RES SOPs (Version 7.6) Summary of Changes, September 2022

How to use this document

This summary of changes document includes all of the revision from version 7.5.1 to version 7.6 of the Research Ethics Service Standard Operating Procedures (RES SOPs). The left-hand column shows the wording which was present in version 7.5.1 and deletions are indicated by ~~strikethrough~~. The right-hand column shows the wording which is now present in version 7.6 and additional text is indicated by <u>underline</u>.

General revisions			
	Updates to reflect changes to process for applications which are submitted and have been approved via the CTIMP combined review service.		
	Updates to remove references to geographical locations and face to face meetings		
	Updates to reflect changes to final report submissions		
	References to Approvals Officer, replaced with Approvals Specialist or Approvals Administrator or 'appropriate member of Approvals Staff'		
Glossary			
Page	SOP 7.5.1	Page	SOP 7.6
	No previous text	20	<u>CTIMP combined review - The combined and co-ordinated review process between the MHRA and REC</u>

Section 1: New applications for ethical review			
Para	SOP 7.5.1	Para	SOP 7.6
1.1	An application for ethical review of a research study should be made by the Chief Investigator (CI) for that study. Applications may not be submitted by the sponsor(s) on behalf of the Chief Investigator. The Chief Investigator should normally be professionally based in the United Kingdom. For international studies with a co-ordinating investigator outside the UK, a health professional based in the UK should normally be nominated as the Chief Investigator responsible for the conduct of the research in the UK. The REC may agree exceptionally to an application being submitted by a CI based outside the UK but should consider as part of the ethical review whether adequate arrangements are in place for supervision of the study in the UK.	1.1	An application for ethical review of a research study should be made by the Chief Investigator (CI) for that study. Applications may not be submitted by the sponsor(s) on behalf of the Chief Investigator. Applications submitted via the combined review service are submitted jointly by the Chief Investigator and the Sponsor. The Chief Investigator should normally be professionally based in the United Kingdom. For international studies with a co- ordinating investigator outside the UK, a health professional based in the UK should normally be nominated as the Chief Investigator responsible for the conduct of the research in the UK. The REC may agree exceptionally to an application being submitted by a CI based outside the UK but should consider as part of the ethical review whether adequate arrangements are in place for supervision of the study in the UK.
Table A	No text to be deleted	Table A	**Clinical trials of investigational medical products (CTIMPs) Type of CTIMP** / **Allocation** Phase 2a trials / Type 3 Recognised NHS REC

1.34	For full meetings, the applicant may decline the first available slot in the UK if ~~he/she~~ has a preference for a particular REC ~~that is either geographically convenient or has prior knowledge of closely related research~~ (for example, it has reviewed an earlier phase trial ~~of the same medicinal product~~).	1.34	For full meetings, the applicant may decline the first available slot in the UK if they have a preference for a particular REC (for example, it has reviewed an earlier phase of the trial).
	No previous text	1.43	Applications which have been submitted via the CTIMP combined review service will be validated by the MHRA. The MHRA will confirm the validation status to the applicant. The REC staff do not need to undertake a formal validation check but should check the application against the validation checklist and request any missing information or clarifications from the applicant if required.
1.4~~3~~	The appropriate validation checklist should always be completed in HARP.	1.44	The appropriate validation checklist should always be completed in HARP (not required for applications submitted via the CTIMP combined review service).
1.4~~7~~	When an application is valid, the Chief Investigator and sponsor should be notified.	1.48	When an application is valid, the Chief Investigator and sponsor should be notified (not required for applications submitted via the CTIMP combined review service).
1.5~~0~~	In the case of an invalid application, the Chief Investigator should be notified of the reasons using SL3. The application is void and should be removed from the assigned meeting in HARP. Time permitting, the meeting	1.51	In the case of an invalid application, the Chief Investigator should be notified of the reasons using SL3. The application is void and should be removed from the assigned meeting in HARP (this does not apply for applications submitted via the

	slot will then become available to be booked into. The Chief Investigator may re-book and re-submit the application, in which case it should be treated as a new application.		CTIMP combined review service, the same meeting slot should be retained where possible). Time permitting, the meeting slot will then become available to be booked into. The Chief Investigator may re-book and re-submit the application, in which case it should be treated as a new application.
1.5~~3~~	Applications should not be made available to REC members unless valid.	1.54	Applications should not be made available to REC members unless valid. For applications submitted via the CTIMP combined review service, applications may be provided to REC members if necessary whilst the outcome of the MHRA validation is awaited.
	No previous text	1.84	For applications submitted via the CTIMP combined review service, applications can only be withdrawn up to the point at which an initial outcome has been issued. If an applicant chooses to withdraw an application after the initial outcome has been issued (e.g. where an applicant chooses not to respond to requests for further information), the application should be set as not approved and an unfavourable opinion letter issued with the reason 'applicant decision to withdraw'.
Section 2: Full meetings of a Research Ethics Committee			
Para	SOP 7.5.1	Para	SOP 7.6
~~2.28~~	~~Members are normally expected to attend in person but may attend by teleconference or videoconference with the permission of an Operational Manager.~~		Text deleted
2.3~~2~~	The following should not be counted for the purpose of the quorum:	2.31	The following should not be counted for the purpose of the quorum:

	• Approvals staff/REC Manager or REC Assistant. • Advisers or referees. • Members who are yet to arrive at the meeting, or who have left early. • Members who submit written comments but do not attend ~~either in person or by teleconference or videoconference~~ (see paragraph 2.4~~3~~). • Deputy members attending alongside the lead member. If a deputy member chooses to attend a REC meeting alongside the lead member, they may take part in the discussion but must not take part in a vote if a vote needs to be taken to agree the ethical opinion (see paragraph 2.7~~5~~).		• Approvals staff/REC Manager or REC Assistant. • Advisers or referees. • Members who are yet to arrive at the meeting, or who have left early. • Members who submit written comments but do not attend (see paragraph 2.4<u>2</u>). • Deputy members attending alongside the lead member. If a deputy member chooses to attend a REC meeting alongside the lead member, they may take part in the discussion but must not take part in a vote if a vote needs to be taken to agree the ethical opinion (see paragraph 2.7<u>4</u>). • <u>Observers to the meeting.</u>
2.7~~1~~	If any observer is present, the Chair should verbally inform any study representative who attends the meeting. The attending study representative should be given the opportunity to object to the presence of an observer (other than an official observer). If there is an objection, the observer should be asked to leave the meeting ~~room~~ for that item. The attendance of observers should be recorded in the minutes.	2.7<u>0</u>	If any observer is present, the Chair should verbally inform any study representative who attends the meeting. The attending study representative should be given the opportunity to object to the presence of an observer (other than an official observer). If there is an objection, the observer should be asked to leave the meeting for that item. The attendance of observers should be recorded in the minutes.

2.7~~7~~	The responsibilities of ~~the Approvals Officer/REC Manager or the Approvals Administrator/REC Assistant~~ in relation to REC meetings are as follows: (i) Publishing the schedule of REC meetings. (ii) Preparing the agenda. (iii) Allocating lead reviewers. (iv) Distributing/making available the agenda ~~and documents as well as making arrangements for the destruction of confidential waste after the meeting~~ (v) Inviting Chief Investigators and, where appropriate, supervisors to attend and making the necessary arrangements. ~~(vi) Preparing the venue/meeting room.~~ (vii) Recording apologies for absence prior to the meeting. (viii) Recording the attendance of members, deputy members, referees and observers for the discussion of each application for ethical review. (ix) Advising the members as necessary on compliance with standard operating procedures and, where relevant, the need for the REC to consider legal requirements applying to the ethical review (e.g. the criteria for approval under the UK Mental Capacity Acts). If clarification on legal or policy matters is required, or the Approvals Officers/REC Managers have any concerns	2.7<u>6</u>	The responsibilities of <u>staff</u> in relation to REC meetings are as follows: (i) Publishing the schedule of REC meetings. (ii) Preparing the agenda. (iii) Allocating lead <u>and second</u> reviewers. (iv) Distributing/making available the agenda and documents <u>on the HARP Reviewer Portal.</u> (v) Inviting Chief Investigators and, where appropriate, supervisors to attend and making the necessary arrangements. (vi) Recording apologies for absence prior to the meeting. (v<u>ii</u>) Recording the attendance of members, deputy members, referees and observers for the discussion of each application for ethical review. (<u>viii</u>) Advising the members as necessary on compliance with standard operating procedures and, where relevant, the need for the REC to consider legal requirements applying to the ethical review (e.g. the criteria for approval under the UK Mental Capacity Acts). If clarification on legal or policy matters is required, or the Approvals Officers/REC Managers have any concerns about the meeting, the Approvals Officers/REC Manager should provide this to the Chair after the meeting, before any ethical opinion is issued. (<u>ix</u>) Providing guidance to members if inappropriate issues are raised during the meeting and advising members on the correct use of ethical decisions.

	about the meeting, the Approvals Officers/REC Manager should provide this to the Chair after the meeting, before any ethical opinion is issued. (x) Providing guidance to members if inappropriate issues are raised during the meeting and advising members on the correct use of ethical decisions. (xi) Making a written record of the meeting. (xii) Recording individual votes where a vote is taken on a decision (e.g. 12 for / 3 against). (xiii) Preparing the minutes of the meeting within 2 working days and obtaining subsequent approval at the following meeting. (xiv) Notifying applicants of ethical decisions taken at the meeting and taking other follow-up action as necessary. (xv) Recording any material Declaration of Interests (DOI) and subsequent actions.		(x) Making a written record of the meeting. (xi) Recording individual votes where a vote is taken on a decision (e.g. 12 for / 3 against). (xii) Preparing the minutes of the meeting within 2 working days and obtaining subsequent approval at the following meeting. (xiii) Notifying applicants of ethical decisions taken at the meeting and taking other follow-up actions, as necessary. (xiv) Recording any material Declaration of Interests (DOI) and subsequent actions. (xv) Checking the meeting is quorate throughout its duration.
2.7~~8~~	The minutes of the REC meeting should be prepared by ~~the secretary~~ to the meeting.	2.77	The minutes of the REC meeting should be prepared by the relevant members of staff to the meeting.
Section 3: Giving an Ethical Opinion			
Para	SOP 7.5.1	Para	SOP 7.6
3.1	Under the Clinical Trials Regulations, a REC is required to give a~~n~~ ethical opinion on an application relating to a CTIMP (except where paragraph 3.2 applies) within 60	3.1	Under the Clinical Trials Regulations, a REC is required to give a final ethical opinion on an application relating to a CTIMP (except where paragraph 3.2 applies) within 60 calendar days

	calendar days of the receipt of a valid application. Where the REC considers that further information is required in order to give an opinion, the REC may give a provisional opinion and make one request in writing for further information from the applicant. The period of 60 days will be suspended pending receipt of this information.		of the receipt of a valid application. Where the REC considers that further information is required in order to give an opinion, the REC may give a provisional opinion (referred to as a request for further information for applications submitted via the CTIMP combined review service) and make one request in writing for further information from the applicant. For applications submitted via the CTIMP combined review service, the initial outcome should be issued within 30 days of receipt of a valid application. The period of 60 days will be suspended pending receipt of this information.
3.10	Notification of the decision should be sent to the Chief Investigator (CI) within at least 10 working days of a full meeting (preferably fewer), or within 5 working days of a proportionate review meeting. In the case of projects undertaken primarily for educational purposes, the decision letter or email and all further correspondence should be addressed to the student (or the first named student on the application if more than one is involved) and copied to the CI if different. All letters should be in the name of the Chair of the REC, it is acceptable for the letter to be signed by a vice- Chair or member of staff supporting the REC acting under delegated authority from the Chair. One of the following letters or email templates should be used: Applications reviewed at a full meeting: SL5 Favourable opinion SL6 Unfavourable opinion	3.10	Notification of the decision should be sent to the Chief Investigator (CI) within at least 10 working days of a full meeting (preferably fewer), or within 5 working days of a proportionate review meeting. For applications submitted via the CTIMP combined review service, the initial outcome should be issued in HARP within 28 days of the receipt of a valid application to allow a period of consolidation with the MHRA prior to the initial outcome being issued to the applicant by day 30. In the case of projects undertaken primarily for educational purposes, the decision letter or email and all further correspondence should be addressed to the student (or the first named student on the application if more than one is involved) and copied to the CI if different. All letters should be in the name of the Chair of the REC, it is acceptable for the letter to be signed by a vice- Chair or member of staff supporting the REC acting under delegated authority from the Chair. One of the following letters or email templates should be used: Applications reviewed at a full meeting:

	Provisional opinion with request for further information (this will usually be ~~be~~ sent as a standalone email rather than as a letter). SL8 Provisional opinion pending consultation with a referee. Applications reviewed by sub-committee under proportionate review: SL5 (PR) Favourable opinion SL6 (PR) Unfavourable opinion SL7 (PR) Provisional opinion with request for further information (this will usually be sent as a standalone email rather than as a letter). SL8 (PR) No opinion – application referred to full meeting		SL5 Favourable opinion SL6 Unfavourable opinion Provisional opinion with request for further information (this will usually be sent as a standalone email rather than as a letter – for applications submitted via the CTIMP combined review service, requests for further information are submitted via HARP). SL8 Provisional opinion pending consultation with a referee. Applications reviewed by sub-committee under proportionate review: SL5 (PR) Favourable opinion SL6 (PR) Unfavourable opinion SL7 (PR) Provisional opinion with request for further information (this will usually be sent as a standalone email rather than as a letter). SL8 (PR) No opinion – application referred to full meeting
3.11	The following information should in all cases be included in the letter or in enclosures: • List of requests for further information from the applicant or additional conditions to be met, including an explanation of the reasons based on the RECs discussion. • A list of all documents reviewed at the meeting, giving correct version numbers and dates.	3.11	The following information should in all cases be included in the letter or in enclosures: • List of requests for further information from the applicant or additional conditions to be met, including an explanation of the reasons based on the RECs discussion. • A list of all documents reviewed at the meeting, giving correct version numbers and dates.

	• A list of the members who were present for the discussion of the application or who submitted written comments on the application prior to the meeting. The list ~~should indicate lay members and give the profession in the case of expert members (this~~ will be issued with the final opinion letter). • Declarations of interest by members, which were material to the application, and whether or not the member concerned took part in the review and voted on the decision (it is not necessary to give details of the interests, only that a declaration was made). This will be included on the final opinion letter. • The names of any observers present at the meeting. • The detail of any requests for further information from the applicant needed before the final opinion can be issued or any conditions of the favourable opinion, this will be confirmed on the final opinion letter.		• For non-CTIMPs a list of the members who were present for the discussion of the application or who submitted written comments on the application prior to the meeting. The list will be issued with the final opinion letter. For CTIMPs the membership list is available on request. • Declarations of interest by members, which were material to the application, and whether or not the member concerned took part in the review and voted on the decision (it is not necessary to give details of the interests, only that a declaration was made). This will be included on the Provisional Opinion status update or final opinion letter (if an outright Favourable Opinion or Unfavourable Opinion is issued). • The names of any observers present at the meeting. • The detail of any requests for further information from the applicant needed before the final opinion can be issued or any conditions of the favourable opinion, this will be confirmed on the final opinion letter.
3.15	The opinion of the REC should be entered on HARP. The date of the opinion is the date on which the final opinion letter is sent.	3.15	The opinion of the REC should be entered on HARP. The date of the opinion is the date on which the final opinion letter is sent. For applications submitted via the CTIMP combined review service, the date of the opinion is the date the UK final opinion is issued to the applicant.
3.16	When giving a favourable opinion, the REC may specify any conditions to be met prior to the start of the study (or the start at each site). These should be clearly set out in the favourable opinion letter. The conditions must be met in order for the favourable opinion to be in place once the study starts; until they are met, the study does not have a	3.16	When giving a favourable opinion, the REC may specify any conditions to be met prior to the start of the study (or the start at each site). These should be clearly set out in the favourable opinion letter. The conditions must be met in order for the favourable opinion to be in place once the study starts; until they are met, the study does not have a favourable opinion and

	favourable opinion and should not start. It is the responsibility of the sponsor to ensure that the specified conditions are met.		should not start. It is the responsibility of the sponsor to ensure that the specified conditions are met. For applications submitted via the CTIMP combined review service, additional conditions should be issued as a request for further information prior to confirmation of a final favourable opinion. Consideration should therefore be given to whether a provisional opinion would be more appropriate.
3.25	In a CTIMP or a clinical investigation of a medical device, the REC should consult the MHRA before giving an unfavourable opinion where the reasons include issues relating to the safety of the trial or the sponsor's planned arrangements for safety monitoring and should take its advice into account. It is strongly recommended that, where the REC is minded to give an unfavourable opinion on such grounds, it should issue a provisional opinion setting out the issues of concern, invite the sponsor to provide further information addressing these points and consult the MHRA in parallel. Procedures for consulting MHRA are set out in Section 14.	3.25	In a CTIMP or a clinical investigation of a medical device, the REC should consult the MHRA before giving an unfavourable opinion where the reasons include issues relating to the safety of the trial or the sponsor's planned arrangements for safety monitoring and should take its advice into account. It is strongly recommended that, where the REC is minded to give an unfavourable opinion on such grounds, it should issue a provisional opinion setting out the issues of concern, invite the sponsor to provide further information addressing these points and consult the MHRA in parallel. Procedures for consulting MHRA are set out in Section 14. For applications submitted via the CTIMP combined review service, the REC should issue the reasons why a favourable opinion cannot be issued as a request for further information. The applicant is permitted to respond prior to the REC confirming the final opinion which may be unfavourable.
3.27	Where the Committee or sub-committee requests further information from the applicant, it should decide in the initial review the procedures for considering that information and determining the REC's final opinion. These responsibilities should normally be delegated to one of the following:	3.27	Where the Committee or sub-committee requests further information from the applicant, it should decide in the initial review the procedures for considering that information and determining the REC's final opinion. This also applies to consolidation with the MHRA for applications submitted via the CTIMP combined review service. These responsibilities should normally be delegated to one of the following:

	(i) Designated REC supporting staff (eg. Approvals Officer/REC Manager). (ii) Officer of the reviewing committee alone. (iii) Officer of the reviewing committee and the designated lead reviewer for the study. (iv) Chair or vice-chair, in oral or written consultation with one or more named members or deputy members that were present at the meeting or who submitted written comments on the application, or with a Scientific Officer. (v) Exceptionally, a Sub-committee involving named members.		(i) Designated REC supporting staff (e.g. Approvals Officer/REC Manager). (ii) Officer of the reviewing committee alone. (iii) Officer of the reviewing committee and the designated lead reviewer for the study. (iv) Chair or vice-chair, in oral or written consultation with one or more named members or deputy members that were present at the meeting or who submitted written comments on the application, or with a Scientific Officer. (v) Exceptionally, a Sub-committee involving named members.
3.30	The application clock should be suspended from the date on which the request for further information was sent to the applicant. It should be re-started on the date when a complete response is received ("the re-start date").	3.30	The application clock should be suspended from the date on which the request for further information was sent to the applicant (for applications submitted via the CTIMP combined review service, the clock should be suspended on the date the Part 1 & Part 2 outcomes are submitted in HARP). It should be re-started on the date when a complete response is received ("the re-start date").
3.33	If the applicant's response is incomplete or does not appear to fully address the matters raised, the REC is entitled to insist on a complete response before issuing its final opinion. The Approvals Officer/REC Manager should write to the applicant using SL11 or SL11 (PR) as applicable, setting out the further information or clarification still required (the letter may be issued more	3.33	If the applicant's response is incomplete or does not appear to fully address the matters raised, the REC is entitled to insist on a complete response before issuing its final opinion. The Approvals Officer/REC Manager should write to the applicant using SL11 or SL11 (PR) as applicable, (issued as an RFI clarification via HARP for applications submitted via the CTIMP combined review service) setting out the further information or

	than once if the response continues to be incomplete). It is recommended that the applicant is contacted to discuss the outstanding points and clarify what is expected. The REC is not entitled to raise any new issues or concerns at this stage of the process. The clock should remain suspended until a complete response is received from the applicant.		clarification still required (the letter may be issued more than once if the response continues to be incomplete). It is recommended that the applicant is contacted to discuss the outstanding points and clarify what is expected. The REC is not entitled to raise any new issues or concerns at this stage of the process. The clock should remain suspended until a complete response is received from the applicant.
3.34	The applicant should normally be allowed a period of no more than two months to respond to the request for further information. The provisional opinion letter will request a response within one month. If the applicant has not responded within one month, a reminder letter should be sent using SL12. If no response is received within one further month, the Approvals Officer/REC Manager should normally send SL13 advising that the REC considers the application to have been withdrawn. The applicant would then be required to submit a new application in order to obtain an ethical opinion. However, the Approvals Officer/REC Manager may extend the two-month period at the request of the applicant where there are reasonable grounds for requiring more time to respond.	3.34	The applicant should normally be allowed a period of no more than two months to respond to the request for further information (14 days for applications submitted via the CTIMP combined review service). The provisional opinion letter will request a response within one month. If the applicant has not responded within one month, a reminder letter should be sent using SL12. If no response is received within one further month, the Approvals Officer/REC Manager should normally send SL13 advising that the REC considers the application to have been withdrawn. The applicant would then be required to submit a new application in order to obtain an ethical opinion. However, the Approvals Officer/REC Manager may extend the two- month period at the request of the applicant where there are reasonable grounds for requiring more time to respond.
Section 4: Proportionate Review			
Para	SOP 7.5.1	Para	SOP 7.6
4.1	The Proportionate Review Service (PRS) provides for proportionate review of research studies raising no material ethical issues, including projects involving	4.1	The Proportionate Review Service (PRS) provides for proportionate review of research studies raising no material ethical issues, including projects involving straightforward

	straightforward issues which can be identified and managed routinely in accordance with standard research practice and existing guidelines. Proportionate Review applications are reviewed by a sub-committee rather than at a full meeting of a REC, with the final decision being notified to the applicant within 21 calendar days of receipt of a valid application. PR sub-committees may meet ~~face to face~~, via ~~teleconference~~ or via email correspondence. The meeting format should be agreed locally.		issues which can be identified and managed routinely in accordance with standard research practice and existing guidelines. Proportionate Review applications are reviewed by a sub-committee rather than at a full meeting of a REC, with the final decision being notified to the applicant within 21 calendar days of receipt of a valid application. PR sub-committees may meet via videoconference or via email correspondence. The meeting format should be agreed locally.
Section 5: Assessing the suitability of research sites			
Para	SOP 7.5.1	Para	SOP 7.6
5.1	In the case of a clinical trial of an investigational medicinal product, the Clinical Trials Regulations provide that a single ethic~~al~~ opinion should be given ~~on any trial,~~ regardless of the number of sites at which the research is to be conducted.	5.1	In the case of a clinical trial of an investigational medicinal product, the Clinical Trials Regulations provide that a single ethics opinion should be given regardless of the number of sites at which the research is to be conducted.
5.2	The policy of the Department of Health and Social Care and the devolved administrations is that ~~the requirement for~~ a single ethic~~al~~ opinion should apply generally to all multi-site research within the UK. The only exception to this is ~~where for~~ non-CTIMPs involving adults unable to consent for themselves and taking place at sites in both England or Wales and Scotland. In this case, two separate opinions must be given under the legislation applying in each jurisdiction (see paragraph 13.40).	5.2	The policy of the Department of Health and Social Care and the devolved administrations is that a single ethics opinion should apply generally to all multi-site research within the UK. The Chief Investigator should therefore submit a single application for ethics review, which should be allocated for review as specified in Section 1. The only exception to this is non-CTIMPs involving adults unable to consent for themselves and taking place at sites in both England or Wales or Northern Ireland **and** Scotland. In this case, two separate submissions are needed and two separate ethics opinions must be given

			under the legislation applying in each jurisdiction (see paragraph 13.40).
5.3	~~The Chief Investigator for any study should therefore submit a single application for ethical review, which should be allocated for review as specified in Section 1.~~	5.3	References to NHS sites should be read to include Health and Social Care (HSC) in Northern Ireland.
5.4	For certain types of study, the ethic~~al~~ review includes an assessment of the suitability of each non-NHS site or sites at which the research is to be conducted in the UK. The site- assessment for participating non-NHS sites is not a separate ~~ethical~~ review, but forms part of the single ethical review of the research.	5.4	For certain types of study, the ethics review includes an assessment of the suitability of each non-NHS Investigator site or sites at which the research is to be conducted in the UK. The site- assessment for participating non-NHS sites is not a separate review, but forms part of the single ethics review of the research.
5.5	An assessment of site suitability is a requirement for the following types of study: (i) Clinical trials of investigational medicinal products (CTIMPs). (ii) Clinical investigations of Medical Devices. (iii) Combined CTIMPs and clinical investigations of medical devices.	5.5	An Ethics assessment of non-NHS Investigator site suitability is a requirement for the following types of study: (i) Clinical trials of investigational medicinal products (CTIMPs). (ii) Clinical investigations of Medical Devices. (iii) Combined CTIMPs and clinical investigations of medical devices.
5.6	For research falling outside the categories listed in paragraph 5.5, an assessment of site suitability is not required for the purposes of ethic~~al~~ review. All ~~research~~ sites listed in the application to the REC, and any other ~~non-NHS~~ sites added during the course of the study, are deemed to be ethically approved as part of ~~a~~ favourable opinion from the REC. ~~Management permission is still required from the organisation responsible for hosting the research before it commences at any site.~~	5.6	For research falling outside the categories listed in paragraph 5.5, an assessment of site suitability is not required for the purposes of ethics review. All Investigator sites listed in the application to the REC, and any other non-NHS sites added during the course of the study, are deemed to be ethically approved as part of the original favourable opinion from the REC. Research should not be conducted by any organisation, or on participants under the duty of care of that organisation, until the relevant management permission/confirmation of capacity and capability (as appropriate to the type and location of the organisation) is given for that organisation.

5.7	~~In the case of any single or multi-site clinical research,~~ the investigator responsible for the conduct of ~~the~~ research at an ~~individual research site will be known as the Principal Investigator (PI) for that site. There should only be one Principal Investigator at each site.~~	5.7	The Principal Investigator (PI is the individual) responsible for the conduct of a research study at an Investigator Site. One Investigator Site may comprise of one or more Trial Sites. The 'Set up of research activity at NHS organisations' guidance in IRAS includes a definition of Investigator Site, Trial Site and information on the appropriate level of PI oversight. The principal scope of this guidance is interventional heath care research in the NHS however, the principles can also be applied to interventional research at non-NHS sites and non-interventional research, generally.
5.8	A "single site study" is a study that the Chief Investigator plans to conduct at one site only in the United Kingdom. In a non-CTIMP, the Chief Investigator should also be the Principal Investigator for the site. In the case of a single-site CTIMP, the CI and PI must be the same person.	5.8	A "single site study" is a study that the Chief Investigator plans to conduct at one Investigator Site only in the United Kingdom. In a non-CTIMP, the Chief Investigator should also be the Principal Investigator (PI) for the site. In the case of a single-site CTIMP, the CI and PI must be the same person.
5.9	A "multi-site study" is a study that the Chief Investigator proposes should be conducted at more than one site in the UK. The Chief Investigator may also be the Principal Investigator for one of the sites ~~(known as the "lead site")~~. ~~At other sites, a Principal Investigator should be appointed.~~ It is the responsibility of the Chief Investigator to ensure that a suitably qualified professional is appointed as the Principal Investigator for each site. In a CTIMP, the Principal Investigator and all other named investigators must be "authorised health professionals" (see definition in the Glossary).	5.9	A "multi-site study" is a study that the Chief Investigator proposes should have more than one Principal Investigator, that is to say that the study should be conducted at more than one site in the UK. The Chief Investigator may also be the Principal Investigator for one of the sites. It is the responsibility of the Chief Investigator to ensure that a suitably qualified professional is appointed as the Principal Investigator for each Investigator site. In a CTIMP, the Principal Investigator and all other named investigators must be "authorised health professionals" (see definition in the Glossary).
5.11	When there is a change of PI at a non-NHS/HSC site in a CTIMP or Clinical Investigation of a Medical Device, a	5.11	When there is a change of PI at a non-NHS/HSC Investigator site in a CTIMP or Clinical Investigation of a Medical Device, a

	substantial amendment should be submitted. The applicant should submit a Substantial Amendment and submit the non-NHS/HSC Site Assessment form and CV/evidence of professional registration for the PI. However, only questions 2 and 3 on the non-NHS/HSC Site Assessment Form need to be completed when the change relates to the appointment of a new PI.		substantial amendment should be submitted. The applicant should submit a substantial amendment and submit the non-NHS/HSC Site Assessment form and CV/evidence of professional registration for the PI. However, only questions 2 and 3 on the non-NHS/HSC Site Assessment Form need to be completed when the change relates to the appointment of a new PI. Substantial amendments to change the PI at a non-NHS/HSC site can be delegated to an operational manager for review on behalf of the REC.
5.12	**Definition of a research site** ~~Under the Clinical Trials Regulations, a "trial site" means a hospital, health centre, surgery or other establishment or facility in the UK at or from which a CTIMP, or any part of a CTIMP, is conducted. For administrative purposes, the guidance set out below applies to the definition of a research site in any study submitted to a REC in the UK.~~	5.12	**Trial sites and Investigator sites** The Medicines for Human Use (Clinical Trials) Regulations 2004 provide the following definitions, specifically for Clinical Trials of Investigational Medicinal Products (CTIMPs): 'trial site' means a hospital, health centre, surgery or other establishment or facility at or from which a clinical trial, or any part of such a trial, is conducted;' 'investigator' means, in relation to a clinical trial, the authorised health professional responsible for the conduct of that trial at a trial site, and if the trial is conducted by a team of authorised health professionals at a trial site, the investigator is the leader responsible for that team;'
5.13	~~In general, the research site should be identified as the single organisation responsible for hosting the research at a particular locality.~~	5.13	Whilst ICH-GCP (E6(R2)) provides the following definitions, specifically for CTIMPs: 'Trial site: The location(s) where trial-related activities are actually conducted.'

			‘Investigator: A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.’
5.14	~~In the case of research conducted within the NHS, the site will in most cases be one of the following:~~ ~~• An NHS Trust (in England).~~ ~~• An NHS Trust and Local Health Board (in Wales).~~ ~~• An NHS Health Board (in Scotland).~~ ~~• A Health and Social Care Trust (in Northern Ireland).~~ ~~• A GP practice or NHS dental practice.~~	5.14	The term 'Investigator Site' means the activities (regardless of their location) with effective oversight by one Principal Investigator.
5.15	~~Where the research will be conducted at more than one location within the same NHS organisation (for example, where the departments involved are dispersed at different hospitals within an acute Trust or Health Board), this should normally be considered as a single site.~~	5.15	Whether research activities performed at different locations are undertaken in one, two, or more Investigator Sites is not determined by whether the locations are within the same legal entity, or are under the same management, nor by whether the personnel undertaking those activities share the same employer, but by the ability of each PI to effectively oversee the work being conducted at their Investigator Site. Further information is included in the ‘Set up of research activities at NHS organisations’ guidance in IRAS
5.16	~~Exceptionally, where the research is to be conducted in two or more entirely discrete operating units within the same NHS organisation, these units may be separately identified as research sites. Each site should have its own Principal Investigator who is accountable for the whole research team. There should be no dual accountability or overlap between research teams. These criteria might apply for example to the~~	5.16	In the case of research conducted within the NHS, each trial site will in most cases be one of the following: • An NHS Trust (in England). • An NHS Trust and Local Health Board (in Wales). • An NHS Health Board (in Scotland). • A Health and Social Care Trust (in Northern Ireland).

	~~operating divisions or community health partnerships established by NHS Health Boards in Scotland. They do not apply to separate clinical departments within the same acute Trust.~~		• A GP practice or NHS dental practice. Guidance on specific scenarios is available in IRAS.
5.17	~~For research conducted by GPs and NHS dentists, the Clinical Commissioning Group (England), Health Board (Scotland), Local Health Board (Wales) or Business Services Organisation (Northern Ireland) is the 'organisation providing care'. In England, primary care organisations may be grouped together by Local Clinical Research Network regions but there is no overarching organisation that provides care. However, the GP or dental practice should normally be identified as the research site as it provides contractual services to the care organisation as an independent practitioner. The following scenarios should be noted:~~ ~~• Where two or more GPs or dentists are conducting a study within the same practice, it should be regarded as a single site and one of the practitioners should be appointed as the Principal Investigator.~~ ~~• In some cases, two or more independent practices may be conducting the research within the same health care centre. These practices should normally be identified as separate research sites.~~ ~~• Where, however, two or more practices have contracted to conduct research collaboratively, whether through a network/consortium or under the direct management of the care organisation, they may be collectively identified as a single site. In such cases, one of the investigators should be appointed as the Principal~~	5.17	To effectively oversee research activity, any one legal entity might have one, or more than one, Principal Investigator, and/or there may be one Principal Investigator for more than one legal entity. Appropriate Principal Investigator oversight in interventional research is described in the Set up of research activity at NHS organisations' guidance in IRAS. Similar principles apply in non-interventional research (that the research activities within one Investigator Site is determined by whether those activities may be most effectively overseen by one Principal Investigator). For example, a large geographical area could be identified as the Investigator site for some studies in public health, epidemiology or needs assessment.

	~~Investigator for the site. Researchers other than GPs and dentists may also be involved in the network/consortium.~~		
5.18	~~A Clinical Commissioning Group, Health Board, Local Health Board or the Business Services Organisation may itself be identified as the research site in the case of research being conducted into primary, community or social care services that it manages directly. However, in England, Wales and Northern Ireland, where the investigator is employed by the primary care organisation but provides services to an acute Trust on its premises, the research site will normally be the acute Trust. In Scotland, both primary and acute care services are managed by Health Boards.~~	5.18	The same principles included in the Set up of research activity at NHS organisations (interventional research) IRAS guidance also apply to non-NHS sites.
5.19	~~On rare occasions, a pragmatic open label clinical trial may involve an investigator at a hospital randomising a participant to a treatment which the GP is then asked to prescribe. As long as it is clear that the intention was always for the GP to prescribe whichever medication the participant is allocated to, that the GP is conducting no other activities in relation to the study or making any decisions in relation to the study protocol, and that this is clearly described in the protocol and REC application form, then the GP surgery would not be classed as a research site. The REC must, however, be satisfied that this is the case. If the REC is not satisfied that these arrangements have been clearly described in the application form and study protocol, then an assessment of the site may be required.~~	5.19	Trial sites outside the NHS could include the following: • an academic institution; • a research centre funded by the voluntary sector; • a Government Department or other public body; • a Prison Service establishment, local authority secure unit or Home Office secure training centre; • a private company or corporation (for example, a pharmaceutical or biotechnology company or clinical research organisation);

			• a private hospital or private clinical practice; • an employee-led social enterprise. Where the research site is outside the NHS in terms of accountability (is not part of an NHS investigator site), but is using NHS facilities by agreement (for example, a private practice based at a GP surgery or a private research unit renting premises at a NHS hospital), the name of the organisation responsible for the research conduct should be clearly distinguished from the NHS organisation concerned(and it should be clear to potential and actual research participants that the NHS is not involved and that they are not under NHS care for the purposes of the research).
5.20	~~A large geographical area in England could be identified as the research site for some research, for example studies in public health, epidemiology or needs assessment.~~	5.20	In some cases, an NHS Investigator site may include activities undertaken by or at non-NHS organisations. For example, MRI scans may be undertaken on premises owned by universities, research charities or private companies. These activities are still within the one NHS Investigator Site, as long as the NHS Principal Investigator is responsible for overseeing them and therefore, no separate Site-Specific Assessment of this non-NHS site or notification to the REC is needed. If separate PI oversight arrangements are needed, the activities are within a separate Investigator Site.

5.21	~~Research sites outside the NHS could include the following:~~ ~~• an academic institution;~~ ~~• a research centre funded by the voluntary sector;~~ ~~• a Government Department or other public body;~~ ~~• a Prison Service establishment, local authority secure unit or Home Office secure training centre;~~ ~~• a private company or corporation (for example, a pharmaceutical or biotechnology company or clinical research organisation);~~ ~~• a private hospital or private clinical practice;~~ ~~• an employee-led social enterprise.~~ ~~Where the research site is outside the NHS in terms of accountability, but the Principal Investigator is using NHS facilities by agreement (for example, a private practice based at a GP surgery or a private research unit renting premises at a NHS hospital), the name of the site should be clearly distinguished from the NHS organisation concerned.~~		Trial sites are organisations responsible for participant-related research procedures specified in the protocol and overseen by a Principal Investigator, including recruitment and informed consent (there may be one or more trial site overseen by one principal investigator, or one trial site may have one or more principal investigator). The following are not considered to be trial sites as they do not undertake activities requiring PI oversight: • Participant Identification Centres (PICs), i.e. organisations from which clinicians or clinical units refer potential participants to the research team based in another organisation, for assessment and possible recruitment to a study. • Data Collection Centres (DCCs) or Tissue Collection Centres (TCCs) in the context of applications for ethical review of research databases or research tissue banks respectively (see paragraph 11.30 and 12.27). • Research units undertaking support functions,

			e.g. project management, site monitoring, data analysis or report writing.
5.22	~~In some cases, a study hosted by an NHS care organisation may involve clinical procedures required by the protocol to be undertaken by non-NHS organisations under contractual arrangements with the NHS organisation. For example, MRI scans or laboratory analysis may be undertaken on premises owned by universities, research charities or private companies. These arrangements may be considered as a single NHS site where all of the following conditions are met:~~ ~~• All the participants are NHS patients recruited through the NHS organisation.~~ ~~• The relevant NHS R&D office (which may be a joint research office acting on behalf of more than one organisation) assumes full responsibility under the UK Policy Framework for Health and Social Care Research for all procedures involving NHS patients at the site, including those undertaken by non-NHS organisations.~~ ~~• Indemnity for all procedures is in place under the Clinical Negligence Scheme for Trusts ("NHS indemnity").~~ ~~Where any of these conditions are not met, the non-NHS organisation should be considered a separate site.~~	5.22	Site specific assessment for NHS sites is delegated to the research management function of the NHS site. The REC does not undertake site specific assessment at NHS sites. A standard condition of a favourable opinion from the REC is that Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) at the organisation level should be obtained prior to any research project activity commencing at an Investigator site within the NHS or Health and Social Care in Northern Ireland (HSC).
5.23	~~Research sites are organisations responsible for participant-related research procedures specified in the protocol, including recruitment and informed consent.~~ ~~The following are not considered to be research sites:~~	5.23	Responsibility for assessing the suitability of non-NHS Investigator sites in the UK lies with the REC and will be carried out by the REC as part of the ethics review

	~~• Participant Identification Centres (PICs), i.e. organisations from which clinicians or clinical units refer potential participants to the research team based in another organisation, for assessment and possible recruitment to a study.~~ ~~• Data Collection Centres (DCCs) or Tissue Collection Centres (TCCs) in the context of applications for ethical review of research databases or research tissue banks respectively (see paragraph 11.30 and 12.27).~~ ~~• Research units undertaking support functions, e.g. project management, site monitoring, data analysis or report writing.~~		for study types which require this assessment (see paragraph 5.5)
5.24	~~Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) at the site level should be obtained prior to any research project activity commencing at a site within the NHS or Health and Social Care in Northern Ireland (HSC). This process is started by submitting the main IRAS application form. Guidance on the UK-nation specific mechanisms for providing site level documentation and information is available within IRAS Help. In England and Wales, research project activity at NHS sites should not commence until HRA and HCRW Approval is also in place.~~	5.24	For CTIMPs and clinical investigations of medical devices, the non-NHS Investigator sites require a site assessment by the REC. However, it may be necessary to arrange for routine clinical procedures required by the protocol to be carried out by other non-NHS organisations in support of the research. For example, routine imaging using standard clinical protocols may be undertaken by a private scanner centre under contractual arrangements with the NHS care organisation where the participants are recruited. These activities are still within the one NHS Investigator Site, **as long as the NHS Principal Investigator is responsible for overseeing them** and there is no need to notify the REC separately of these non-NHS subsidiary sites. If separate PI oversight arrangements are needed, the activities are within a separate Investigator Site, and management

			permission is required from the organisation responsible for the non-NHS site.
5.25	~~A standard condition of a favourable opinion from the REC is that Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) at the site level should be obtained prior to any research project activity commencing at a site within the NHS or Health and Social Care in Northern Ireland (HSC).~~	5.25	If a non-NHS Investigator site is using a non-NHS subsidiary site, the Chief Investigator or sponsor may request an exemption for the non-NHS subsidiary site from the requirement for site assessment by writing to the REC giving the name and address of the subsidiary site, the name of the person who will act as local Principal Investigator and brief details of the routine procedures to be conducted. Alternatively, this can be requested by listing all of the non-NHS subsidiary sites on the non-NHS site assessment form for the investigator site. The request may be reviewed by the Chair or by sub-committee or at a meeting of the Committee. The Chief Investigator and sponsor should be notified of the decision by email or by incorporating the relevant text into the validation or opinion outcome. **Non-NHS sites functioning under an NHS PI and NHS investigator site do not require an exemption from the REC. These activities are still within the one NHS Investigator Site, as long as the NHS Principal Investigator is responsible for overseeing them. If separate PI oversight arrangements are needed, the activities are within a separate Investigator Site**.
5.26	~~Responsibility for assessing the suitability of non-NHS sites in the UK lies with the REC will be carried out by the REC as part of the ethical review.~~	5.26	For CTIMPs and clinical investigations of medical devices the non-NHS site assessment form should be electronically submitted from IRAS as part of the main application or added at a later date as an amendment.

5.27	~~For CTIMPs and clinical investigations of medical devices, the main sites undertaking recruitment and administering the interventions will always require a site assessment. However, it may be necessary to arrange for routine clinical procedures required by the protocol to be carried out by other organisations sites in support of the research. For example, routine imaging using standard clinical protocols may be undertaken by a private scanner centre under contractual arrangements with the NHS care organisation where the participants are recruited. Unless the NHS organisation accepts full governance responsibility for these procedures and assures NHS indemnity (see paragraph 5.22), the responsible non-NHS organisation should be considered a separate research site or 'subsidiary site'. Management permission is required from the organisation responsible for the subsidiary site. However, the Chief Investigator or sponsor may request exemption of non-NHS subsidiary sites from the requirement for site assessment by writing to the REC giving the name and address of the subsidiary site, the name of the person who will act as local Principal Investigator (i.e. take responsibility for the conduct of study procedures) and brief details of the routine procedures to be conducted. The request may be reviewed by the Chair or by sub-committee or at a meeting of the Committee. The Chief Investigator and sponsor should be notified of the decision by email or by incorporating the relevant text into the validation or opinion letter. (Note however that where the NHS organisation accepts full governance responsibility for~~	5.27	The application for site assessment should be accepted as valid if it meets all the following criteria: i. The non-NHS site assessment Form and all supporting documentation have been submitted electronically from IRAS. ii. All relevant sections in the form have been completed, and the text is in English and legible. iii. The form has been electronically authorised on behalf of the Site Management Organisation. iv. A short curriculum vitae (maximum two pages) has been submitted for the Principal Investigator. (It is not necessary to submit CVs for other staff.) v. The site is located in the United Kingdom. vi. The name of the site has been correctly stated, vii. Evidence of insurance or indemnity (not required for Phase 1 trials in healthy volunteers where the site is accredited by the MHRA). viii. When appropriate, local versions have been provided on headed paper of any documentation which differs substantially in content to the documentation reviewed as part of the main ethical review. For example, this may be where there are differing arrangements in place for reimbursement of costs between sites.

	~~procedures at the non-NHS organisation, this is considered a single site).~~		
5.28	~~For CTIMPs and clinical investigations of medical devices the non-NHS/HSC site assessment form should be electronically submitted from IRAS as part of the main application.~~	5.28	The main issue to be considered as part of the assessment is the suitability of the site for the conduct of the research. This involves consideration of the following: (i) The suitability of the Principal Investigator, taking into account their professional qualifications, knowledge of the research field, expertise in the procedures involved, previous research experience, training in research methods (including informed consent), training in Good Clinical Practice (if applicable), and ability to take professional oversight for the local research team. (ii) The adequacy of the local facilities available for the research. (iii) The arrangements for notifying other local health or social care staff, who may have an interest in the care of the participants, about the research. (iv) The availability of any extra support that might be required by research participants as a result of their participation. (v) The practical arrangements to be made at the site for providing information to potential participants who might not adequately understand verbal explanations or written information given in English, where it is planned to include such groups in the study as a whole. (vi) Inclusion of relevant site-specific information in the local

			version of the information sheet for the study. This is only required where there are substantial differences. (vii) Evidence of insurance or indemnity to cover the potential liabilities of the Principal Investigator. (Note: This is not required for commercial Phase 1 trials in healthy volunteers as the sponsor makes an undertaking to compensate a volunteer who has suffered harm as a result of taking part in the trial whether or not the sponsor is liable. The sponsor company will make its own arrangements to ensure that the CRO and Principal Investigator have sufficient insurance or indemnity cover so that it can recover any losses from them where the harm resulted from their negligence). (viii) Evidence that the Principal Investigator has appropriate professional registration. (ix) Additional documentation may be requested relating to the governance of the research site, for example, internal SOPs, protocols, quality standards, job descriptions, training policies, evidence of audit and inspection.
5.29	~~The application for site assessment should be accepted as valid if it meets all the following criteria:~~ ~~i. The non-NHS/HSC site assessment Form and all supporting documentation have been submitted electronically from IRAS.~~	5.29	The Principal Investigator is formally accountable for the whole research team, and it is not necessary for the REC to give detailed scrutiny to the suitability of other local investigators or support staff, or to require submission of other CVs. Questions about the proposed

	~~ii. All relevant sections in the form have been completed, and the text is in English and legible.~~ ~~iii. The form has been electronically authorised on behalf of the Site Management Organisation.~~ ~~iv. A short curriculum vitae (maximum two pages) has been submitted for the Principal Investigator. (It is not necessary to submit CVs for other staff.)~~ ~~v. The site is located in the United Kingdom.~~ ~~vi. The name of the site has been correctly stated, taking into account the guidance in paragraphs 5.12-5.23.~~ ~~vii. Evidence of insurance or indemnity (not required for Phase 1 trials in healthy volunteers where the site is accrediated by the MHRA).~~ ~~viii. When appropriate, local versions have been provided on headed paper of any documentation which differs substantially in content to the documentation reviewed as part of the main ethical review. For example, this may be where there are differing arrangements in place for reimbursement of costs between sites.~~		conduct and management of the research at the local site may be raised directly with the Principal Investigator, including the allocation of research tasks to staff with relevant expertise and procedures for monitoring and supervision. Any assurances or clarifications given by the Principal Investigator should be noted as part of the ethical review.
5.30	~~In assessing the site, the main issue to be considered is the suitability of the site for the conduct of the research. This involves consideration of the following:~~ ~~100~~ ~~(i) The suitability of the Principal Investigator, taking into account his/her professional qualifications, knowledge of the research field, expertise in the procedures involved, previous research experience, training in research methods (including informed consent), training in Good Clinical Practice (if applicable), and ability to take professional responsibility for the local research team.~~	5.30	The assessment of a non-NHS/HSC site is a documentary check, supplemented where necessary by discussion with the Investigator where the REC requires additional information or clarification. It is not normally necessary for the REC to visit a site, especially where it is already familiar with the site and the type of research it undertakes. However, the REC has the discretion to arrange a site visit. This might be appropriate where the studies carried out at the site involve significant risk to participants, the site is unfamiliar, and a visit is considered essential to gain an understanding of the

	~~(ii) The adequacy of the local facilities available for the research.~~ ~~(iii) In a CTIMP, arrangements for receipt and storage of trial medication, Qualified Person Certification (if applicable), reconstitution (if applicable), labelling, control of access, dispensing, record-keeping and destruction.~~ ~~(iv) The arrangements for notifying other local health or social care staff, who may have an interest in the care of the participants, about the research.~~ ~~(v) The availability of any extra support that might be required by research participants as a result of their participation.~~ ~~(vi) The practical arrangements to be made at the site for providing information to potential participants who might not adequately understand verbal explanations or written information given in English, where it is planned to include such groups in the study as a whole.~~ ~~(vii) Inclusion of relevant site-specific information in the local version of the information sheet for the study. This is only required where there are substantial differences.~~ ~~(viii) Evidence of insurance or indemnity to cover the potential liabilities of the Principal Investigator. (Note: This is not required for commercial Phase 1 trials in healthy volunteers as the sponsor makes an undertaking to compensate a volunteer who has suffered harm as a result of taking part in the trial whether or not the sponsor is liable. The sponsor company will make its own arrangements to ensure that the CRO and Principal Investigator have sufficient insurance or indemnity cover~~		<u>context in which the research will be undertaken and assess the suitability of the staff and facilities.</u>

	~~so that it can recover any losses from them where the harm resulted from their negligence).~~ ~~(ix) Evidence that the Principal Investigator has appropriate professional registration.~~ ~~(x) Additional documentation may be requested relating to the governance of the research site, for example, internal SOPs, protocols, quality standards, job descriptions, training policies, evidence of audit and inspection.~~		
5.31	~~The Principal Investigator is formally accountable for the whole research team, and it is not necessary for the REC to give detailed scrutiny to the suitability of other local investigators or support staff, or to require submission of other CVs. Questions about the proposed conduct and management of the research at the local site may be raised directly with the Principal Investigator, including the allocation of research tasks to staff with relevant expertise and procedures for monitoring and supervision. Any assurances or clarifications given by the Principal Investigator should be noted as part of the ethical review.~~	5.31	Where the site is a specialist research unit with which the REC is already familiar, it may be helpful to arrange occasional visits to maintain the Committee's knowledge of the site, facilities, key personnel and operating procedures.
5.32	~~The assessment of a non-NHS/HSC site is a documentary check, supplemented where necessary by discussion with the Investigator where the REC requires additional information or clarification. It is not normally necessary for the REC to visit a site, especially where it is already familiar with the site and the type of research it undertakes. However, the REC has the discretion to arrange a site visit. This might be appropriate where the studies carried out at the site involve significant risk to participants, the site is unfamiliar, and a visit is~~	5.32	The MHRA GCP Inspectorate operates a voluntary scheme of accreditation for commercial trial units undertaking Phase 1 trials in healthy volunteers. Details of the scheme and a list of accredited units are published on the MHRA website.

	~~considered essential to gain an understanding of the context in which the research will be undertaken and assess the suitability of the staff and facilities.~~		
5.33	~~Where the site is a specialist research unit with which the REC is already familiar, it may be helpful to arrange occasional visits to maintain the Committee's knowledgeof the site, facilities, key personnel and operating procedures.~~	5.33	The site assessment for Phase 1 trial sites should take the accreditation status of the site into account. It is not necessary for the REC to review issues routinely addressed by the GCP inspectors as part of the process leading to accreditation. The inspectors will notify the HRA when a unit has been accredited and will provide a copy of the application form submitted by the unit, the inspection report and closing statement, and the accreditation certificate. This information will be made available centrally to all Phase 1 RECs. Any critical findings identified during inspection will be promptly notified to RES so that these can be considered in any reviews undertaken prior to the issues being resolved and accreditation confirmed.
5.34	~~The MHRA GCP Inspectorate operates a voluntary scheme of accreditation for commercial trial units undertaking Phase 1 trials in healthy volunteers. Details of the scheme and a list of accredited units are published on the MHRA website.~~	5.34	Reassurance as to the suitability of the site may be gained from the registration of the site within the MHRA Phase 1 Accreditation Scheme.
5.35	~~The site assessment for Phase 1 trial sites should take the accreditation status of the site into account. It is not necessary for the REC to review issues routinely addressed by the GCP inspectors as part of the process leading to accreditation. The inspectors will notify the HRA when a unit has been accredited and will provide a copy of the application form submitted by the unit, the~~	5.35	Clinical trial units, particularly Phase 1 units, may undertake general advertising and screening procedures to recruit potential trial participants to a pool of volunteers, prior to inviting such volunteers to participate in a specific trial. This activity constitutes preparations for undertaking a trial and is not part of the conduct of a trial under the Clinical Trials Regulations. It is therefore

	~~inspection report and closing statement, and the accreditation certificate. This information will be made available centrally to all Phase 1 RECs. Any critical findings identified during inspection will be promptly notified to RES so that these can be considered in any reviews undertaken prior to the issues being resolved and accreditation confirmed.~~		not a legal requirement for the procedures to be reviewed by an ethics committee and a favourable opinion obtained. However, Phase 1 trial units should seek ethical advice on these generic procedures. Requests for advice should be submitted in writing to phase1.advertreview@hra.nhs.uk enclosing relevant documentation such as advertising material or screening protocols. The request should not form part of the main application relating to a particular trial.
5.36	~~Reassurance as to the suitability of the site may be gained from the registration of the site within the MHRA Phase 1 Accreditation Scheme.~~	5.36	Procedures for extension of a study to new Investigator sites, appointment of new Principal Investigators or other site-specific amendments are set out in paragraphs 6.67 – 6.84.
5.37	~~Clinical trial units, particularly Phase 1 units, may undertake general advertising and screening procedures to recruit potential trial participants to a pool of volunteers, prior to inviting such volunteers to participate in a specific trial. This activity constitutes preparations for undertaking a trial and is not part of the conduct of a trial under the Clinical Trials Regulations. It is therefore not a legal requirement for the procedures to be reviewed by an ethics committee and a favourable opinion obtained. However, Phase 1 trial units should seek ethical advice on the procedures. Requests for advice should be submitted in writing to phase1.advertreview@hra.nhs.uk enclosing relevant documentation such as advertising material or screening protocols. The request should not form part of the main application relating to a particular trial.~~	5.37	There is no requirement for the Chief Investigator or sponsor to notify the REC where an approved site is closed or withdrawn from the study prematurely for example, if the Principal Investigator withdraws from the study or the sponsor decides that the site is no longer suitable. There is no requirement for the Chief Investigator or sponsor to notify the REC of the routine closure of active sites at the conclusion of a study. The Chief Investigator or sponsor must declare the end of a study to the REC, and MHRA as appropriate, using the appropriate end of study form.

5.38	~~Procedures for extension of a study to new sites, appointment of new Principal Investigators or other site-specific amendments are set out in paragraphs 6.67 – 6.85.~~	5.38	A substantial amendment is required only for a temporary halt at a study site, if this temporary halt is to protect participants from harm (see paragraph 6.26). The REC may request further information regarding the reasons for the closure of the sites if it has any concerns (For example, if there are concerns regarding the welfare of participants who had already been recruited).
5.39	~~For CTIMPs and Clinical Investigations of Medical Devices, the Chief Investigator or sponsor should notify the REC where an approved site is closed or withdrawn from the study prematurely, for example if the care organisation withholds research governance approval, or the Principal Investigator withdraws from the study, or the sponsor decides that the site is no longer suitable. Notification may be made by correspondence which should be reviewed by the Chair. A substantial amendment is required only for a temporary halt at a study site to protect participants from harm (see paragraph 6.26). The REC may request further information regarding the reasons for the closure of the sites if it has any concerns (For example, if there are concerns regarding the welfare of participants who had already been recruited).~~	5.39	Operational policy on the monitoring of research is set out in Section 10. In general, the REC is not responsible for proactive monitoring of research. However, it has a duty to keep the favourable ethical opinion under review in the light of progress reports and significant developments and may review the opinion at any time.
5.40	~~There is no requirement for the Chief Investigator or sponsor to notify the REC of the routine closure of active sites at the conclusion of a study.~~	5.40	The REC is not responsible for proactive monitoring of the conduct of the research at individual sites. However, where information comes to the attention of the REC that raises questions about the suitability of the site or investigator, the favourable opinion for the site may be reviewed. Procedures for review of opinions and for

			suspension or termination of opinions in non-CTIMPs are set out in paragraphs 10.100ff. Only the REC has authority to suspend or terminate an opinion, whether for the study as a whole or an individual site.
5.41	~~Operational policy on the monitoring of research is set out in Section 10. In general, the REC is not responsible for proactive monitoring of research. However, it has a duty to keep the favourable ethical opinion under review in the light of progress reports and significant developments and may review the opinion at any time.~~	5.41	The REC may request additional information for a particular site at any time in the light of concerns brought to its attention from any source. It may do so by writing to the Chief Investigator and sponsor
5.42	~~The REC is not responsible for proactive monitoring of the conduct of the research at individual sites. However, where information comes to the attention of the REC that raises questions about the suitability of the site or investigator, the favourable opinion for the site may be reviewed. Procedures for review of opinions and for suspension or termination of opinions in non-CTIMPs are set out in paragraphs 10.100ff. Only the REC has authority to suspend or terminate an opinion, whether for the study as a whole or an individual site.~~	5.42	Procedures for reviewing amendments to multi-site research are set out in Section 6, including extension to additional Investigator sites), appointment of new Principal Investigators and site-specific protocol amendments (paragraphs 6.67-6.84).
Section 6: Amendments to research given a favourable opinion			
Para	SOP 7.5.1	Para	SOP 7.6
6.19	A substantial amendment should be accepted as valid if all the following criteria are met:	6.19	A substantial amendment should be accepted as valid if all the following criteria are met (this does not apply for CTIMPs submitted via the combined review service):

6.20	It is the responsibility of the Approvals Officer/REC Manager to decide whether or not the amendment is valid and to notify the sponsor and Chief Investigator using SL27 (valid notice) or SL28 (invalid notice). Notification should normally be given within 5 working days of receipt, except that there is no need to issue a validation letter if the sub-committee is able to review the amendment and reach an opinion within 5 working days. (Where the amendment relates solely to the addition of a new site or investigator in a CTIMP or Clinical Investigation of a Medical Device, special procedures apply – see paragraph 6.67-6.72). The agreement of the Chair is not required.	6.20	It is the responsibility of the Approvals Officer/REC Manager to decide whether or not the amendment is valid and to notify the sponsor and Chief Investigator using SL27 (valid notice) or SL28 (invalid notice). Validation is confirmed by the MHRA for amendments submitted via the CTIMP combined review service. Notification should normally be given within 5 working days of receipt, except that there is no need to issue a validation letter if the sub-committee is able to review the amendment and reach an opinion within 5 working days. (Where the amendment relates solely to the addition of a new site or investigator in a CTIMP or Clinical Investigation of a Medical Device, special procedures apply – see paragraph 6.67-6.72). The agreement of the Chair is not required.
6.21	Where a substantial amendment is invalid, but the outstanding information or documentation appears relatively straightforward, this can be followed up with the applicant without needing to issue SL28. Where this occurs, the validation date is the date on which the last part of the information required for a valid application is received by the REC. The Substantial Amendment should be marked as 'validation under consideration' on HARP. If the Substantial Amendment cannot be made valid prior to the cut-off date for the REC meeting, it should be changed from 'validation under consideration' to 'invalid' on HARP and withdrawn from the meeting.	6.21	Where a substantial amendment is invalid, but the outstanding information or documentation appears relatively straightforward, this can be followed up with the applicant without needing to issue SL28 (this does not apply for amendments submitted via the CTIMP combined review service). Where this occurs, the validation date is the date on which the last part of the information required for a valid application is received by the REC. The Substantial Amendment should be marked as 'validation under consideration' on HARP. If the Substantial Amendment cannot be made valid prior to the cut-off date for the REC meeting, it should be changed from 'validation under consideration' to 'invalid' on HARP and withdrawn from the meeting.
6.27	There will, however, be changes to the details of research that have no significant implications for participants or for the conduct, management or scientific	6.27	There will, however, be changes to the details of research that have no significant implications for participants or for the conduct, management or scientific value of the study and can be regarded as non-substantial amendments.

	value of the study and can be regarded as non-substantial amendments. • Changes to the research team at particular trial sites (other than appointment of a new Principal Investigator in a CTIMP at an NHS/HSC site). • Addition of any new NHS/HSC sites, or addition of any new non-NHS/HSC sites (except in CTIMPs and Clinical Investigations of Medical Devices (see paragraphs 6.73-6.74).		• Changes to the research team at particular trial sites (other than appointment of a new Principal Investigator in a CTIMP at a non-NHS/HSC site - see paragraph 6.75). • Addition of any new NHS/HSC sites, or addition of any new non-NHS/HSC sites (except for the addition of non-NHS/HSC sites in CTIMPs and Clinical Investigations of Medical Devices (see paragraphs 6.67-6.74).
6.38	The decision reached should be either a favourable or unfavourable opinion of the amendment. It is not permitted to give a favourable opinion for part of the amendment only. However, when giving an unfavourable opinion the REC may indicate which parts of the amendment would have been acceptable and give guidance on the submission of a modified amendment taking account of its concerns. The sponsor and Chief Investigator should be notified of the decision using one of the following letters: SL32 Favourable opinion of substantial amendment SL33 Unfavourable opinion of substantial amendment The opinion letter should include the same information that would be included in an opinion letter on a new application (see paragraph 3.11), including a contact point for receipt of queries from the applicant.	6.38	The decision reached should be either a favourable or unfavourable opinion of the amendment, unless it relates to a Section 30 amendment where a provisional opinion can be issued (13.44). It is not permitted to give a favourable opinion for part of the amendment only. However, when giving an unfavourable opinion the REC may indicate which parts of the amendment would have been acceptable and give guidance on the submission of a modified amendment taking account of its concerns. The sponsor and Chief Investigator should be notified of the decision using one of the following letters: SL32 Favourable opinion of substantial amendment SL33 Unfavourable opinion of substantial amendment The opinion letter should include the same information that would be included in an opinion letter on a new application (see paragraph 3.11), including a contact point for receipt of queries from the applicant.

6.44	Where the REC gives an unfavourable opinion of a substantial amendment, the sponsor or Chief Investigator may submit a modified amendment taking account of the Committee's concerns. The amendment should be re-submitted, amended as necessary, and should be accompanied by any supporting documents that have been modified. The amendment should be clearly marked to indicate that it relates to a modified amendment.	6.44	Where the REC gives an unfavourable opinion of a substantial amendment, the sponsor or Chief Investigator may submit a modified amendment taking account of the Committee's concerns. The amendment should be re-submitted, amended as necessary, and should be accompanied by any supporting documents that have been modified. The amendment should be clearly marked to indicate that it relates to a modified amendment. For modified amendments submitted via the CTIMP combined review service, there is no modified amendment workflow in HARP but the 14 day timeline should be complied with.
6.59	Where a REC requests submission of a new application, it should give reasons to the applicant with reference to the above criteria.	6.59	Where a REC requests submission of a new application, it should give reasons to the applicant with reference to the above criteria. Where a substantial amendment relates to a CTIMP, the decision whether a new application should be submitted is primarily the responsibility of the MHRA. The MHRA's decision should therefore be taken into consideration; this is regardless of whether the CTIMP was approved under the combined review service or the standard review service. If the MHRA decision is unknown, the REC is encouraged to liaise with the MHRA via ctdhelpline@mhra.gov.uk.
6.60	By virtue of their design, studies which have been set up as Complex Innovative Trials (sometimes referred to as adaptive, platform or umbrella trials) may add different interventions or may recruit new categories of participants as the study progresses. For Complex Innovative Trials, it is acceptable for these changes to be submitted as a substantial amendment rather than as a new application. However, for trials to come under the heading of a Complex Innovative Trial, the protocol must	6.60	By virtue of their design, studies which have been set up as Complex Innovative Trials (sometimes referred to as adaptive, platform or umbrella trials) may add different interventions or may recruit new categories of participants as the study progresses. For Complex Innovative Trials, it is acceptable for these changes to be submitted as a substantial amendment rather than as a new application. However, for trials to come under the heading of a Complex Innovative Trial, the protocol must have been approved by the REC on this basis when the

	have been approved by the REC on this basis when the study was originally reviewed and the methodology included in the protocol should have been clear about the scope for future phases, treatment arms or other adaptive features. Where the changes included in the amendment are particularly significant, the amendment may be reviewed by a sub-committee involving a larger number of members or by reviewing the amendment at a full REC meeting.		study was originally reviewed and the methodology included in the protocol should have been clear about the scope for future phases, treatment arms or other adaptive features. Where the changes included in the amendment are particularly significant (this applies beyond CTIMPs which fall under the category of Complex Innovative Design Trials), the amendment may be reviewed by a sub-committee involving a larger number of members or by reviewing the amendment at a full REC meeting.
Section 7: Sub-committees			
Para	SOP 7.5.1	Para	SOP 7.6
7.6	Sub-committee business may be conducted ~~at face-to-face meetings~~, by video conference~~/telephone meetings (see paragraphs 7.13-7.14)~~ or by correspondence between the members (see paragraphs 7.1~~7~~-7.1~~9~~). Consideration should be given to the significance of the matters to be discussed.	7.6	Sub-committee business may be conducted by video conference or by correspondence between the members (see paragraphs 7.15-7.17). Consideration should be given to the significance of the matters to be discussed.
~~7.13~~	~~**Telephone meetings**~~ ~~Sub-committee meetings may be conducted over the telephone. Where available, teleconferencing or video-conferencing facilities should be used.~~		Text deleted
~~7.14~~	~~Where a meeting will be held by video-conference or tele-conference, the Approvals Officer/REC Manager should issue documents for the meeting according to normal procedure. Matters on the agenda may be~~		Text deleted

	~~considered in written correspondence or email between the members concerned prior to the telephone meeting, provided that the decisions of the sub-committee are then formally made at the meeting. The Chair should provide written notes for incorporation in the minutes.~~		
7.~~20~~	Investigators are not normally invited to sub-committee meetings. However, exceptionally the REC may invite the Chief Investigator, local Principal Investigator or sponsor's representative for a research study to attend a sub-committee meeting ~~or to be available by phone (or by teleconference or videoconference~~) where this would be helpful in providing further clarification, resolving issues of concern to the REC and reaching an early decision.	7.18	Investigators are not normally invited to sub-committee meetings. However, exceptionally the REC may invite the Chief Investigator, local Principal Investigator or sponsor's representative for a research study to attend a sub-committee meeting, where this would be helpful in providing further clarification, resolving issues of concern to the REC and reaching an early decision.
7.2~~6~~	The requirements of paragraphs 2.78~~ff~~ apply to the minutes of sub-committee meetings in the same way as for REC meetings, ~~whether undertaken by correspondence, teleconference or face to face.~~	7.24	The requirements of paragraphs 2.78 apply to the minutes of sub-committee meetings in the same way as for REC meetings.
Section 8: Further review of research given a unfavourable opinion			
Para	SOP 7.5.1	Para	SOP 7.6
8.17	Notice should be given by the applicant in writing to the Appeal Manager, The Appeal Manager should then make arrangements to allocate the application to another REC for review, taking into account ~~geographical proximity to the Chief Investigator's professional base and~~ any legal or regulatory requirement for review by a particular REC, and for an agenda slot to be booked at its next meeting.	8.17	Notice should be given by the applicant in writing to the Appeal Manager, The Appeal Manager should then make arrangements to allocate the application to another REC for review, taking into account any legal or regulatory requirement for review by a particular REC, and for an agenda slot to be booked at its next meeting.

Section 10: Monitoring of research given a favourable opinion			
Para	SOP 7.5.1	Para	SOP 7.6
10.12	Progress reports should be in the format prescribed by RES and published on the website. Reports may be submitted by the sponsor or the Chief Investigator ~~but should always be signed by the Chief Investigator.~~	10.12	Progress reports should be in the format prescribed by RES and published on the website. Reports may be submitted by the sponsor or the Chief Investigator.
10.18	The Clinical Trials Regulations provide that the sponsor or the Chief Investigator, or the local Principal Investigator at a trial site, may take appropriate urgent safety measures in order to protect the subjects of a CTIMP against any immediate hazard to their health or safety. The REC and the MHRA must be notified ~~immediately and in any event~~ within 3 days that such measures have been taken and the reasons why. The policy from RES is that these requirements should apply to all other research with a favourable opinion from a REC.	10.18	The Clinical Trials Regulations provide that the sponsor or the Chief Investigator, or the local Principal Investigator at a trial site, may take appropriate urgent safety measures in order to protect the subjects of a CTIMP against any immediate hazard to their health or safety. The REC and the MHRA must be notified within 3 days that such measures have been taken and the reasons why. The policy from RES is that these requirements should apply to all other research with a favourable opinion from a REC. For trials which have been approved via the CTIMP combined review service, one USM notification is made via IRAS and received by the MHRA. No additional notification is required directly to the REC – the REC notification will be via the substantial amendment which follows the USM notification.
10.19	The initial notification to the REC should be ~~by telephone. Notice~~ in writing and should be sent within 3 days (this does not apply for trials approved via the CTIMP combined review service). The notice should set out the reasons for the urgent safety measures and the plan for further action.	10.19	The initial notification to the REC should be in writing and should be sent within 3 days (this does not apply for trials approved via the CTIMP combined review service). The notice should set out the reasons for the urgent safety measures and the plan for further action.

10.23	Suspected Unexpected Serious Adverse Reactions (SUSARs), which are associated with the use of an investigational medicinal product (IMP) in the trial, must be notified both to the MHRA and to the REC in accordance with the requirements of the Directive for expedited reporting. This includes SUSARs associated with an active comparator drug used in the trial. In the case of the REC, the sponsor is only required to report in expedited fashion SUSARs occurring in the concerned trial in the UK. SUSARs occurring in the trial outside the UK are subject to expedited reporting to all relevant competent authorities, but do not need to be notified in this way to ethics committees in the UK. They should however be included in line listings submitted with annual safety reports once the trial has started in the UK (see paragraphs 10.36-10.47). Where RECs receive expedited reports of non-UK SUSARs, these should be confidentially destroyed and there is no requirement to acknowledge receipt.	10.23	Suspected Unexpected Serious Adverse Reactions (SUSARs), which are associated with the use of an investigational medicinal product (IMP) in the trial, must be notified both to the MHRA and to the REC in accordance with the requirements of the Directive for expedited reporting. For CTIMPs approved under the combined review service, notification of SUSARs should be to the MHRA only - the MHRA will liaise with the REC if deemed appropriate. This includes SUSARs associated with an active comparator drug used in the trial. In the case of the REC, the sponsor is only required to report in expedited fashion SUSARs occurring in the concerned trial in the UK. SUSARs occurring in the trial outside the UK are subject to expedited reporting to all relevant competent authorities, but do not need to be notified in this way to ethics committees in the UK. They should however be included in line listings submitted with annual safety reports once the trial has started in the UK (see paragraphs 10.36-10.47). Where RECs receive expedited reports of non-UK SUSARs, these should be confidentially destroyed and there is no requirement to acknowledge receipt.
10.29	An adverse event associated with placebo will not normally satisfy the criteria for a SUSAR. If this occurred exceptionally (e.g. a reaction due to an excipient or impurity) it should be reported.	10.29	An adverse event associated with placebo will not normally satisfy the criteria for a SUSAR. If this occurred exceptionally (e.g. a reaction due to an excipient or impurity) it should be reported. This guidance also applies to safety reporting of other research (10.62-10.67).
10.35	For each IMP being tested in the trial, the sponsor should provide the REC with an annual report on the safety of subjects, in all clinical trials of the product for which the sponsor is responsible, whether in the UK or elsewhere. The reporting requirement ends when the conclusion or	10.35	For each IMP being tested in the trial, the sponsor should provide the REC with an annual report on the safety of subjects, in all clinical trials of the product for which the sponsor is responsible, whether in the UK or elsewhere. For trials approved via the CTIMP combined review process, the annual safety report is submitted by the applicant via IRAS to

	early termination of the trial has been notified in the UK (even if the trial is continuing in other countries).		the MHRA. A separate submission directly to the REC is not required. Where there is action taken by the sponsor in relation to information contained in the annual safety report, this will require the sponsor to submit a substantial amendment and the REC will be informed via this route. The reporting requirement ends when the conclusion or early termination of the trial has been notified in the UK (even if the trial is continuing in other countries).
10.66	Individual reports of SAEs should be reviewed at a sub-committee or Committee meeting.	10.66	Individual reports of SAEs should be reviewed at a sub-committee or Committee meeting. The purpose of the ethics review is to check the accuracy of the risk/benefit analysis as described in the participant information sheet and to consider the possible need for new information to be given to participants and their consent sought to continue in the study if necessary. The Committee should also consider any other issue that may be relevant to the ethics of the trial.
10.137	~~A summary of the~~ final report on the research should be submitted to the ~~REC~~ within one year of the conclusion of the research. In the case of early termination, provision of a final report is at the discretion of the sponsor. ~~This applies to both CTIMPs and all other research. There is no standard format for final reports. As a minimum, the REC should receive information on whether the study achieved its objectives, the main findings, and arrangements for publication or dissemination of the research including any feedback to participants.~~	10.137	For all project based research (i.e. not research tissue banks or research databases) that have received a favourable ethical opinion from a REC a summary of the final report on the research should be submitted to the Research Ethics Service within one year of the conclusion of the research. In the case of early termination, provision of a final report is at the discretion of the sponsor.
10.138	~~All such reports should be acknowledged and reviewed by the Chair or, at the Chair's discretion, by another member of the Committee or a Scientific Officer.~~ The	10.138	All final reports will be acknowledged within 30 days. The Committee should be notified of the receipt of the report in the

	Committee should be notified of the receipt of the report in the REC Report. ~~At the discretion of the Chair, copies or summaries may be distributed to members. No further action is required unless the Chair considers that issues are raised requiring discussion at a meeting of the REC or sub-committee.~~		REC Report. The Committee can ask to see a copy of the final report on request.
Section 11: Research databases			
Para	SOP 7.5.1	Para	SOP 7.6
11.23	Applicants may also seek generic approval on behalf of external researchers receiving non-identifiable data to undertake valuable scientific studies. Data sharing is encouraged in the interests of maximising the research potential of stored data, provided that adequate safeguards are in place to protect confidentiality. The REC may give generic approval extending to studies by external researcher's subject to conditions (see paragraph 11.27).	11.27	Applicants may also seek generic approval on behalf of external researchers receiving non-identifiable data to undertake valuable scientific studies, without the need for applying for a separate ethics review each time. Data sharing is encouraged in the interests of maximising the research potential of stored data, provided that adequate safeguards are in place to protect confidentiality. The REC may give generic approval extending to studies by external researcher's subject to conditions (see paragraph 11.27). Where generic ethical approval has not been granted for the research database, a separate ethics review for any individual research projects' conducted using the data would need to be applied for.
11.27	Where ethical approval is given, the REC should issue a set of approval conditions appropriate to Research Databases, normally including the following: (c) Research has been subject to scientific critique, is appropriately designed in relation to its objectives and ~~(with the exception of student research below doctoral~~	11.27	Where ethical approval is given, the REC should issue a set of approval conditions appropriate to Research Databases, normally including the following: (c) Research has been subject to scientific critique, is appropriately designed in relation to its objectives and is likely to add something useful to existing knowledge.

	~~level)~~ is likely to add something useful to existing knowledge.		
Section 12: Research involving human tissue			
Para	SOP 7.5.1	Para	SOP 7.6
12.11	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 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. Similarly,~~ for tissue collections in Scotland, RECs should consider the requirements of the accreditation scheme for NHS Scotland biorepositories (section 12.2).	12.11	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. For tissue collections in Scotland, RECs should consider the requirements of the accreditation scheme for NHS Scotland biorepositories (section 12.2).
12.32	The REC should issue a set of approval conditions appropriate to RTBs, which should normally include the following: (c) Where the applicant has applied for generic ethical approval for projects receiving tissue - without further project-specific applications being required - the following conditions apply to the release of tissue:	12.32	The REC should issue a set of approval conditions appropriate to RTBs, which should normally include the following: (c) Where the applicant has applied for generic ethical approval for projects receiving tissue - without further project-specific applications being required - the following conditions apply to the release of tissue:

	• The RTB should have management arrangements in place to be satisfied that the research has been subject to scientific critique, is appropriately designed in relation to its objectives and ~~(with the exception of student research below doctoral level)~~ is likely to add something useful to existing knowledge.		• The RTB should have management arrangements in place to be satisfied that the research has been subject to scientific critique, is appropriately designed in relation to its objectives and is likely to add something useful to existing knowledge.
Section 13: Research involving adults unable to consent for themselves			
Para	SOP 7.5.1	Para	SOP 7.6
13.44	Where the amendment relates to a CTIMP, the usual SOPs apply to the review (paragraph 6.36 - 6.41). Where it relates to a non-CTIMP, a 60-day timescale applies to the review and the REC may stop the clock once to request further information or clarification in the same way as for a new application. The amendment should be reviewed at a full committee meeting.	13.44	Where the amendment relates to a CTIMP, the usual SOPs apply to the review (paragraph 6.36 - 6.41). Where it relates to a non-CTIMP, a 60-day timescale applies to the review and the REC may stop the clock once <u>and issue a provisional opinion</u> to request further information or clarification in the same way as for a new application. The amendment should be reviewed at a full committee meeting.
Annex C: Notification of substantial amendments to CTIMPs			
	Amendments normally requiring both authorisation and a favourable ethical opinion		**Amendments normally requiring both authorisation and a favourable ethical opinion**

	• New toxicological or pharmacological data or new interpretation of toxicological or pharmacological data which is likely to impact on the risk/benefit assessment.		• Protocol amendments due to new toxicological or pharmacological data or new interpretation of toxicological or pharmacological data which is likely to impact on the risk/benefit assessment.
Annex I: The Social Care Research Ethics Committee			
Para	SOP 7.5.1	Para	SOP 7.6
~~3~~	~~Researchers unsure about their options for seeking ethical review should seek guidance from the Social Care REC (see paragraph 6 below).~~		Text deleted