://www.gov.uk/government/publications/notify-clinical-investigation-medical-device)

# **Appendix A: Areas of review in HRA assessment which are additional to the UK study wide governance criteria**

## **Human Resources Good Practice Resource Pack**

The Initial Assessment and HRA and HCRW Approval letters will confirm whether a Letter of Access (LoA), Honorary Research Contract (HRC) or neither would be appropriate for the research activities specified in the IRAS application, were these to be undertaken by non-commercial research staff not already holding a substantive or honorary contractual relationship with the NHS organisation responsible for the activities. The Initial Assessment and HRA and HCRW Approval letters will also specify the appropriate pre-engagement checks, in accordance with the HR Good Practice Resource Pack.

For clarity, the term ‘if in NHS facilities’, used in the Algorithm of Research Activity and Pre-Engagement Checks for the purposes of specifying when a Letter of Access is expected for research involving staff or their data, should be taken as referring to areas within NHS premises where care is provided. Offices and other non-care areas should be regarded as business premises and letters of access will therefore not be expected for access to such locations for staff research. External researchers working under such arrangements are expected to comply with the off-site working policies and procedures of their employing organisation.

In commercially sponsored studies, commercial research staff should not be given a Research Passport or issued with an HRC or LoA or any other document that could be construed as indicating that the NHS organisation is accepting liability for their actions. With the exception of clinical study data monitors, the model agreements do not cover issues relating to commercial organisations providing staff to undertake commercial research activities in the NHS (e.g. commercial research nurses).

Therefore, the NHS organisation needs to ensure that a contract for the provision of these services is put in place with the commercial organisation. This contract should address all issues relating to the activities and suitability of the commercial staff, for example, pre-engagement check requirements (Disclosure and Barring service (DBS), occupational health, professional registration, right-to work, qualification etc, training, accountability and management arrangements, insurance for negligent actions. For access by commercial staff to NHS facilities the Initial Assessment and HRA and HCRW Approval letters will be clear where such other arrangements are appropriate

## **Oversight Arrangements**

The Initial Assessment and HRA and HCRW Approval letters will confirm, for each group of organisations that are identified in the application as undertaking different activities within the study, whether those activities should be overseen by a Principal

Investigator and, if so, whether the Principal Investigator should hold a contract of employment with the participating organisation or may provide effective oversight from another organisation. Where oversight by a Principal Investigator is not needed, the letters will set out the appropriate alternative arrangements to be made at the participating organisation, for example, support by a Local Collaborator.

Non-commercial sponsors are expected to state their intentions through the outline Organisational Information Document/s in their IRAS submission. The HRA/HCRW will assess the appropriateness of the sponsor's proposal and confirm expectations by group of organisations in the Initial Assessment and HRA and HCRW Approval letters. Where there should be Principal Investigators, Co-Investigators and/or Local Collaborators, the sponsor should be clear as to whether these have been identified or whether they require local assistance in identifying suitable staff.

Where there should be a Principal Investigator HRA and HCRW assessment will ensure that any specific training expectations of the sponsor for them and/or their team are clear. Where a Principal Investigator will be locally employed it is the responsibility of each participating NHS organisation to assess the suitability of the individual selected, in line with the general and specific training expectations outlined by the sponsor and to consider any possible conflict of interest. Where requested, the NHS organisation should support the sponsor in identifying an appropriate Principal Investigator. In the case of a remote Principal Investigator, it is the responsibility of the NHS organisation at which the Principal Investigator is physically present to assess the suitability of the Principal Investigator and to provide appropriate assurances to other relevant NHS organisations that it has done so in line with the UK Policy Framework for Health and Social Care Research.

By confirming the Organisational Information Document and Schedule of Events/SoECAT (or agreeing the site agreement) the participating NHS organisation will be taken to have confirmed the suitability and appropriateness of any Principal Investigator selected.

## **Interventional Research Studies**

Sponsors should refer to the Set-up of Interventional Research guidance, for information on risk assessment of oversight arrangements. The guidance sets out principles and examples relating to whether different activities require Principal Investigator oversight, locally or from a distance, and details other arrangements to be made in relation to such oversight (for example, relating to the type of contracting and capacity and capability confirmation that should be in place). IRAS submissions should specify oversight arrangements for participating organisations in the study, in accordance with the guidance. Where applicable, a copy of the relevant parts of the sponsor risk assessment should be provided to facilitate HRA and HCRW review of the proposed arrangements. HRA and HCRW assessment will be undertaken accordingly.

## **Non-Interventional Research Studies**

A Principal Investigator should be in place where oversight is required of local staff conducting activities in relation to the research study. The Principal Investigator may be locally employed, or may provide oversight from another organisation, depending

on the ability of the PI to effectively oversee the work being conducted, as determined by the sponsors risk assessment.

Where local staff will not be conducting activities in relation to the research study, but where central study staff will be present at the participating organisation to undertake research procedures, it is expected that a Local Collaborator will be identified. The role of the Local Collaborator is to support practical arrangements to facilitate the presence of the external research staff, for example by making appropriate arrangements as per the HR Good Practise Resource Pack.

IRAS submissions should specify oversight arrangements for participating organisations in the study. HRA and HCRW assessment will be undertaken accordingly.

Further guidance on the set up of non-interventional research is currently in preparation.

## **Level of capacity and capability assessment expected of participating organisations**

NHS organisations in England or Wales should assess, arrange and confirm their capacity and capability to undertake a study in a manner proportionate to the nature of the study and their specific roles and responsibilities within it. Not all organisations connected with the management of a participant in a study are considered to have a role in the study, particularly if they are not processing personal data under the instruction of the sponsor and are undertaking no activities beyond standard of care.

In most cases, the mechanism for formal confirmation of capacity and capability is the participating NHS organisation entering into the site agreement with the sponsor (providing to the sponsor, i. the agreed Organisation Information Document for a non-commercial, non-interventional study, or, for all interventional studies; ii. the NHS organisation signed agreement). Where a participating NHS organisation is also the sponsor, confirmation is not by contract exchange (as a legal entity cannot contract with itself) and local arrangements will be in place to confirm when the study may start.

The agreement (including, where applicable, the Organisation Information Document), used to confirm that the NHS organisation has made the necessary arrangements to deliver the study, should be used without modification to its templated elements. Sponsors should include in their IRAS submissions the template of each site and/or PIC agreement that they intend to use for the study. Where the sponsor is proposing modifications to a template agreement, each proposed modification should be highlighted and justified. Where the sponsor is of the opinion that no suitable template agreement exists for their study, or for some sites within their study, this should be explained in the application. The HRA and HCRW assessment will consider the suitability of any proposed modifications and the Initial Assessment and HRA and HCRW Approval letters will detail the arrangements agreed with the sponsor.

NHS organisations in England are obliged by their standard form provider contracts with NHS England to use only the appropriate unmodified model agreement for commercial contract research. NHS organisations in Wales are under an equivalent policy expectation. This requirement/expectation may only be set aside if expressly waived in the letter of HRA and HCRW Approval. The negotiation of proposed modifications prior to any such waiver is likely to cause significant delay.

In some cases, it is not necessary for an NHS organisation to formally confirm its capacity and capability, by provision of an agreed Organisation Information Document or signed contract, prior to research activity commencing at that organisation. In other cases, whilst formal confirmation is needed prior to research activity commencing, the nature of the activity means that this confirmation should be given within a specified timeframe. Sponsors should give consideration as to whether some or all sites within their study should be regarded as not requiring confirmation of capacity and capability, or whether some or all sites within their study should be given confirmation within a specified timeframe. Sponsors should include within their application an explanation and justification for their plans. This will be assessed, and appropriate arrangements confirmed in the Initial Assessment and HRA and HCRW Approval letters.

The following table provides an example of some common scenarios in which different levels of assessing, arranging and confirming may be expected and should be used by sponsors to guide their own risk assessment and statement of intent and justification in their IRAS submission. The Initial Assessment letter will provide initial instructions regarding whether formal confirmation of capacity and capability is expected by participating organisations (including, where applicable, when different organisation are delivering different research activities within the study), the likely extent of any assessment and key considerations for arranging capacity and capability. These instructions will be finalised and explicitly stated in the HRA and HCRW Approval letter. Sponsors and participating NHS organisations should note that it is possible that these instructions will change between these communications if further information about the study becomes available.

## **Assessing and arranging capacity and capability**

- **Full:** In terms of the ‘assess’ and ‘arrange’ steps of assessing, arranging and confirming capacity and capability, it is expected that the organisation will need to fully consider the implications of participating in the study and put specific arrangements in place to be able to undertake their activities.
- **Minimal:** In terms of the ‘assess’ and ‘arrange’ steps of assessing, arranging and confirming capacity and capability, it is expected to be relatively straightforward for organisations to consider the implications of participating in the study, and that minimal arrangements would need to be in place to be able to undertake the activities: for example, ‘do we have the staff/resources to undertake the activities?’, ‘do we hold the data being requested?’, ‘will the systems in place locally make it easy or difficult to undertake the activities?’ (for example, accessing electronic vs. hard copy records).

## **Confirmation of capacity and capability**

- 1. Formal confirmation of capacity and capability will be expected:**  
The organisation will formally confirm that it has capacity and capability in place to undertake the activities by entering into an agreement with the sponsor. Even where there is no expected timeframe stated for the organisation to assess, arrange, and provide formal confirmation of capacity and capability, organisations should arrange the capacity and capability to deliver the study as soon as is possible, in accordance with timelines agreed with the sponsor, and formally confirm as soon as they have done so.
- 2. Formal confirmation of capacity and capability will be expected within a specified timeframe:** The organisation will formally confirm that it has capacity and capability in place to undertake the activities by entering into an unmodified model agreement with the sponsor. However, due to the nature of the activities involved, organisations will be expected to provide that confirmation to the sponsor within a specified timeframe (usually 35 days from receipt of the local information pack but may be less, as specified in the Initial Assessment and HRA and HRA Approval letters). Where the sponsor proposes use of any agreement other than an unmodified model agreement, formal confirmation of capacity and capability will usually be expected (as it would not usually be appropriate to expect an NHS organisation to review a non-standard agreement within an expedited timeframe) and no time limit will be specified (option 1).

The timeframe will be specified during assessment and detailed in the Initial Assessment and HRA and HCRW Approval Letters. If the organisation is not able to formally confirm capacity and capability within this timeframe, a justification for this must be provided to the sponsor within the specified timeframe. If the sponsor is not satisfied with the justification, then the sponsor may escalate to the HRA and / or HCRW as appropriate

- 3. No formal confirmation of capacity and capability is required:** In circumstances where no study agreement is expected, because there is no expectation that the NHS organisation needs to undertake significant assessing or arranging and because it will not be processing personal data under the instructions of the sponsor, the organisation may be given a set amount of time (usually 35 days from receipt of the local information pack, but may be less) to consider the expected activities and to opt out if they are not able to participate.

The sponsor may assume that capacity and capability has been confirmed if the organisation does not raise any objections within the given time. Even in such cases, organisations are encouraged to informally confirm capacity and capability to the sponsor (or their delegate) at the earliest opportunity, rather than unnecessarily waiting for the specified number of days to elapse. In some cases, Participating organisations will be informed of the study, but the specified study

activity may commence

Uncontrolled when printed

<b>Study / Site type Description</b>	<b>Assess?</b>	<b>Arrange?</b>	<b>Confirm?</b>
<p>1. Participating organisation will be conducting activities outside of usual care competence, such as</p> <ul style="list-style-type: none"> <li>a) Recruitment and Consent of participants</li> <li>b) Activities not within usual care competence, such as specialised tissue collection, imaging, or other protocol specific measurements/ assessments.</li> <li>c) Study specific visits</li> <li>d) Administration of IMP not within usual care competence (or within usual care competence, but the risk assessment requires that this is done only at a Trial Site with a locally employed PI)</li> <li>e) Accountability of IMP is required for overall evaluation of results</li> <li>f) Complex data collection and transfer where monitoring is required or use of participant recorded outcomes that may need support from the study team for training</li> </ul>	Yes: Full	Yes: Full	Formal confirmation of capacity and capability will be expected
<p>2. PIC activity involving the Identification of potential participants for a study by means of study specific data processing under the controllership of the sponsor. Potential participants are then put in touch with the recruiting site (no specific consent or recruitment takes place).</p>	Yes: Minimal	Yes: Minimal	<p>Formal confirmation of capacity and capability will be expected</p> <p>Where an appropriate unmodified model agreement is proposed formal confirmation of capacity and capability will be expected within a specified timeframe.</p>

<p>3. Organisation is responsible for taking blood (or other) tests within usual care competence but <b>are not</b> part of standard of care (i.e. would not be performed if the participant was not in a trial). This should be taken to include where samples are collected and sent to a central laboratory using a trial-specific kit provided by the sponsor</p>	<p>No</p>	<p>No</p>	<p>Where such activity falls within usual care competence and therefore does not need PI oversight, nor detailed instruction from the sponsor (such that the participating organisation should be regarded as the data processor of the sponsor) the activity may occur without formal confirmation. Where the sponsor will make payment for the activity, a contract or other mechanism for payment may still be appropriate (but may be negotiated in good faith without delaying the activity in question)</p>
<p>4. Use of organisations (Organisation B) as continuing care Investigator Sites</p> <p>Participants are recruited at a specialist centre (Organisation A) and undergo the research intervention there. However, participants may have care continued at a hospital closer to their home (Organisation B) which would be required to undertake research specific activity in addition to standard of care <b>outside of usual care competence</b> (such as continued administration of the IMP). In some instances, Organisation B is known prior to participant recruitment, in other instances the organisation</p>	<p>Yes: Full</p>	<p>Yes: Full</p>	<p>Formal confirmation of capacity and capability will be expected</p> <p>Where an appropriate unmodified model agreement is proposed formal confirmation of capacity and capability will be expected within a specified timeframe</p> <p><b>Note - This may need to be done quickly to ensure the patient's continued</b></p>

<p>will not be identified until the participant is recruited or transferred.</p> <p><b>Note - The transfer of a research participant is expected to be facilitated by the ‘transferring’ organisation, providing all relevant information to the ‘receiving’ organisation to support the receiving organisation’s continuation of the research. The sponsor should factor this into the study design so that the activities do not differ significantly from what is already in place.</b></p>			<b>participation on the study.</b>
5. Activities that are performed on behalf of Organisation A, under the usual care competence of a contracted Service Provider (Organisational B), including where Organisation B is an NHS Organisation and undertakes the activities to be performed as usual as part of normal care pathways.	No	No	No formal confirmation of capacity and capability is required from organisation B, as it is assumed to have been already provided by Organisation A, including through consideration that the applicable Service Contract is suitable to cover the activities in question as research activities. Study activities can commence once HRA and HCRW Approval is in place and Organisation A has provided its confirmation, as applicable.
6. Questionnaire or focus group study where no study specific data processing is required to identify potentially eligible participants (for example an opportunity will be brought to the attention of staff through pre-existing, routine, communications or general advertisement)	No	No	No formal confirmation of capacity and capability is required. The organisation will be given a set amount of time to opt out if they are not

			able to participate (if for example they do not have eligible staff to participate). The sponsor may assume that capacity and capability has been confirmed if the organisation does not raise any objections within the given time.
7. Questionnaire or focus group study that does require study specific data processing on the part of participating NHS organisations (for example to identify and approach specific participant groups).	Yes: Minimal	Yes: Minimal	Formal confirmation of capacity and capability will be expected  Where an appropriate unmodified model agreement is proposed formal confirmation of capacity and capability will be expected within a specified timeframe.
8. No change to local activity but automated data extraction by central team	No	No	No formal confirmation of capacity and capability is required. The organisation will be given a set amount of time to opt out if they are not able to participate (if for example they do not have the right patient population). The sponsor may assume that capacity and capability has been confirmed if the

			organisation does not raise any objections within the given time.
9. Data extraction by central research team where the central research team require access to the organisation to undertake the data extraction.  <b>Note – It would be important to consider in this scenario the central research team's legal basis under the common law duty of confidentiality if the data extraction activity will require disclosure of confidential personal information.</b>	Yes: Minimal	Yes: Minimal	No formal confirmation of capacity and capability is required. The organisation will be given a set amount of time to opt out if they are not able to participate (if for example they do not have the right patient population). The sponsor may assume that capacity and capability has been confirmed if the organisation does not raise any objections within the given time.
10. Provision of existing personal data, or data collected through the course of routine care by the staff at Organisation A to the central study team or provision of personal data following processing (e.g. extraction, anonymisation, etc.)	Yes: Minimal	Yes: Minimal	Formal confirmation of capacity and capability will be expected  Where an appropriate unmodified model agreement is proposed formal confirmation of capacity and capability will be expected within a specified timeframe
11. Transfer, including processing for the purposes of transfer, of existing data, or data collected through the course of routine care, which is not considered to be personal data (for example it relates to service users	Yes: Minimal	Yes: Minimal	No formal confirmation of capacity and capability is required. The organisation will be given a set amount of time

	who are deceased) by the staff at Organisation A to the central study team.			to opt out if they are not able to participate (if for example they do not have the right patient population). The sponsor may assume that capacity and capability has been confirmed if the organisation does not raise any objections within the given time.
12.	Rare genetic disease study under the <a href="#">Musketeers Memorandum Consortium Agreement</a> . N.B. HRA Organisational Information Document(s) completed for these studies should clearly state that the study is covered under the Consortium Agreement.	No. Studies covered by the consortium agreement are within the capacity and capability of consortium member Trusts.	No. Studies covered by the consortium agreement are within the capacity and capability of consortium member Trusts.	No. The study may commence locally once HRA Approval is in place and in line with the timelines set out in the consortium agreement.
13.	Provision of previously collected tissue samples that have personal data associated with them to another organisation for a specific study	Yes: Minimal	Yes: Minimal	Formal confirmation of capacity and capability will be expected  Where an appropriate unmodified model agreement

			is proposed formal confirmation of capacity and capability will be expected within a specified timeframe
14. Provision of previously collected tissue samples that do not have personal data associated with them to another organisation for a specific study	Yes: Minimal	Yes: Minimal	No formal confirmation of capacity and capability is required. The organisation will be given a set amount of time to opt out if they are not able to participate (if for example they do not have samples/resources available). The sponsor may assume that capacity and capability has been confirmed if the organisation does not raise any objections within the given time.
15. Processing or analysing tissue samples for a specific study received from another organisation  <b>Note – This applies where the processing is being undertaken as a research activity. Where this processing is undertaken under an existing service level agreement then the arrangements detailed at example 8 will apply</b>	Yes: Minimal	Yes: Minimal	Formal confirmation of capacity and capability will be expected  Where an appropriate unmodified model agreement is proposed formal confirmation of capacity and capability will be expected within a specified timeframe

### Organisations considered to have no role in the study

16. Referral activity not involving Participant	Organisations B and C have <b>no role in the study</b> as they are
---	--

<p>Identification Centres (PICs), e.g.</p> <ul style="list-style-type: none"> <li>a) Organisation A wants Organisation B to display a poster and advertising materials about the study</li> <li>b) A consultant at organisation C becomes aware of the study and has a patient with the relevant condition. The consultant mentions the study taking place at Organisation A and the patient is interested in participating. The consultant refers the patient to Organisation A to explore the treatment options available there.</li> </ul>	<p>undertaking no activities beyond standard of care and are not acting as data processors of the sponsor by processing personal data under sponsor instruction. Therefore, the concepts of assessing, arranging and confirming capacity and capability are not expected to apply as HRA and HCRW Approval is not required in relation to these organisations.</p>
<p>17. Organisation is undertaking only activities that <b>are</b> part of standard of care (i.e. would be performed if the participant was not in a trial). For example</p> <ul style="list-style-type: none"> <li>a) Blood (or other) tests taken at a GP site, or satellite clinic or local hospital, that the HCPs/staff that are part of standard of care (i.e. would be performed if the participant was not in a trial).</li> <li>b) Recording of visits and results in the patients' medical records as part of standard of care; this would include treatment of a patient in hospital for example in an emergency setting, where the data is retrieved by the PI to ensure patient safety</li> <li>c) Staff who visit patients at home to provide standard of care, for example district nurses,</li> </ul>	<p>The organisation has <b>no role in the study</b> as they are undertaking no activities beyond standard of care. Therefore, the concepts of assessing, arranging and confirming capacity and capability are not expected to apply as HRA and HCRW Approval is not required in relation to these organisations.</p>

or part of a contracted service provider	
<p>18. Activities under the duty of care of one organisation that are physically embedded at another (for example, Satellite Clinics)</p> <p>Organisation A acts as the regional centre for treatment of patients. The regional centre has network clinics embedded in other organisations (Organisation B). Patients are considered to be patients of Organisation A but they may be seen at the geographical location of Organisation B in order to receive their care from Organisation A</p>	<p>If staff from Organisation A undertake all protocol related procedures and take full responsibility for all Research specific activity undertaken with the study participants then Organisation B is considered to have no role in the study. Therefore, the concepts of assessing, arranging, and confirming capacity and capability are not expected to apply as HRA/HCRW Approval is not required in relation to this organisation.</p>
<p>19. Provision of surveillance data to Organisation A through the orange, yellow etc. reporting card systems, (including provision of further routine non-identifiable data once a card has been returned).</p>	<p>This activity falls within the definition of 'usual practice' according to the HRA's Defining Research table. As this is not research activity, it is outside the remit of the approval processes in England and Wales so the concepts of assessing, arranging and confirming capacity and capability are not expected to apply.</p> <p>Where NHS organisations need to undertake additional activities (e.g. provide data from notes, samples, approach patients etc.) to the routine monthly returns, then it would be considered if that additional activity is significant enough to constitute 'research' activity, or just an extension of the standard surveillance programme. If it is considered a research study by the sponsor, then participating NHS organisations are participating organisations and the above examples should be followed (dependent on activities).</p>

## Appendix B Summary of Changes

Area of Change	Description of change
General changes throughout	<ul style="list-style-type: none"> <li>Updated further guidance links</li> <li>Additional minor textual changes to improve readability and provide additional context and guidance</li> <li>Clearer distinction between study wide considerations as opposed to introductory and contextual guidance in each area of assessment.</li> </ul>
Section A (Areas of review HRA assessment which are additional to the UK study wide governance criteria	<ul style="list-style-type: none"> <li>Section A moved to the end of the document and retitled ‘Additional areas of review for the purposes of HRA/HCRW Approval’. Amended to reflect changes in expectations following adoption of these checks by Wales, and to reflect the position agreed with the MHRA in respect to Principal Investigator oversight.</li> </ul>
1.1 IRAS application completed correctly	<ul style="list-style-type: none"> <li>Amended to reflect current policy positions regarding student research, as expressed <a href="#">here and to add further clarity regarding</a> the position agreed with the MHRA in respect to participating site types.</li> </ul>
2.1 Participant information / consent documents and consent process	<ul style="list-style-type: none"> <li>General updates to reflect policy expectations regarding the common law duty of confidentiality and the information that should be provided to study participants</li> <li>Addition of detailed requirements regarding child participants, the nature of consent (in line with <a href="#">ICO position</a>), <a href="#">in respect to the management of Potential ‘health-related findings’ and</a> the use of Electronic Consent methods (in line with the <a href="#">Joint HRA/MHRA statement</a>)</li> </ul>
3.1 Protocol assessment	<ul style="list-style-type: none"> <li>Additional clarification regarding the need for the protocol to provide instructions to participating NHS/HSC organisations to enable them to deliver the research, including regarding the definition of the end of the study.</li> </ul>
4.1 Allocation of responsibilities and	<ul style="list-style-type: none"> <li>Updates to reflect changes in the availability of, and expectations regarding the use of, model agreements</li> </ul>

rights are agreed and documented	<ul style="list-style-type: none"> <li>Updates to reflect the contractual requirements of GDPR.</li> </ul>
4.2 Insurance / indemnity arrangements assessed	<ul style="list-style-type: none"> <li>Updates to insurance expectations in line with the <a href="#">UK Policy Framework for Health and Social Care Research, in particular in respect to management and design.</a></li> <li><a href="#">Changes to insurance expectations as these relate to primary care following disestablishment of PCTs and equipment indemnity following changes in expectations relating to the Master indemnity agreement.</a></li> </ul>
4.3 Financial arrangements assessed	<ul style="list-style-type: none"> <li>No additional significant changes</li> </ul>
5.1 Compliance with Data Protection law and data security issues assessed	<ul style="list-style-type: none"> <li>Additional criteria with respect to situations where a study requires the installation of specific software on NHS systems, or the utilisation of hardware additional to standard NHS equipment</li> <li>Redrafted to include requirements of Data Protection Act 2018 and GDPR and to more clearly express the requirements of the Common Law duty of confidentiality</li> </ul>
5.2 CTIMPs – Arrangements for compliance with the Clinical Trials Regulations assessed	<ul style="list-style-type: none"> <li>Redrafting to more clearly describe expectations regarding the conduct and management of the CTIMP at participating NHS/HSC organisations.</li> <li>Additional criteria in relation to the inclusion of minors in a CTIMP and in relation to incapacitated adults</li> <li>Additional information provided regarding HRA Pharmacy Technical Assurance</li> </ul>
5.3 Compliance with national legislation regarding Adults unable to consent for themselves in a non-CTIMP	<ul style="list-style-type: none"> <li>Additional section added to separate the requirements more clearly in relation to Adults unable to consent for themselves in a non-CTIMP in line with relevant legislation and policy guidance, and reflecting the differences in legislation between the four nations, including the Mental Capacity Act (NI) 2016</li> </ul>
5.4 Compliance with national legislation	<ul style="list-style-type: none"> <li>Additional section added to separate the requirements more clearly in relation to compliance with national legislation regarding Human Tissue in line with relevant legislation and policy guidance and reflecting the differences in legislation between the four nations.</li> </ul>

regarding Human Tissue	
5.5 Compliance with any other applicable laws or regulations	<ul style="list-style-type: none"> <li>Deletion of criteria in relation to Adults unable to consent for themselves and Human Tissue</li> <li>Updated criteria in relation to the requirements of the Welsh Language Act 1993</li> <li>Additional criteria in relation to The Ionising Radiation (Medical Exposure) Regulations 2017 and the Ionising Radiation (Medical Exposure) Regulations (Northern Ireland) 2018 including the Radiation Technical Assurance programme.</li> </ul>
6.1 NHS Research Ethics Committee favourable opinion received for applicable studies	<ul style="list-style-type: none"> <li>No additional significant changes</li> </ul>
6.2 CTIMPs – Clinical Trial Authorisation (CTA) letter received	<ul style="list-style-type: none"> <li>No additional significant changes</li> </ul>
6.3 Devices – MHRA Notice of no objection received	<ul style="list-style-type: none"> <li>Amended to reflect changes in medical device regulations for MHRA assessment in Great Britain (England, Wales and Scotland) differ from those applicable to Northern Ireland. The Northern Ireland Protocol requires Northern Ireland to continue to align with EU rules for devices after 1 January 2021. Therefore, the Medical Device Regulation (EU) 2017/745 (MDR) and the In Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR) will apply in Northern Ireland from 26 May 2021, and 26 May 2022 respectively, in line with the EU's implementation timeline.</li> </ul>
6.4 Other regulatory approvals and authorisations received	<ul style="list-style-type: none"> <li>Redrafting of requirements when accessing patient information without consent</li> <li>Updated criteria in relation to access to Criminal Offenders</li> <li>Additional criteria in relation to Genetically Modified Organisms (GMOs)</li> </ul>