9.93 It is also an offence to provide false or misleading information to a recognised REC in the course of an application for an ethical opinion relating to a CTIMP or when giving a notice of amendment.

9.94 Where a REC receives information suggesting that a criminal offence may have been committed, it should proceed as in paragraph 9.89.

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GCP inspections

9.95 The Clinical Trials Regulations together with internationally recognised guidelines for Good Clinical Practice (GCP) provide a standard for the conduct of CTIMPs. Compliance with this standard provides public assurance that the rights, safety and well-being of clinical trial subjects are protected (consistent with the principles that have their origin in the Declaration of Helsinki), and that clinical trial data are credible and accurate. MHRA GCP inspectors assess compliance with the Regulations and GCP by conducting inspections at the sites of pharmaceutical companies, contract research organisations, non-commercial organisations, investigational trial sites, clinical laboratories, GCP archives and other facilities involved in CTIMPs.

9.96 Inspections are carried out to protect the public (both trial participants and future patients), to meet legal obligations and enforce applicable legislation, to provide assurance of compliance with the Regulations and GCP, to detect and take action relating to serious non-compliance (including fraud and misconduct) and to assist with quality improvements in clinical research. All these activities provide support to the regulatory assessment process on which licence approvals and renewals depend.

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Non-compliance in CTIMPs

9.97 RECs should draw serious concerns about compliance issues in CTIMPs to the attention of the OREC Manager and appointing authority under the procedures for notifying possible fraud or misconduct (see paragraph 9.89). The OREC Manager

should notify the Operations Director. In consultation with the OREC Manager and the appointing authority, the Operations Director will be responsible for deciding whether the information should be shared with the GCP Inspectorate at the MHRA. Where appropriate, the Operations Director or OREC Manager will notify the Operations Manager for GCP by email.

9.97A The MHRA should always be notified where one of the following is suspected:

- Conduct of a trial without a CTA or favourable opinion.
- Conduct of the trial at a particular site without a favourable opinion for the site or the Principal Investigator.
- Provision of false or misleading information to the main REC in relation to an application for ethical opinion or notification of substantial amendment.
- Implementation of a substantial amendment without authorisation and/or a favourable opinion as appropriate.
- Failure to notify SUSARs occurring in the trial in the UK in an expedited manner or to provide an Annual Safety Report.
- Failure to notify urgent safety measures.
- Failure to notify the early termination or conclusion of the trial.
- A serious breach of GCP or the protocol.
- Any other fraud or serious misconduct.

A breach of the conditions and principles of GCP or the protocol should be regarded as "serious" if it is likely to affect to a significant degree the safety or physical or mental integrity of the participants or the scientific value of the trial.

9.97B Consideration should also be given to notifying the MHRA where a pattern emerges of repeated minor breaches of GCP or the protocol.

9.97C A recognised REC may notify the MHRA directly of possible non-compliance if it considers it appropriate to do so, although it is recommended that RECs follow the reporting procedure in paragraph 9.89. When writing direct to the MHRA, the REC should copy the notification to the OREC Manager and appointing authority.

9.97D All reports received by MHRA will be acknowledged. Feedback will be provided to the Operations Director on the findings of any resulting inspections or investigations.

The Operations Director will arrange for relevant RECs and OREC Managers to be notified.

9.97E Where the MHRA takes regulatory or enforcement action in relation to the conduct of a CTIMP, the Operations Director will be notified and a copy of the relevant inspection report provided. The Operations Director will arrange for relevant RECs and OREC Managers to be notifed and to receive a copy of the inspection report.

9.97F Copies of inspection reports will not be routinely disclosed to RECs. However:

- Any report on a Phase 1 trial site will be provided to the REC responsible for undertaking SSA for the site.
- Reports will be disclosed in any case where regulatory or enforcement action is taken (see paragraph 9.97F).
- Relevant information from other inspections (or copies of reports where appropriate) may be disclosed on request to the GCP Inspectorate from the main REC, OREC Manager or Operations Director.

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Co-operation with inspections and investigations

9.98 GCP Inspections do not include assessment of the compliance of RECs with the Regulations or the SOPs. They may however seek to ensure that trials have a favourable opinion from a recognised REC and are being conducted in accordance with the terms of the opinion. This may require verification of the application documentation and correspondence held by the main REC. Any request from the GCP Inspectorate to inspect documentation will be made in writing to the Co-ordinator of the main REC, copied to the OREC Manager. The main REC should normally facilitate the inspection. Any concern on the part of the REC about the inspection should be referred to the appointing authority and the OREC Manager. If the matter cannot be resolved locally with the GCP Inspectorate, the OREC Manager should notify the Operations Director, who will contact the Operations Manager for GCP at the MHRA.

9.98A The REC should co-operate fully if asked to assist with criminal investigations. The appointing authority and OREC Manager should be kept informed.

9.99 Requests to provide information or assistance in connection with investigations by other bodies into suspected fraud or misconduct should be referred initially to the OREC Manager for discussion as appropriate with the Operations Director and appointing authority. With the permission of the OREC Manager, the REC should co-operate fully. The REC should not under any circumstances undertake its own investigations.

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Section 10: Transitional arrangements

Summary

The EU Directive and the Clinical Trials Regulations came into force in the UK on 1 May 2004. This section gives guidance on ongoing review by the "main REC" of studies that received ethical approval before 1 May 2004. The transitional provisions for CTIMPs are set out in the Clinical Trials Regulations and have statutory force.

"Ongoing review" means all responsibilities of the main REC following approval. This includes ethical review of substantial amendments, approval of new sites and PIs, review of progress and safety reports, and all other monitoring responsibilities.

Transitional arrangements depend on whether:

(i) The study is a CTIMP or non-CTIMP.

(ii) The REC is recognised to review the study by UKECA (in the case of a CTIMP).

(iii) The study is single- or multi-site.

The guidance covers each scenario in detail. Key points are as follows:

- An ethical opinion given to a CTIMP by a REC that is recognised for the relevant type of trial remains valid until the conclusion of the trial. The REC continues as the main REC.
- An ethical opinion given to a CTIMP by a REC that was not recognised by UKECA remained valid until 1 May 2006. At this point UKECA took steps to give a limited form of recognition to RECs without recognition to review *new* CTIMPs or with only type ii recognition. This "transitional recognition" allows them to continue as the main REC for the trial on a UK-wide basis after 1 May 2006. New applications will not therefore be required from Chief Investigators.
- For non-CTIMPs with ethical approval from one REC, this REC continues as the main REC. This applies whether or not the study is extended to sites in other domains.
- All multi-site studies previously approved by Type 3 RECs continue with the Type 3 REC as main REC. Local RECs that gave "locality approval" - under Annex D of the previous MREC application form - continue as site-specific assessors but have no other responsibilities.
- Where a multi-site study was ethically reviewed and approved by more than one REC, a single REC must be appointed by NRES Head Office as the main REC before any further decisions can be taken on the study. Normally this will be one of the RECs that approved the study. If it is a CTIMP, the REC should be recognised.

Guidance is given on re-designating studies as SSA-exempt under the new SOPs.

Guidance is also given on transfer of responsibilities where a REC ceases to function following abolition or merger, or has its recognition revoked. OREC Managers are responsible for arranging for another REC to take over as main REC for outstanding applications and existing studies.

Section 10 Transitional arrangements

Introduction

10.1 This section gives guidance on the transitional arrangements applicable to:

- Ongoing ethical review of studies that received a favourable ethical opinion before 1 May 2004, i.e. responsibility for amendments, new sites and monitoring; and procedures for submission of fresh applications where legally required.
- Transfer of studies from a REC that ceases operation or has its recognition revoked, including both outstanding applications and ongoing ethical review of studies.

10.2 Applicants and REC Co-ordinators should contact OREC Managers wherever necessary for further advice on the interpretation of these procedures.

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Studies with a favourable ethical opinion given before 1 May 2004

10.3 In this section all references to "favourable ethical opinion" include ethical approvals given by any duly constituted NHS REC prior to 1 May 2004. They do not apply to "locality approvals" given by local RECs under the procedures for multi-centre studies prior to 1 March 2004.

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Single-site CTIMPs

10.4 Where the favourable ethical opinion was given by a REC that is now recognised by UKECA for the appropriate type of research, the opinion remains legally valid until the conclusion of the research. Except where paragraph 10.8 applies, the REC will continue as the main REC for all purposes, including the review of substantial amendments, approval of new sites and monitoring. Where it is proposed to add new

sites, other local RECs will be responsible for site-specific assessment in the normal way.

10.5 Where the favourable ethical opinion was given by a REC that was not recognised by UKECA[1], or was not recognised for the appropriate type of research, the opinion remained legally valid until 1 May 2006. At this point, UKECA took steps to give a limited form of type iii recognition to RECs that would not have been recognised to review such trials if they had been new applications. This "transitional recognition" means that:

- Type ii recognised RECs continue as the main REC for a trial being conducted anywhere in the UK
- RECs without recognition to review any new CTIMPs continue as the main REC for a trial being conducted anywhere in the UK.

10.6 RECs receiving "transitional recognition" under paragraph 10.5 may therefore give an opinion on a substantial amendment or the addition of a new site, receive progress reports and carry out other monitoring functions. However, RECs without recognition to review *any* new CTIMPs should note the following guidance:

- If a substantial amendment is submitted to a trial, it should not give an opinion without consulting another REC with recognition to review new CTIMPs.
- Advice should be sought from the OREC Manager on an appropriate REC to consult. This REC should then be sent copies of the amendment documentation, together with any other necessary information for background (e.g. the current protocol and patient information sheet).
- The REC whose advice is requested should review the amendment in sub-committee (either at a meeting or by correspondence) and provide written advice to the main REC indicating what its opinion would be.
- Taking this advice into account, the main REC should then review the amendment at a sub-committee meeting in accordance with normal procedures and issue its opinion.

[1] Where an ethics committee ceased to exist and all its functions were transferred to another ethics committee prior to 1 May 2004, and this committee is then recognised, all the ethical opinions of the former committees are treated as having been given by a recognised committee in accordance with paragraph 10.4. This applies particularly to the opinions given under the previous ethics committee system in Northern Ireland.

10.8 Where the CTIMP has ethical approval from a Type 2 recognised REC, this REC may continue as the main REC except that its authority to give an opinion on research sites in another domain(s) would expire on 1 May 2006. At this point the Chief Investigator would be required to submit a new application for review by a Type 3 REC if proposing to extend the trial to become multi-domain.

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Multi-site CTIMPs

10.9 Where the favourable ethical opinion was given by a Type 3 REC, paragraph 10.4 applies.

10.10 Where favourable ethical opinions were given by more than one REC, these opinions remain valid. However, no further opinions should be given in relation to the study, in particular on substantial amendments or new sites, until one of the RECs has been appointed by NRES Head Office as the main REC. The sponsor or Chief Investigator for any such study should apply as soon as possible in writing to the Operations Director at NRES, giving the following information:

- Full title of study
- Details of the Chief Investigator
- Names and references of the RECs that gave a favourable opinion.

10.11 The application may indicate which of the RECs the sponsor or Chief Investigator would prefer to be appointed as the main REC. The primary criterion should be that the REC is recognised to review the appropriate type of research. The secondary criterion is geographical proximity to the Chief Investigator's professional base.

10.12 NRES Head Office should appoint the main REC by writing to the sponsor or Chief Investigator, copied to all the RECs concerned. The RECs not appointed as main REC continue to be responsible for any advice required by the main REC on issues relating to their own sites.

10.13 Where none of the RECs concerned would be recognised to review a new CTIMP application, the Operations Director should nevertheless appoint one of the RECs as the main REC for the trial. The guidance in paragraph 10.6 applies to the continuing review of the trial by this REC.

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Single-site non-CTIMPs

10.14. The favourable opinion remains valid for the duration of the study and the REC concerned should continue to carry out all the functions of the main REC, including the review of substantial amendments, approval of new sites and monitoring.

10.15 Where the Chief Investigator proposes to extend the study to another site, whether in the same domain or another domain, the REC should continue as main REC. If the study involves procedures requiring SSA, this should be carried out in the normal way.

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Multi-site non-CTIMPs

10.16 Where the favourable ethical opinion was given by a Type 3 REC, the opinion remains valid. The Type 3 REC will continue as the main REC for all purposes, including the review of substantial amendments, approval of new sites and monitoring. Where it is proposed to add new sites requiring SSA, other RECs will be responsible for site-specific assessment in the normal way.

10.17 Where favourable ethical opinions were given by more than one REC, these opinions remain valid. However, no further opinions should be given in relation to the study, in particular on substantial amendments or new sites, until one of the RECs has been appointed by NRES Head Office as the main REC. The procedures in paragraphs 10.10–10.13 apply.

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Previous "locality approval" for multi-site studies

10.18 Issues arise in relation to multi-site studies given "locality approval" by local RECs under the Annex D scheme prior to 1 March 2004. Such studies are likely to fall within the category now requiring site-specific assessment under SOPs (see

paragraphs 4.19–4.32). However, the previous locality approval may not be quite in accordance with the new procedures. For example:

- There may not be a clearly defined Principal Investigator for the site
- The site may not be defined in accordance with the new guidance in section 4 of SOPs.

10.19 As a general rule, it should be assumed that the research has a valid ethical opinion for the site, however it has been defined. It is a matter for the sponsor to ensure that the local investigators comply with the protocol and other ethically approved documentation, and that they are accountable to the Chief Investigator whether directly or through an appointed Principal Investigator.

10.20 Where significant changes are proposed to the conduct of the research at the site, in particular the appointment of a new Principal Investigator, an application for SSA should be submitted by completing the SSI Form. The opportunity should be taken by the local REC to conduct a full SSA under SOPs and advise the main REC accordingly. This could include a re-definition of local research site(s) and designated Principal Investigators. These arrangements should then be confirmed in writing to the Chief Investigator by the main REC.

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SSA exemption

10.21 An issue may arise in relation to SSA exemption where a main REC is appointed for a multi-site study with previous ethical approval from more than one REC. The Chief Investigator may ask the main REC to consider designating the study as SSA-exempt, taking account of the guidance in paragraphs 4.19-4.32. If the main REC agrees, there would then be no requirement for the main REC to give an opinion on the extension of the study to other sites, and no need to apply for SSA.

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Transfer of functions between RECs

10.22 The following guidance applies to all types of research.

10.23 The OREC Manager is responsible for arranging the transfer of functions from the "former REC" to the "new REC" in the following circumstances:

(i) Abolition of a REC by its appointing authority
(ii) Any other circumstance in which a REC ceases to operate (including mergers)
(iii) Revocation of recognition.

10.24 In the case of (i) and (ii) above, all studies for which the former REC was the main REC, and all outstanding applications, should be formally transferred to other appropriate RECs. In the case of (iii), only those CTIMPs that the REC is no longer recognised to review need to be transferred.

10.25 The choice of the new REC should take account of the following:

- In the case of CTIMPs, the new REC should be recognised to review new applications for the appropriate type of trial.
- Non-CTIMPs being conducted in more than one domain should normally be transferred to a Type 3 REC.
- As far as possible, studies should be transferred to new RECs within the same domain, or within the same OREC area.
- When transferring outside the OREC area, relevant OREC Managers should be consulted.

10.26 The new REC has full authority to give ethical opinions on outstanding applications, amendments or new sites.

10.27 In the case of outstanding applications, the new REC should continue to review the application in accordance with SOPs, taking account of the issues identified by the former REC and information requested of the applicant. There is no provision for making a second request for information or extending the normal 60 day time period.

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Section 11 Research involving human tissue

Statutory provisions

11.1 Detailed guidance on the provisions of the *Human Tissue Act 2004* relating to research involving human tissue is at Annex H. The Human Tissue Act ("HT Act") applies only in England, Wales and Northern Ireland, except for provisions relating to DNA and the storage of relevant material for transplantation, which are UK-wide.

11.2 Under the *Human Tissue (Scotland) Act 2006* the statutory provisions relating to research apply only to research involving tissue and organs from the deceased. A summary of these provisions is at Annex H. The Scottish Executive intends issuing guidance in the near future on how the principles of the HT Act apply to Scottish research generally. However, where a Scottish REC is considering an application for research involving human tissue from England, Wales or Northern Ireland, the full procedures set out in this section will apply.

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General policy

11.3 The general policy from NRES Head Office is that the NHS REC system should:

- Provide ethical review of research using human tissue collected, stored and used within the UK as required by legislation and/or GAfREC.
- Undertake ethical review in a proportionate way, taking account of any material risk of harm or distress to donors, their families and other research participants.
- Facilitate valuable research using human tissue of benefit to society, within the legal framework established by statute and common law within each country of the UK.

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Requirements for ethical review of research involving human tissue

England, Wales and Northern Ireland

11.4 Under the HT Act and the HT Regulations, researchers in England, Wales and Northern Ireland will legally require ethical approval in order to carry out the following activities:

- Storing or using the tissue of living or deceased persons for a research project without a licence from the Human Tissue Authority (HTA) (see paragraph 1.23 of Annex H).
- Storing or using tissue from the living for a research project without consent where the samples are anonymised to the researcher, i.e. in circumstances where the researcher is unable to identify the tissue donor and not likely to be able to do so in future (see paragraph 1.9(ii) of Annex H).
- Analysing human DNA in material from the body of a living person (or using the results of DNA analysis) without consent, in circumstances where they are unable to identify the tissue donor and not likely to be able to do so in future (see paragraph 1.18 of Annex H).
- Storing or using tissue for a research project where consent is required and the tissue is from adults unable to consent for themselves (see paragraphs 1.15-1.17 of Annex H).

11.5 The HT Regulations provide that, where ethical approval is required for research involving tissue in England, Wales or Northern Ireland, it must be given by:

- Any committee established or recognised under the Clinical Trials Regulations (including recognised RECs in Scotland), or
- Any other committee or persons appointed to advise on the ethics of research on human tissue and recognised for that purpose by or on behalf of the Secretary of State, National Assembly for Wales or the Department of Health, Social Services and Public Safety in Northern Ireland. (For health-related research this means any NHS REC in England and Wales or a HPSS REC in Northern Ireland.)

11.6 These provisions mean that, in general, researchers requiring ethical approval for the purpose of the HT Act will need to apply to a recognised REC under the Clinical Trials Regulations or to any NHS or HPSS REC in England, Wales or Northern Ireland.

With the exception of applications relating solely to the storage or use of imported tissue (see paragraph 11.38), the REC system should provide ethical review even where the research would not be within the normal remit of RECs under paragraph 3.1 of GAfREC. RECs are encouraged to use their discretion under paragraph 3.2 of GAfREC to accept applications relating to research not involving the tissue of NHS patients. Where a REC feels unable to consider an application, the OREC Manager should be informed so that the application can be allocated to another REC.

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Scotland

11.7 Under the Human Tissue (Scotland) Act 2006, research must be approved in writing where it takes place on an organ retained from a post-mortem examination carried out on the instructions of the Procurator Fiscal. Approval is also required for new research on organs retained from a post-mortem examination that took place before 1 September 2006. An Order made by Scottish Ministers under the Act specifies that such approvals must be given by:

- Any ethics committee established or recognised under the Medicines for Human Use (Clinical Trials) Regulations 2004, or
- Any other committee established to advise on the ethics of research investigations in human beings, and recognised for that purpose by or on behalf of the Secretary of State or the Scottish Ministers. This includes all NHS RECs in Scotland and England.

11.8 The Human Tissue (Scotland) Act 2006 does not require ethical approval where the research involves tissue blocks and slides retained from a post-mortem examination carried out on the instructions of the Procurator Fiscal, or tissues and organs retained from a hospital post-mortem examination, and there is authorisation for its use in research. However, under guidance issued on the Act in Scotland those responsible for the research project would be expected to obtain REC approval.

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Ethics and compliance with the law

11.9 When reviewing research involving human tissue, the role of the REC is to give an ethical opinion rather than to apply the law. The REC's opinion should be informed by and take account of legal requirements but is not limited by them. Where difficult issues of legal interpretation arise it is not the role of the committee to provide legal advice. RECs may provide researchers with essential information about the legal requirements. However, researchers should seek their own legal advice and/or consult the HTA for advice where appropriate.

11.10 In some cases, consent to the storage and use of tissue in research is not legally required by the HT Act, in particular for *existing holdings* and, subject to ethical approval, *tissue from living persons not identifiable to the researcher*. However, this does not mean that all such tissue should be used freely and without regard to issues of consent or other ethical considerations. The Human Tissue Authority (HTA) Code of Practice on Consent gives advice (see paragraphs 114-115) on questions to be considered in relation to the use of existing holdings in research. RECs should take compliance with this advice into account in a proportionate way in discussion with applicants.

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Applications for ethical approval

11.11 There are two possible routes to obtaining ethical approval for research involving storage or use of human tissue or analysis of DNA:

(i) Application for approval of a specific project using the normal REC application form (see paragraphs 11.13-11.17). Such approval lasts only for the duration of the project as described in the protocol and the application form.

(ii) Application for approval of a research tissue bank (RTB), which may confer generic ethical approval prospectively for a range of research to be carried out by the establishment responsible for the bank and/or by other researchers to whom tissue is released by the bank within the conditions of the ethical approval (see paragraphs 11.19-11.31). Such approval may be given for a

period of up to 5 years and will be renewable. A storage licence will be required from the HTA.

11.12 The same options apply where ethical approval:

- Is required by the HT Act in England, Wales or Northern Ireland in order to confer exemption from licensing or consent provisions (see paragraph 11.4)
- Is required by Departmental policy under research governance systems anywhere in the UK (broadly speaking, wherever the research involves the tissue of NHS patients), or
- Is not required by law or policy as the research involves material which is outside the definition of "relevant material", but is sought on a voluntary basis (for example, research involving cell lines).

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Project-based applications

11.13 Project-based applications should be made in the following cases:

(a) CTIMPs involving storage or use of human tissue.

(b) Research involving removal of human tissue or other bodily material from the living as part of the protocol (i.e. primarily for research purposes).

(c) Research involving the use of stored tissue or data in circumstances where the researcher is able, or could be able, to identify the donor(s).

(d) Research involving any contact with donors or relatives to seek consent, obtain further data or undertake any other research procedure.

(e) Research involving use of stored tissue from a research tissue bank which does not have ethical approval from a REC.

(f) Research involving use of stored tissue from a research tissue bank, which has ethical approval from a REC, but (a) the terms of the approval do not extend to generic approval for projects receiving tissue from the bank (see paragraph 11.29(c)), or (b) the tissue bank manager requires the researcher to obtain project-specific approval before agreeing to release tissue.

(g) Research involving stored tissue from a clinical diagnostic archive that is not licensed to store tissue for use in research and is not ethically approved.

(h) Research in Scotland involving organs, tissue blocks and slides no longer required for Procurator Fiscal purposes following post-mortem examinations, or research involving organs and tissue retained from hospital post-mortem examinations.

11.14 Project-based applications should be made using the normal REC application form and in accordance with normal booking procedures (see section 1). The application should be allocated as follows:

- CTIMPs should be allocated to recognised committees in accordance with normal procedures (see section 1).
- Non-CTIMPs seeking ethical approval for the purposes of the HT Act should normally be allocated for review by a REC in England, Wales or Northern Ireland. However, they could be reviewed by a recognised REC in Scotland and this might be appropriate where for example the research is being conducted in (or involves tissue from) both Scotland and another part of the UK. Where any of the participants are adults with incapacity in Scotland, the application should be made to Scotland A REC.
- Other non-CTIMPs taking place anywhere in the UK and submitted for ethical review under departmental policy or on a voluntary basis, but not seeking ethical approval for the purposes of the HT Act, may generally be allocated to any REC in the UK. Where any of the participants are adults with incapacity in Scotland, the application should be made to Scotland A REC.
- In Scotland, non-CTIMPs seeking ethical approval for the purposes of the Human Tissue (Scotland) Act 2004 and associated guidance should normally be allocated to a Scottish REC but may be allocated to a REC in England if necessary (see paragraph 11.7).

11.15 "Participants" includes any living person whose tissue is to be stored or used for the purpose of the research, even if the research requires no contact with them.

11.16 Applications should be reviewed in accordance with normal procedures. The standard approval conditions should be issued when issuing a favourable opinion.

11.17 Ethical approval for project-specific applications is confined to the specific project described in the protocol and the application form. It is permitted to seek approval for a project to be undertaken in several stages provided that these are clearly defined in the protocol and relate to the same set of research questions. It is not acceptable to use the project-specific application form to seek open-ended approval for use of stored tissue in future research programmes (although the terms of the consent itself may be generic and open-ended, allowing for future approved research using the same samples). Applications not relating to specific projects with a study protocol may be invalidated by Co-ordinators. Nor is it acceptable to submit substantial amendments to approved projects in order to use tissue for another project with a different set of research questions.

11.18 Where a researcher in *England, Wales or Northern Ireland* makes a specific project-based application but also plans to store the tissue beyond the life of the project for use in further projects, the following options are available:

- At the end of the project (assuming it is given a favourable opinion), the researcher may make a further project-based application. The application must be submitted no later than the date on which the first project ends (as defined in the protocol), otherwise continued storage of the tissue would require a licence from the HTA. If the second application is also granted a favourable opinion, continued storage of the tissue for use in this project will be lawful without a licence. At the end of the second project the options set out in this paragraph apply in the same way.
- At the end of the project the researcher may make an application for review of a RTB, including details of the plans for further research. The RTB will also require a storage licence from the HTA.
- Applications may be made simultaneously at the outset for review of the project and the longer term RTB, using both application forms. The two forms should be

submitted to the same REC and reviewed in conjunction. A storage licence will be required from the HTA at the end of the initial project.

- If none of the above steps are taken, the researcher will need to arrange for disposal of the tissue or transfer to an appropriately licensed tissue bank, or apply to HTA for a licence.
- The researcher may hold on to the tissue without a licence under the original REC approval provided it is being held as a record of the completed research project, for example to verify research data. Storage for this purpose without a licence should continue for no longer than necessary. If the tissue continues to be stored without a licence for the purpose of any other research project, further ethical approval should be sought using either the project-specific or RTB application process.

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Applications for ethical review of research tissue banks

11.19 Organisations responsible for the management of research tissue banks (RTB) anywhere in the UK may apply for ethical review of their arrangements for collection, storage, use and distribution of tissue. A "research tissue bank" (or "biobank") is defined for the purpose of these SOPs as:

> *A collection of human tissue or other biological material, which is stored for potential research use beyond the life of a specific project with ethical approval or for which ethical approval is pending.*

11.20 Tissue banks storing human tissue for use in as yet unspecified research must obtain a licence from the HTA (except in Scotland). There is no requirement for tissue banks to obtain ethical approval under the HT Act or under NHS research governance systems or GAfREC. Applications will therefore be made on a voluntary basis, but ethical approval for a bank may have benefits by facilitating programmes of research without a need for individual project-based ethical approval.

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Application form for RTB

11.21 An applicant seeking review of a RTB should select the relevant option on the application form sieve. This will produce a customised version of the form suited to review of tissue banking arrangements rather than a specific research project.

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Booking, allocation and validation of RTB applications

11.22 New applications should normally be booked via CAS and allocated to one of the panel of flagged RECs (see paragraph 1.38B).

11.23 The normal validation criteria in paragraph 1.48 do not apply. RTB applications should meet the following validation criteria:

(a) The appropriate version of the application form for a RTB has been submitted. The form must be in typescript

(b) The applicant's checklist has been completed and submitted. All documents listed in the checklist have been submitted.

(c) All relevant sections and questions have been completed, the text is in English and the print is clearly legible.

(d) The application form has been signed by the applicant.

(e) Where consent is to be sought from new donors, or fresh consent is to be sought from previous donors, copies of all information sheets and consent forms have been enclosed.

(f) All supporting documents have been marked with version numbers and dates.

(g) The applicant is based within the United Kingdom.