Health Research Authority

RES SOPs (Version 7.4) Summary of Changes, June 2019

How to use this document

This summary of changes document includes all of the revision from version 7.3 to version 7.4 of the Research Ethics Service Standard Operating Procedures (RES SOPs). The left hand column shows the wording which was present in version 7.3 and deletions are indicated by ~~strikethrough~~. The right hand column shows the wording which is now present in version 7.4 and additional text is indicated by <u>underline</u>.

General revisions			
Para	SOP 7.3	Para	SOP 7.4
	References to Head of RES		Changed to Head of Approvals Operations or Head of Approvals Support as relevant
	Regional Manager		This role no longer exists in England and Wales so references have been deleted and in most cases have not had to be replaced as the wording has been made more generic. Where the wording has been replaced the role 'Operational Manager' has been inserted and is defined in the glossary.
	RES Project & Support Manager		Quality and Performance Manager
	RES Managers		This role no longer exists in England and Wales so references have been deleted and in most cases have not had to be replaced as the wording has been made more generic. Where the wording has been replaced the role

			'Operational Manager' has been inserted and is defined in the glossary.
	REC Assistant		Approvals Administrator/REC Assistant
	REC Manager		Approvals Officer/REC Manager
Introduction to RES SOPs			
Page	SOP 7.3	Page	SOP 7.4
16.	Introduction to RES SOPs – version 7.~~3~~	13.	Introduction to RES SOPs – version 7.4
16.	Under the UK Health Departments' Governance Arrangements for Research Ethics Committees (GAfREC) (~~issued on 9 May 2011 and in effect from 1 September 2011~~), each REC within the Research Ethics Service is required to adopt SOPs approved by or on behalf of its appointing authority. The REC is required to act in accordance with its SOPs and is ultimately accountable to its appointing authority for its governance in this respect.	13.	Under the UK Health Departments' Governance Arrangements for Research Ethics Committees (GAfREC) (published 18 June 2018 and valid from 17 September 2018), each REC within the Research Ethics Service is required to adopt SOPs approved by or on behalf of its appointing authority. The REC is required to act in accordance with its SOPs and is ultimately accountable to its appointing authority for its governance in this respect.
18.	Version 7 of the RES SOPs is effective from ~~1 September 2016~~ and applies retrospectively to all research already underway with a favourable opinion from a REC. Where the SOPs state that a particular procedure "should" be followed - without qualification - all RECs adopting the SOPs will be expected to comply fully. Compliance will be monitored ~~through Regional Managers~~. The system of	15.	Version 7.4 of the RES SOPs is effective from 5 June 2019 and applies retrospectively to all research already underway with a favourable opinion from a REC. Where the SOPs state that a particular procedure "should" be followed - without qualification - all RECs adopting the SOPs will be expected to comply fully. Compliance will be monitored. ~~through Regional Managers~~. The system of

	audit and accreditation of RECs developed by RES is based on GAfREC and the SOPs.		audit and accreditation of RECs developed by RES is based on GAfREC and the SOPs.
18.	~~RECs may develop additional local operating procedures to deal with local matters not addressed in these SOPs or where discretion is permitted. Local operating procedures should be agreed between the Chair and the REC Manager.~~	~~18.~~	Text deleted
18.	The standard letters and other documents listed in Annex A are available in HARP ~~and on the HRA Hub for use alongside these SOPs~~. A small number of the standard letters are not available in HARP and need to be produced using the templates on the HRA Hub.	15.	The standard letters and other documents listed in Annex A are available in HARP. A small number of the standard letters are not available in HARP and need to be produced using the templates on the HRA Hub.
19.	~~***Further information***~~ ~~16. RECs requiring further information or advice should in the first instance contact their Regional Manager.~~ ~~17. Researchers and other enquirers may seek advice by contacting hra.queries@nhs.net or the appropriate REC Manager or Centre staff.~~	19.	Text deleted

Glossary			
Page	SOP 7.3	Page	SOP 7.4
~~29.~~	~~Regional Manager- The manager with line management responsibility for leading the Centre team to ensure that all research taking place within the jurisdiction of the REC Centre committees receives ethical review within relevant guidelines *(where this term is used throughout SOPs, it should be read as referring to the member of staff with equivalent responsibilities in Northern Ireland, Scotland and Wales).*~~ ~~RES Manager - The manager responsible for co-ordinating the work of REC Centre teams to ensure that all research receives ethical review within relevant guidelines *(where this term is used throughout SOPs, it should be read as referring to the member of staff with equivalent responsibilities in Northern Ireland, Scotland and Wales)*,~~ ~~SSA - Site-specific assessment - an assessment of the suitability of the investigator, site and facilities for each research site. SSA is undertaken for certain types of study only. See section 5 of the SOPs.~~ ~~Site-specific assessor - The body responsible for undertaking a site-specific assessment, either the R&D office for a NHS site or an appropriate REC for a non-NHS site.~~		Text deleted

	~~SSI Form - Site-Specific Information Form~~		
			Operational Manager – This could be the Scientific Officer in Scotland, the Head of the Office for Research Ethics Committees in Northern Ireland or an Approvals Operations Manager in England & Wales.
Section 1: New applications for ethical review			
Para	SOP 7.3	Para	SOP 7.4
1.21	Detailed guidance on the remit of GTAC is at Annex J. ~~Any queries about the allocation of particular studies should be referred to the GTAC Manager.~~	1.21	Detailed guidance on the remit of GTAC is at Annex J.
1.28	~~Queries about the appropriate source of review for social care research to be conducted in England and another UK country should be referred to the Social Care REC Manager for advice.~~		Text deleted
1.33	~~An applicant who requires general advice on the booking and submission process should contact their local REC office.~~		Text deleted
1.34	~~The applicant should also contact their local REC office to seek advice on whether the study is suitable for review through the Proportionate Review Service taking into account the criteria published on the HRA website (see paragraph 4.3).~~		Text deleted

1.48 (l)	~~In the case of a non-CTIMP, either the sponsor or the sponsor's legal representative is established within the UK.~~	1.45 (l)	In the case of a CTIMP, where the sponsor has appointed a legal representative, evidence has been provided (in the form of a letter from the legal representative or contract with the sponsor) confirming that the legal representative has agreed to undertake this role. The legal representative may be a person or an organisation. No legal qualifications are required.
1.48 (m)	Where the sponsor has appointed a legal representative, evidence has been provided (in the form of a letter from the legal representative or contract with the sponsor) confirming that the legal representative has agreed to undertake this role. The legal representative may be a person or an organisation. No legal qualifications are required.	1.45 (m)	In the case of a CTIMP, Clinical Investigation of a Medical Device or combined CTIMP and Device studies that include non-NHS/HSC sites, a short non-NHS/HSC Site Assessment form has been submitted along with the required supporting documentation (paragraph 5.36)
1.51	~~An SSI form may be submitted after the application has been validated but before the date of the meeting, if the study requires site-specific assessment (SSA) and is to be conducted at a non-NHS site. In such cases, the REC should carry out the SSA for this site alongside the ethical review.~~		Text deleted
1.53	~~Evidence from care organisations of their agreement *in principle* to the conduct of the research is highly desirable and should be encouraged, particularly for single-site research, but is not a criterion for validation except where the care organisation is the sponsor (see 1.48(d)). The process for securing final research governance approval to proceed with the research from care organisations and/or~~		Text deleted

	~~employing organisations is separate to the process of ethical review.~~		
1.58	~~REC Managers should also send a copy of the validation letter via e-mail to the lead NHS R&D office for any research to be conducted within the NHS.~~		Text deleted
1.63	Applications should not ~~be sent~~ to REC members unless valid (with the exception of 1.50).	1.57	Applications should not be made available to REC members unless valid (with the exception of 1.50).
1.86	~~When considering revisions to applications for multi-site studies requiring SSA, the REC should also note the guidance in paragraph 5.69.~~		Text deleted
Section 2: Full meetings of a Research Ethics Committee			
Para	SOP 7.3	Para	SOP 7.4
2.6	The schedule of Committee meetings for the year commencing on 1 January ~~should be agreed between the REC Manager and the Regional Manager~~ by 30 September in the previous year. The schedule should set out the dates, times and venues of meetings, and the closing date for applications to each meeting. All members and deputy members of the REC should be issued with details of the schedule.	2.6	The schedule of Committee meetings for the year commencing on 1 January should be agreed by 30 September in the previous year. The schedule should set out the dates, times and venues of meetings, and the closing date for applications to each meeting. All members and deputy members of the REC should be issued with details of the schedule.
2.8	The REC Manager should seek the approval of the Regional Manager for any proposed changes to their meeting schedule during the year. ~~RES Managers may request changes to meeting schedules to ensure that the system as a whole has sufficient operational capacity at all times.~~	2.8	There may be proposed changes to the meeting schedules during the year. Any changes will be cascaded to the members of staff dealing with the REC and to the Chair, and the meeting dates will be updated on the website.

2.9	~~Report by the REC Manager (see 2.13ff).~~	2.9	REC Report
2.12	Section 7 describes arrangements for REC business that may be conducted by sub-committees. The agenda for REC meetings may include items that would normally be reviewed in sub-committee, in particular where the Chair considers it important that a wider discussion takes place. ~~In allocating business between the Committee and sub-committee meetings, the REC Manager and the Chair should weigh carefully the requirement to give ethical opinions within statutory time limits, the need to conduct REC business both efficiently and with due care, and the overall demands of the agenda on members.~~	2.12	Section 7 describes arrangements for REC business that may be conducted by sub-committees. The agenda for REC meetings may include items that would normally be reviewed in sub-committee, in particular where the Chair considers it important that a wider discussion takes place.
2.19	It is strongly recommended that RECs appoint one or more members as lead reviewers for each application for *full applications*. ~~The REC Manager must appoint a~~ lead reviewer for each application to be reviewed by a *proportionate review* sub-committee~~, in consultation with the Chair as necessary.~~ ~~Use of the lead reviewer sheets published on the HRA Hub~~ is mandatory, however, there is no requirement for the lead reviewer to ~~give a copy of the~~ lead reviewer sheet ~~to the REC Manager~~ in advance at the meeting.	2.19	It is strongly recommended that RECs appoint one or more members as lead reviewers for each application for *full applications*. A lead reviewer must be appointed for each application to be reviewed by a proportionate review sub-committee is mandatory, however, there is no requirement for the lead reviewer to share their lead reviewer sheet in advance of the meeting.
2.22	~~All members should receive and review the application form and all supporting documentation for each new application, except that RECs have discretion as follows:~~ ~~• The protocol for the study should be available at least to the lead reviewer(s) and to members with relevant~~		Text deleted

	~~expertise. Other members should be able to access the protocol via the HARP member portal.~~ • ~~The Investigator Brochure for an investigational medicinal product should be sent/made available only to members with relevant expertise (in particular, to the pharmacist or clinical pharmacologist).~~ • ~~CVs and validated questionnaires made available to members, other than the Chair and lead reviewer(s), via the HARP member portal only~~		
2.43	A member or deputy member who is unavailable to attend a meeting may submit comments in writing on any agenda item. These should normally be ~~received by the REC Manager~~ at least three working days prior to the meeting so that copies may be made available in advance to members. Where later comments are received, they ~~may~~ be tabled at the meeting ~~at the discretion of the Chair~~. The minutes should record that written comments were submitted from the member or deputy member concerned and reflect unattributably any specific points addressed by the REC in the ethical review.	2.42	A member or deputy member who is unavailable to attend a meeting may submit comments in writing on any agenda item. These should normally be entered in the Member Portal at least three working days prior to the meeting so that copies may be made available in advance to members. Where later comments are received, they should be tabled at the meeting. The minutes should record that written comments were submitted from the member or deputy member concerned and reflect unattributably any specific points addressed by the REC in the ethical review.
2.48 (iii)	The Committee may decide at the meeting to give a provisional opinion and seek *written advice following the meeting*. The REC Manager or Chair should ~~normally write to the~~ referee within 5 days of the meeting using SL9. The written advice received should then be considered promptly in accordance with procedures agreed at the meeting (see paragraphs ~~3.42-3.46~~ for further guidance).	2.47 (iii)	The Committee may decide at the meeting to give a provisional opinion and seek written advice following the meeting. The Approvals Officer/REC Manager or Chair should email the referee within 5 days of the meeting using the template available on the HRA Hub. The written advice received should then be considered promptly in

			accordance with procedures agreed at the meeting (see paragraphs 3.39-3.43 for further guidance).
2.75	Vice-chairs should chair at least one meeting per year when the Chair is present. ~~This is for training purposes and should be undertaken with the agreement of the Regional Manager.~~ When doing so, they carry the normal responsibilities of the Chair.	2.74	Vice-chairs should chair at least one meeting per year when the Chair is present for training purposes. When doing so, they carry the normal responsibilities of the Chair.
2.78	~~The secretary to the meeting will normally be the REC Manager or REC Assistant.~~		Text deleted
2.78 (viii)	~~Raising with the Regional Manager any concern that a meeting may not be quorate.~~		Text deleted
2.78 (xiv)	Preparing the minutes of the meeting within ~~3~~ working days ~~for review by the Chair~~, and subsequent approval at the following meeting.	2.77(xiii)	Preparing the minutes of the meeting within 2 working days and subsequent approval at the following meeting.
2.80	The minutes of the REC meeting should be prepared by the secretary to the meeting ~~in accordance with the guidance issued by the Head of RES. The substantive content of letters should be approved by the Chair before letters are issued to applicants giving the Committee's decision (see paragraph 3.11). Local procedures should be agreed.~~	2.78	The minutes of the REC meeting should be prepared by the secretary to the meeting.
Section 3: Giving an Ethical Opinion			
Para	SOP 7.3	Para	SOP 7.4
3.11	~~The REC Manager should ensure that~~ notification of the decision is sent to the Chief Investigator within 10 working days of a full meeting, or within 5 working days of	3.11	Notification of the decision should be sent to the Chief Investigator within at least 10 working days (preferably fewer) of a full meeting, or within 5 working days of

	proportionate review by sub-committee. In the case of projects undertaken primarily for educational purposes, the decision letter 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~~, who has ultimate responsibility for, and should approve, the content~~. It is acceptable for the letter to be signed by a vice-Chair or member of the REC office acting under delegated authority from the Chair. ~~Local procedures should be agreed (see also paragraph 2.80).~~ One of the following letters should be used: SL7 Provisional opinion with request for further information		proportionate review by sub-committee. In the case of projects undertaken primarily for educational purposes, the decision letter 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 the REC office acting under delegated authority from the Chair. One of the following letters should be used: SL7 Provisional opinion with request for further information <u>(this may be sent as a standalone email rather than as a letter).</u>
3.19	A standard condition of any favourable opinion is that the sponsor must obtain management permission or approval from relevant host organisations prior to the start of the study at each site. ~~In the case of studies requiring SSA (see Section 4), the suitability of NHS sites is assessed by the NHS R&D office as part of standard site set up.~~ The favourable opinion therefore applies to all NHS sites on condition that NHS management permission is confirmed prior to the start of the study at that site.	3.19	A standard condition of any favourable opinion is that the sponsor must obtain management permission or approval from relevant host organisations prior to the start of the study at each site. The favourable opinion therefore applies to all NHS sites on condition that NHS management permission is confirmed prior to the start of the study at that site.
3.24	The Chief Investigator or sponsor should notify the REC for information in writing once the conditions have been	3.24	The Chief Investigator or sponsor should notify the REC for information in writing once the conditions have been met

	met (except for management permission or approval at individual sites) and provide copies of final documentation for reference purposes where appropriate. ~~The REC Manager~~ should acknowledge receipt within 5 working days using SL44 and giving a complete list of the final documentation approved for the study. ~~Neither the REC nor the REC Manager is required to undertake any further review of the actions taken.~~		(except for management permission or approval at individual sites) and provide copies of final documentation for reference purposes where appropriate. Receipt should be acknowledged within 5 working days using SL44 and giving a complete list of the final documentation approved for the study.
3.26	~~In the case of studies requiring site-specific assessment (SSA), the REC reviewing the application should confirm approval of each non-NHS site as part of the ethical opinion~~		Text deleted
3.27	~~Where a study requires SSA and includes non-NHS sites, there may be occasions where the REC is in a position to issue a favourable opinion but no SSA has yet been carried out. In such cases, the Approvals Officer/REC Manager should issue the favourable opinion without delay (see paragraph 5.56).~~		Text deleted
~~3.32~~	~~Following proportionate review, the further information or changes to documentation requested with the provisional opinion will normally be reviewed by the Chair or the lead reviewer.~~	3.32	Text deleted
3.43	In some cases, the REC may decide at the meeting it wishes to consult a referee. If so, this decision and the area of expertise required should be recorded in the minutes. ~~If not~~, either the Chair or the REC Manager should be appointed to identify a suitable referee urgently following the meeting. ~~The REC may wish to seek advice~~	3.40	In some cases, the REC may decide at the meeting it wishes to consult a referee. If so, this decision and the area of expertise required should be recorded in the minutes. Either the Chair or the Approvals Officer/REC Manager should be appointed to identify a suitable referee

	~~from the Regional Manager, who may be aware of members of other RECs with the relevant expertise, or from the RES Manager. The referee may be another REC or specialist body.~~		urgently following the meeting. The referee may be another REC <u>member or an expert in the specialist field</u>
3.45	When advice is being sought from ~~someone who is not a REC member,~~ the REC Manager should ~~write to the referee using SL9~~. ~~Where advice is being sought from another REC member, direct contact may be made by e-mail.~~ The request should be as specific as possible about the issues of concern to the REC and the expert advice required. A copy of the application form should be provided, together with any supporting documentation required by the referee. Where possible, the letter should be sent within 5 working days of the meeting. The referee should be asked to respond in writing within a further 10 days.	<u>3.42</u>	When advice is being sought from a referee, the <u>Approvals Officer</u>/REC Manager should <u>email the referee using the template available on the HRA Hub.</u> The request should be as specific as possible about the issues of concern to the REC and the expert advice required. A copy of the application form should be provided, together with any supporting documentation required by the referee. Where possible, the letter should be sent within 5 working days of the meeting. The referee should be asked to respond in writing within a further 10 days.
3.50 (ii)	~~Where the study involves NHS sites, the REC should send copies of correspondence to the lead R&D office for the study.~~ The Chief Investigator and sponsor will be expected to arrange for other care organisations to be kept informed and in particular to receive copies of letters from the REC confirming the favourable opinion for the study and for the site.	<u>3.47</u> (ii)	The Chief Investigator and sponsor will be expected to arrange for other care organisations to be kept informed and in particular to receive copies of letters from the REC confirming the favourable opinion for the study and for the site.

Section 5: ~~Site Specific Assessment~~ Assessing the suitability of research sites			
Para	SOP 7.3	Para	SOP 7.4
5.4	**Requirement for site-~~specific~~ assessment** For ~~certain types of study~~, the ethical review includes an assessment of the suitability of each site or sites at which the research is to be conducted in the UK. The "site-~~specific~~ assessment" ~~(SSA)~~ is not a separate ethical review, but forms part of the single ethical review of the research. ~~Where there is no objection from the assessor on site-specific grounds, a site is deemed to be approved as part of the favourable ethical opinion given by the REC.~~	5.4	**Requirement for site assessment** For certain types of study, the ethical review includes an assessment of the suitability of each site or sites at which the research is to be conducted in the UK. The site assessment is not a separate ethical review, but forms part of the single ethical review of the research.
5.5	~~Except where paragraphs 5.29-5.32 apply, SSA is required for all sites in the following types of study~~: i) Clinical trials of investigational medicinal products (CTIMPs) ~~ii)~~ Clinical investigations of ~~non-CE marked~~ medical devices or ~~CE marked devices~~ ~~which have been modified or are being used for a new intended purpose~~ iii) Combined CTIMPs and clinical investigations of medical devices	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

	~~iv) Other clinical trials to study a novel intervention or randomised clinical trials comparing interventions in clinical practice~~ ~~v) Intrusive research involving adults unable to consent for themselves in England or Wales and requiring approval under the Mental Capacity Act 2005, and similar research in Northern Ireland~~ ~~vi) Research involving adults unable to consent for themselves and requiring approval under the Adults with Incapacity (Scotland) Act 2000.~~		
5.6	For research falling outside the categories listed in paragraph 5.5, ~~SSA is~~ not required for the purposes of ethical review. All research sites listed in the application to the REC, and any other 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, <u>assessment of site suitability</u> is not required for the purposes of ethical review. All research sites listed in the application to the REC, and any other 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.**
5.11	When there is a change of PI at a site requiring ~~SSA, a new SSA should be submitted to the REC.~~	5.11	When there is a change of PI at a site <u>in a CTIMP or clinical investigation of a medical device a Notice of Substantial Amendment should be submitted.</u>
5.24	NHS management permission at the site level ~~("NHS management permission")~~ should be obtained prior to any research project activity commencing at a site within the	5.24	<u>Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland)</u> at the site level should be

	NHS or Health and Social Care in Northern Ireland (HSC). ~~The NHS management permission~~ process is started by submitting the main IRAS application form ~~(England), or the R&D application form (Northern Ireland, Scotland or Wales) in IRAS~~. Guidance on the UK-nation specific mechanisms for providing site level documentation and information, ~~to obtain NHS management permission~~, ~~is~~ available at ~~http://www.rdforum.nhs.uk~~ and ~~and~~ within IRAS. In England, research project activity at NHS sites should not commence until HRA Approval is also in place.		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.
5.25	~~The governance review conducted before NHS permission by the R&D office satisfies the requirement for a SSA to be undertaken. SSI Forms do not need to be submitted to the REC~~	5.25	Text deleted.
5.26	A standard condition of a favourable opinion from the REC is that management permission is obtained before the start of the study at each site ~~(see paragraph 3.19). There is no requirement for the outcome of the final decision on NHS management permission to be notified to the REC by the R&D office, or for the REC to confirm ethical approval for each NHS site. Once NHS management permission has been given, the site is deemed to be ethically approved as part of the favourable opinion.~~	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).
5.27	~~SSA~~ at non-NHS sites Responsibility for ~~undertaking SSA~~ at non-NHS sites in the UK lies with the REC system itself and will be carried out by the REC, ~~normally in parallel with the main ethical review. Guidance on SSA at non-NHS sites is available on~~	5.26	Site Assessment at non-NHS sites Responsibility for assessing the suitability of non-NHS sites in the UK lies with the REC system itself and will be carried out by the REC as part of the ethical review.

	~~the HRA website: http://www.hra.nhs.uk/resources/applying-for-reviews/site-specific-assessment-ssa/ .~~		
5.28	~~Individual RECs may be identified for non-NHS sites regularly involved in research requiring SSA, e.g. research units in the commercial, higher education or voluntary sectors. The main REC may then seek advice from that local REC, with knowledge of the trial unit, when undertaking the SSA.~~		Text deleted
5.29	~~***Exemption from the requirement for SSA at non-NHS sites Non-clinical research involving adults lacking capacity to consent***~~ ~~The REC has the discretion to waive the requirement for SSA at non-NHS sites in the case of research involving adults lacking capacity to consent for themselves where the study involves no clinical interventions *and* either of the following applies:~~ ~~(i) Studies with no local investigator. All recruitment procedures and all study procedures involving participants (e.g. questionnaires, observations) are undertaken directly by the Chief Investigator's team. The role of local staff at the site is limited to facilitating the study, for example, by helping to identify potential participants and relatives/consultees, who are then approached by the Chief Investigator's team.~~		Text deleted

	~~(ii) Low risk studies. In this case, SSA may be waived where the REC is satisfied that the risk to participants lacking capacity is likely to be negligible and will not interfere with their freedom of action or privacy in a significant way or be unduly invasive or restrictive. These criteria could apply for example to studies limited to use of personal data, or the administration of a simple questionnaire involving minimal burden.~~		
5.30 5.31	~~When giving exemption for SSA under paragraph 5.29, the REC should be satisfied from review of the main application that the Chief Investigator's team will make adequate arrangements for the conduct of the study locally, including procedures for identifying suitable sites, participants and relatives/consultees. Where local site staff will be responsible for undertaking recruitment or other study procedures, the REC should be satisfied that they will have appropriate training. Approval conditions may be included in the ethical opinion where appropriate (see paragraphs 3.18ff).~~ ~~The REC has the discretion to waive the requirement for SSA at non-NHS sites in the case of research under the category 'Other clinical trials to study a novel intervention or randomised clinical trials comparing interventions in~~		Text deleted

5.32	~~clinical practice' where the REC is satisfied that the study poses minimal risk to participants.~~ ~~The Chief Investigator or sponsor may submit a request for SSA exemption under paragraph 5.29 either with the main application or in further correspondence at any time. However, the Committee may decide to give exemption without receiving such a request. Decisions to give exemption may be made at a meeting of the Committee or sub-committee, or by the Chair acting alone. The Chief Investigator and sponsor should be notified using SL1A or by incorporating the relevant text into the validation or opinion letter.~~		
5.33	In clinical research the main sites undertaking recruitment and administering the interventions will always require ~~SSA~~. 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	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

	the requirement for ~~SSA~~ 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 ~~using SL1A~~ or by incorporating the relevant text into the validation or opinion letter. (Note however that where the NHS organisation accepts full governance responsibility for procedures at the non-NHS organisation, this is considered a single site ~~and SSA exemption is not required)~~.		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 procedures at the non-NHS organisation, this is considered a single site)
5.34	**Application for site-specific assessment at non-NHS sites** Applications for SSA ~~can only be submitted once the main application has been validated. The ethical review and the SSA will normally proceed in parallel, so that the outcome of the SSA will be included in the ethical opinion given by the REC. However, applications for SSA may also be submitted at any time after a favourable ethical opinion has been given. The REC has 14 days (for a Phase 1 trial) or 25 days (for other studies) from receipt of a Site Specific Assessment application to notify the Chief Investigator for the study of the decision for the SSA. SSAs should never be reviewed before the full application review, regardless of when it is received. The clock on HARP will~~	5.28	**Application for site assessment at non-NHS sites** For CTIMPs and devices the non NHS/HSC site assessment form should be electronically submitted from IRAS as part of the main application.

	~~automatically re-set to 0 days when the application receives a favourable opinion.~~		
5.35	~~Applications for SSA should be submitted via e-submissions in IRAS.~~		Text deleted
5.36	The application should be accepted as valid if it meets all the following criteria: i. The ~~Site Specific Information~~ Form and all supporting documentation have been submitted electronically from IRAS. ii. All relevant sections ~~and questions~~ in the ~~SSI~~ form have been completed, and the text is in English and legible. iii. The ~~SSI~~ form has been electronically authorised ~~by the Principal Investigator and~~ the Site Management Organisation. iv. 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 ~~on the SSI~~ form, taking into account the guidance in paragraphs 5.12-5.23.	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. 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. 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 ~~cover for the Principal Investigator has been provided *(except for commercial Phase 1 trial sites)*~~. ~~viii. Evidence of professional registration for the Principal Investigator has been provided.~~ ix. 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.		vii. Evidence of insurance or indemnity (not required for Phase 1 trials in healthy volunteers where the site is accredited by the MHRA). vii. 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.
5.37	~~If the application is valid, the REC Manager should acknowledge receipt by writing to the Principal Investigator using SL17. A copy should be sent to the sponsor's contact point.~~		Text deleted
5.38	~~If the application is not valid, the Principal Investigator should be notified of the reason(s) using SL18.~~		Text deleted
5.39	**Issues relevant to the site ~~-specific~~ assessment** In ~~making a site-specific~~ assessment, the main issue to be considered 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 his/her professional qualifications, knowledge of	5.30	**Issues relevant to the site assessment** 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: (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. (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) For studies involving adults unable to consent for themselves, the local arrangements for identifying and approaching a legal representative (CTIMPs), the guardian, welfare attorney or nearest relative (non-CTIMPs in Scotland), a consultee under section 32 of the Mental Capacity Act (non-CTIMPs in England and Wales) or a close relative or friend (non-CTIMPs in Northern Ireland).~~		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. (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.

	~~This includes consideration of the appointment and training of professional legal representatives or nominated consultees. The REC may request additional documentation where appropriate.~~ (vii) 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. (~~Where the Chief Investigator proposes in the main application that such groups are to be excluded, and the REC does not accept the reasons given and requires their inclusion, the SSI form should be revised and new applications for SSA should be made.)~~ (viii) 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. (ix) 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*		(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 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.

	so that it can recover any losses from them where the harm resulted from their negligence. ~~*The sponsor's insurance cover will be reviewed by the main REC.)*~~ (x) Evidence that the Principal Investigator has appropriate professional registration. (xi) 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.		
5.41	~~Site-specific assessment does not involve any consideration of other issues relating to the ethical review of the application.~~		Text deleted
5.42	~~***Procedures for SSA for additional non-NHS sites***~~ ~~When carried out separately to the main ethical review (eg for new sites added at a later date) the assessment should be made by at least two members, including the Chair or a vice-chair. It may be carried out in correspondence, including e-mail. Alternatively the assessment may be made at a meeting of the sub-committee or at a full meeting of the REC.~~		Text deleted
5.43	~~Where the assessment is made in correspondence, the Chair or vice-chair is responsible for reviewing the comments made by other members and for making a final decision on behalf of the REC. Any relevant questions or~~		Text deleted

	~~concerns should be addressed appropriately with the Investigator. Where there are significant objections, or a difference of view among members, these may be discussed further at a meeting of the sub-committee or the Committee at the discretion of the Chair. The REC Manager should prepare minutes of assessments made in correspondence which should include the names of the members involved, all comments received and the outcome of the assessment.~~		
5.44	~~Every effort should be made to address relevant questions with the Investigator within the time allowed for the SSA. The Investigator may be required to respond to questions in writing or by telephone, or invited to attend a Committee or sub-committee meeting. A file record should be kept of any telephone conversation. If the Investigator does not respond or provide adequate assurances, an unfavourable opinion for the addition of that site should be given.~~		Text deleted
5.45	~~SSA~~ 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 ~~for the purpose of trial-specific SSA~~, 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 context in which the research will be undertaken and assess the suitability of the staff and facilities.	5.32	The assessment of a non-NHS 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 context in which the research will be undertaken and assess the suitability of the staff and facilities.

5.49	~~Trial-specific SSA~~ 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 taken into account in any ~~SSAs~~ undertaken prior to the issues being resolved and accreditation confirmed.	5.36	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 taken into account in any reviews undertaken prior to the issues being resolved and accreditation confirmed.
5.50	~~SSA in non-NHS sites will usually be undertaken by the REC in parallel with the ethical review of the full application.~~ Reassurance as to the suitability of the site may be gained from the registration of the site within the MHRA Phase 1 Accreditation Scheme.	5.37	Reassurance as to the suitability of the site may be gained from the registration of the site within the MHRA Phase 1 Accreditation Scheme.
5.51	~~Where any new sites are added after the initial ethical review and approval, the SSA can be undertaken by a sub-committee.(see 5.34) If the REC has any concerns in respect of a site, it may raise those concerns with the identified local REC and seek their advice.~~		Text deleted
5.53	~~***Action by the REC following SSA for a non-NHS site***~~ ~~On taking a decision on site-specific assessment, the REC should proceed as follows.~~		Text deleted

5.54	~~***No objection on site-specific grounds***~~ ~~No non-NHS sites should be approved by the REC until it is in a position to give a favourable ethical opinion to the application.~~		Text deleted
5.55	~~When giving a favourable ethical opinion for any study requiring SSA, the REC should at the same time give specific approval for all non-NHS sites for which it has no objection (SL5 or SL14 as appropriate).~~		Text deleted
5.56	~~Where the REC is in a position to issue a favourable opinion but no SSA has yet been submitted, it may be necessary to advise the Chief Investigator about the procedures.~~ ~~In the meantime the favourable opinion letter (SL5 or SL14) should be issued to the Chief Investigator without delay in all cases. (The letter should make it clear the study cannot start at any non-NHS site.) As soon as one or more SSAs for non-NHS sites have been agreed, approval for these sites should be confirmed by sending SL23C to the Chief Investigator, copied to the sponsor's contact point.~~		Text deleted
5.57	~~It is the responsibility of the Chief Investigator to notify the Principal Investigator at each non-NHS site that the study has a favourable ethical opinion and approval for the site, and for the Principal Investigators then to seek final approval to proceed from the host organisation.~~		Text deleted
5.58	~~Where, following the issue of a favourable ethical opinion, a further SSA is submitted, the REC should confirm the~~		Text deleted

	~~favourable opinion for the new site by issuing SL23C to the Chief Investigator, copied to the sponsor.~~		
5.59	~~***Representations by the Chief Investigator***~~ ~~Where the REC issues an unfavourable opinion for a research site, there is no formal process of appeal. However, the Chief Investigator may make representations in writing to the REC. Any such representations should be given due consideration by the REC.~~		Text deleted
5.60	~~***Revision of the main application with implications for SSA***~~ ~~Where the Chief Investigator revises the main application during the ethical review, the information given in the SSI form may no longer be complete or accurate. In such cases, the REC should consider the following options:~~ • ~~Where the revisions are ethically acceptable but in the judgement of the REC the implications for site-specific assessment are minor (e.g. modification of the schedule of study procedures), any SSAs already underway should continue. Where the revisions are ethically acceptable but could have significant implications for the site-specific assessment (e.g. addition of new study procedures requiring special facilities), the Chief Investigator may be required to modify the SSA.~~		Text deleted

	• ~~Where the revisions are not ethically acceptable, the REC should give an unfavourable opinion (see section 8).~~		
5.61	~~***Delegation of SSA to another body***~~ ~~The RES Manager may make Arrangements for SSAs relating to a particular site or sites to be delegated to another local body with expertise in the management of health-related research. The terms of the delegation should be set out in a written agreement, which should be approved by the Head of RES. The REC system remains accountable for the process of site-specific assessment and for the provision of appropriate advice on the outcome of the SSA within 25 days.~~		Text deleted
5.62	~~The agreement between the RES Manager and the assessment body should include provision for the following:~~ • ~~Definition of the research site(s) and/or geographical area covered by the agreement;~~ • ~~Procedures for referral of valid applications for SSA to the assessment body by the REC Manager;~~ • ~~All SSAs to be reviewed by at least two assessors, including an individual of appropriate seniority;~~		Text deleted

	~~• Compliance with the guidance in paragraph 5.38 on the issues to be considered in the SSA, with no consideration of any other issues;~~ ~~• The outcome of SSAs to be notified to the REC Manager in writing within 25 calendar days of the receipt of the valid application;~~ ~~• There may be further discussion of the SSA directly between the REC and the assessors, in particular where the REC is considering over-ruling objections, but the RES Manager should be kept informed;~~ ~~• Monitoring of the agreement by the RES Manager, with a formal review at least annually.~~		
5.63	Procedures for extension of a study to new sites, appointment of new Principal Investigators or other site-specific amendments are set out in paragraph ~~6.75.~~	5.39	Procedures for extension of a study to new sites, appointment of new Principal Investigators or other site-specific amendments are set out in paragraphs 6.66 – 6.83
5.64	~~In a study requiring SSA,~~ 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 Notice of	5.40	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

	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).		the Chair. A Notice of 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).
5.68	The REC may request ~~a new SSA at~~ 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~~, requiring formal submission of a new application for SSA.~~	5.44	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
5.69	Procedures for ~~reviewing amendments to multi-site research are set out in Section 6, including~~ extension to additional sites ~~(paragraphs 6.75-6.76)~~, appointment of new Principal Investigators (~~paragraphs 6.77-6.80)~~ and site-specific ~~protocol~~ amendments ~~(paragraphs 6.81-6.83).~~	5.45	Procedures for extension of a study to new sites, appointment of new Principal Investigators or other site-specific amendments (paragraphs 6.66-6.83).
Section 6: Amendments to research given a favourable opinion			
Para	SOP 7.3	Para	SOP 7.4
6.20	It is the responsibility of the REC Manager to decide whether or not the notice of amendment is valid and to notify the sponsor and Chief Investigator using SL27 (valid notice) or SL28 (invalid notice). Notification should	6.20	It is the responsibility of the Approvals Officer/REC Manager to decide whether or not the notice of amendment is valid and to notify the sponsor and Chief Investigator using SL27 (valid notice) or SL28 (invalid

	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, special procedures apply – see paragraph 6.67). The agreement of the Chair is not required.		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 6.66-6.72). The agreement of the Chair is not required.
6.23	Sponsors and CIs may seek ~~advice from REC offices or the HRA Queries Line~~ on whether an amendment should be considered substantial. ~~REC Managers may give advice in straightforward cases, or may seek advice from the Regional Manager or the Chair.~~ When giving advice, it should always be made clear that it is ultimately the sponsor's responsibility to determine whether an amendment is substantial.	6.23	Sponsors and CIs may seek advice on whether an amendment should be considered substantial. When giving advice, it should always be made clear that it is ultimately the sponsor's responsibility to determine whether an amendment is substantial.
6.26	Guidance from RES is that the following changes should normally be regarded as substantial: • Changes to the design or methodology of the study, or to background information, likely to have a significant impact on its scientific value • Changes to the procedures undertaken by participants • Changes likely to have a significant impact on the safety or physical or mental integrity of participants, or to the risk/benefit assessment for the study	6.26	Guidance from RES is that the following changes should normally be regarded as substantial: • Changes to the design or methodology of the study, or to background information, likely to have a significant impact on its scientific value • Changes to the procedures undertaken by participants • Changes likely to have a significant impact on the safety or physical or mental integrity of participants, or to the risk/benefit assessment for the study

	• Significant changes to study documentation such as participant information sheets, consent forms, questionnaires, letters of invitation, letters to GPs or other clinicians, information sheets for relatives or carers • A change of sponsor(s) or sponsor's legal representative • Appointment of a new Chief Investigator, or temporary arrangements to cover the absence of a CI reference ~~6.84-6.86~~ • In a CTIMP, addition of a new site and/or new PI not listed in the original application • A change to the insurance or indemnity arrangements for the study • A change to the payments, benefits or incentives to be received by participants or researchers in connection with taking part in the study, or any other change giving rise to a possible conflict of interest on the part of any investigator/collaborator • Temporary halt of a study or temporary halt at a study site to protect participants from harm, and the planned restart of a study following a temporary halt (see paragraph ~~10.91-10.93)~~ • A change to the definition of the end of the study (see paragraph ~~10.96)~~ • Any other significant change to the protocol or the terms of the REC application. • ~~Amendment to the number of UK participants to be recruited into the study~~		• Significant changes to study documentation such as participant information sheets, consent forms, questionnaires, letters of invitation, letters to GPs or other clinicians, information sheets for relatives or carers • A change of sponsor(s) or sponsor's legal representative • Appointment of a new Chief Investigator, or temporary arrangements to cover the absence of a CI reference 6.81-6.83 • In a CTIMP, addition of a new site and/or new PI not listed in the original application • A change to the insurance or indemnity arrangements for the study • A change to the payments, benefits or incentives to be received by participants or researchers in connection with taking part in the study, or any other change giving rise to a possible conflict of interest on the part of any investigator/collaborator • Temporary halt of a study or temporary halt at a study site to protect participants from harm, and the planned restart of a study following a temporary halt (see paragraph 10.89-10.91) • A change to the definition of the end of the study (see paragraph 10.94) • Any other significant change to the protocol or the terms of the REC application.

6.27	• ~~In a non-CTIMP,~~ addition of any new NHS site, or addition of a non-NHS site ~~in a study not requiring SSA~~ (see paragraphs 6.71-6.73)	6.27	• 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 6.72-6.73).
6.34	~~Non-substantial amendments do not need to be reported to the Committee. The REC Manager is not required to acknowledge receipt of any non-substantial amendment. If a non substantial amendment is received, an e-mail response may be sent informing the applicant that non substantial amendments do not need to be submitted to the REC). Referral of non-substantial amendments to the Chair or other members for information is at the discretion of the REC Manager.~~	6.34	Non-substantial amendments do not require an ethical opinion.
6.42	Where a substantial amendment relates solely to the addition of a new site, appointment of a new Principal Investigator or other changes to the management or conduct of the study at a particular site, the procedures in paragraphs 6.66ff should be followed. ~~This is still a substantial amendment but there is no requirement for the amendment to be formally reviewed by the Committee or sub-committee of the REC.~~ Site-specific amendments to the protocol, participant information sheet or other study documentation should be reviewed by the REC according to normal procedures.	6.42	Where a substantial amendment relates solely to the addition of a new site, appointment of a new Principal Investigator or other changes to the management or conduct of the study at a particular site, the procedures in paragraphs 6.66ff should be followed. Site-specific amendments to the protocol, participant information sheet or other study documentation should be reviewed by the REC according to normal procedures.

6.67	Where the amendment relates to the addition of a new NHS site, not listed on the original application form, and/or PI, ~~the REC Manager~~ should issue SL23B within 5 working days, confirming a favourable opinion on condition that permission is given or continued by the R&D office(s) for the care organisation(s) involved. New sites should be manually added to the list of approved sites in HARP. Responsibility for ~~SSA~~ lies with the NHS care organisation. It is not necessary for the amendment to be reviewed or notified to the Committee. If any doubt arises whether the site(s) concerned are NHS sites, ~~the REC Manager~~ should seek clarification from the sponsor and/or the care organisation concerned.	6.67	Where the amendment relates to the addition of a new NHS site, not listed on the original application form, and/or PI, SL23B should be issued within 5 working days, confirming a favourable opinion on condition that permission is given or continued by the R&D office(s) for the care organisation(s) involved. New sites should be manually added to the list of approved sites in HARP. Responsibility for site assessment lies with the NHS care organisation. It is not necessary for the amendment to be reviewed or notified to the Committee. If any doubt arises whether the site(s) concerned are NHS sites, staff should seek clarification from the sponsor and/or the care organisation concerned.
6.69	Where the amendment includes any changes at non-NHS sites, the responsibility for ~~SSA~~ lies with the REC system. ~~The REC Manager should validate the amendment in the normal way. If the amendment is valid, SL23A should be sent within 5 working days of receipt. The sponsor should arrange to apply for SSA by submitting the SSI Form and accompanying documentation in the normal way (5.33).~~	6.69	Where the amendment includes any changes at non-NHS sites, the responsibility for site-assessment lies with the REC system. The non-NHS/HSC Site Assessment form should be submitted as part of the amendment and the amendment should be validated and reviewed by the REC.
~~6.70~~	~~Following SSA for a new non-NHS site, the REC should issue an opinion using either SL23C (favourable opinion) or SL23 (unfavourable opinion).~~		Text deleted
~~6.71~~	~~The REC should not issue the opinion until it has received both the Notice of Substantial Amendment form and decided the outcome of the SSA. REC Managers should note that the validation date for an amendment relating to a non-NHS site is the date by which *both* a valid Notice of Substantial Amendment form and a valid application for~~		Text deleted

	~~SSA have been received by the REC. If only the SSA is received, the REC Manager should contact the sponsor to request that the notice of amendment be provided. When the notice of amendment is received, the opinion should be issued.~~		
6.72	~~Other studies requiring SSA~~ Where the study is to be extended to a new non-NHS site, ~~specific approval for the site is required from the REC. An application for site-specific assessment should be made to the REC.~~	6.71	**Clinical Investigations of Medical Devices** Where the study is to be extended to a new non-NHS site, the NHS/HSC site assessment form should be submitted to the REC as part of a Notice of Substantial Amendment.
6.74	~~There is no requirement to submit a Notice of Substantial Amendment form to the REC, either for NHS or non-NHS sites. See paragraph 6.41~~		Text deleted
6.75	***Research not requiring ~~SSA~~*** ~~The~~ sponsor may extend the study to additional NHS and non-NHS sites, subject to obtaining permission from the NHS care organisation or other organisation responsible for participants at the site. ~~There is no requirement for the REC to be notified of the new site(s) or for application to be made for SSA.~~ The site(s) are deemed to be approved within the terms of the favourable opinion for the study from the REC.	6.72	**Research not requiring site assessment** The sponsor may extend the study to additional NHS and non-NHS sites, subject to obtaining permission from the NHS care organisation or other organisation responsible for participants at the site. The site(s) are deemed to be approved within the terms of the favourable opinion for the study from the REC.
6.80	~~There is no requirement to notify the REC of the appointment of a new Principal Investigator or Local Collaborator in a study not requiring SSA. At NHS sites,~~		Text deleted as this duplicates information which is provided in paragraph 6.79.

	~~the R&D office should be notified and continued permission sought.~~		
6.85	If the new Chief Investigator will also be appointed as a new local Principal Investigator at a research site, this should be made clear on the notice of amendment form. If it is a NHS site, the R&D office should be notified. If it is a non-NHS site in a study requiring ~~SSA~~, the REC should be notified. It is not necessary for a further ~~SSA~~ to be carried out but if the REC has any concerns about the appointment of the new PI it should inform the CI.	6.82	If the new Chief Investigator will also be appointed as a new local Principal Investigator at a research site, this should be made clear on the notice of amendment form. If it is a NHS site, the R&D office should be notified. If it is a non-NHS site in a study requiring site assessment, the REC should be notified. It is not necessary for a further assessment of the site to be carried out but if the REC has any concerns about the appointment of the new PI it should inform the CI.
6.88	In some cases it may be necessary to appoint an acting or new CI or PI. The following guidance may be given to CIs, PIs and sponsors: ~~•~~ Where the absence is likely to exceed 3 months or is indefinite, it is mandatory to appoint an acting or new CI or PI. (see paragraphs ~~6.66-6.71, 6.77-6.80 and 6.84-6.85.)~~ • Where the absence is likely to exceed 4 weeks but will be less than 3 months, the sponsor should ensure that appropriate cover arrangements are made. The REC should be notified by letter about cover arrangements for absent CIs. R&D offices at NHS sites should be notified about cover arrangements for absent PIs. For non-NHS sites in studies requiring ~~SSA~~, the REC should be notified. If it has any concerns about the suitability of the	6.85	In some cases it may be necessary to appoint an acting or new CI or PI. The following guidance may be given to CIs, PIs and sponsors: • Where the absence is likely to exceed 3 months or is indefinite, it is mandatory to appoint an acting or new CI or PI. (see paragraphs 6.66-6.85.) • Where the absence is likely to exceed 4 weeks but will be less than 3 months, the sponsor should ensure that appropriate cover arrangements are made. The REC should be notified by letter about cover arrangements for absent CIs. R&D offices at NHS sites should be notified about cover arrangements for absent PIs. For non-NHS sites in studies requiring site assessment, the REC should be notified. If it has any concerns about the suitability of the

	arrangements, it should notify the sponsor. The REC has the discretion to request formal appointment of an acting CI or PI. • For absences shorter than 4 weeks, it is not generally necessary to notify the REC.		arrangements, it should notify the sponsor. The REC has the discretion to request formal appointment of an acting CI or PI. • For absences shorter than 4 weeks, it is not generally necessary to notify the REC.
~~6.90~~	Return of a CI or PI following a period of absence is not considered to be a substantial amendment. The REC should be notified for information only of the return of a CI (in any study), or a PI in a CTIMP or the return of a PI at a non-NHS site requiring SSA.	6.87	Return of a CI or PI following a period of absence is not considered to be a substantial amendment. The REC should be notified for information only of the return of a CI (in any study), or a PI in a CTIMP or the return of a PI at a non-NHS site requiring site assessment.
Section 7: Sub-Committees			
Para	SOP 7.3	Para	SOP 7.4
7.3 (i)	Sub-committees may exercise the following functions on behalf of the REC: (i) Review of new applications submitted for proportionate review (see Section ~~3~~)	7.3 (i)	Sub-committees may exercise the following functions on behalf of the REC: (ii) Review of new applications submitted for proportionate review (see Section ~~4~~)
7.14	Where a telephone meeting is necessary, the Approvals Officer/REC Manager should issue an agenda and papers	7.14	Where a telephone meeting is necessary, the Approvals Officer/REC Manager should issue an agenda and papers

	for the meeting according to normal procedure. Matters on the agenda may be considered in written correspondence or e-mail between the members concerned prior to the telephone meeting, provided that the decisions of the sub-committee are then formally made at the meeting. Minutes of telephone meetings should be prepared by the REC Manager. ~~Where he/she is unable to follow the telephone discussion,~~ the Chair should provide written notes for incorporation in the minutes.		for the meeting according to normal procedure. Matters on the agenda may be considered in written correspondence or e-mail 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.
7.27	The requirements of paragraphs 2.80ff 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~~, including review of SSA.~~	7.27	The requirements of paragraphs 2.80ff 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.
Section 8: Further review of research given a unfavourable opinion			
SOP 7.4	SOP 7.3	Para	SOP 7.4
8.3	~~A~~ new application ~~should be entered on HARP by the REC Manager, and~~ will receive a new REC reference number. The validation procedures in Section 1 apply. In addition to the usual validation criteria, the following requirements apply (see paragraph 1.4~~8~~(n)ff):	8.3	The new application ~~should be entered on HARP by the REC Manager, and~~ will receive a new REC reference number. The validation procedures in Section 1 apply. In addition to the usual validation criteria, the following requirements apply (see paragraph 1.45(n)ff):
8.4	The application should be ethically reviewed according to normal procedures. In the case of studies requiring ~~SSA~~ for non-NHS sites, new applications for ~~SSA~~ should be submitted and processed in the normal way.	8.4	The application should be ethically reviewed according to normal procedures. In the case of studies requiring an assessment of site suitability for non-NHS/HSC sites, new applications for site assessment should be submitted and processed in the normal way.

8.31	~~In the case of studies requiring SSA, the second REC assumes all responsibilities relating to the approval of non-NHS sites and should be reviewed alongside the main application. There is no need for new applications to be submitted. Any SSAs which have been suspended should restart with a new clock.~~		Text deleted
Section 10: Monitoring of research given a favourable opinion			
SOP 7.4	SOP 7.3	Para	SOP 7.4
10.3	~~Where a study received ethical approval from more than one REC under the system in operation prior to 1 March 2004, the sponsor or Chief Investigator should contact the Head of RES to request that a single REC is appointed to take responsibility for monitoring of the research.~~		Text deleted
10.14	Progress reports should be acknowledged ~~by the REC Manager~~ (SL37 may be used) and reviewed at least by the ~~Chair or, at the Chair's discretion, by one or more members of the~~ Committee ~~(for example, the lead reviewer for the study) or a Scientific Officer~~. The Committee should be notified of the receipt of the report (see paragraph 2.13). Copies or summaries may be distributed to members.	10.13	Progress reports should be acknowledged (SL37 may be used) and reviewed by the Committee (or reviewed by a member of staff on behalf of the Committee). The Committee should be notified of the receipt of the report (see paragraph 2.13). Copies or summaries may be distributed to members.
10.52	Expedited and annual safety reports will normally be submitted by the sponsor, but may also be submitted by the sponsor's legal representative or the Chief Investigator for the study. Reports should normally be sent by email.	10.51	Expedited and annual safety reports will normally be submitted by the sponsor, but may also be submitted by the sponsor's legal representative or the Chief Investigator for the study. Reports should normally be sent by email.

	~~Extensive line listings may be submitted on CD at the discretion of the REC office (three copies of the CD should be provided).~~		
Section 11: Research databases			
SOP 7.4	SOP 7.3	Para	SOP 7.4
11.30	~~SSA is not required~~ for Research Database applications. The ethical review applies to the management of the database as a whole, including arrangements made with collaborators. There is no requirement for specific ethical approval for Data Collection Centres who provide data under the terms of a supply agreement between their organisation and the database. DCCs are not regarded as research sites for the purpose of the UK Policy Framework for Health and Social Care Research. However, local collaborators at Data Collection Centres within the NHS will require internal permission from their NHS care organisation to collect and supply data relating to NHS patients.	11.30	An assessment of the site is not applicable for Research Database applications. The ethical review applies to the management of the database as a whole, including arrangements made with collaborators. There is no requirement for specific ethical approval for Data Collection Centres who provide data under the terms of a supply agreement between their organisation and the database. DCCs are not regarded as research sites for the purpose of the UK Policy Framework for Health and Social Care Research. However, local collaborators at Data Collection Centres within the NHS will require internal permission from their NHS care organisation to collect and supply data relating to NHS patients.
Section 12: Research involving human tissue			
SOP 7.4	SOP 7.3	Para	SOP 7.4
		12.7	Arrangements for collaboration between the Human Tissue Authority and the HRA have been agreed in a Memorandum of Understanding between HRA and the Human Tissue Authority.

Section 13: Research involving adults unable to consent for themselves			
Para	SOP 7.3	Para	SOP 7.4
13.52	~~SSA is required for any new application involving adults unable to consent for themselves (except for applications for section 30 approval under the MCA submitted under transitional arrangements). The normal procedures for SSA in Section 5 of the SOPs apply. Where the site is outside the NHS, the SSA should be undertaken by the main REC.~~	~~13.52~~	Text deleted
Section 14: Communication with other regulators and review bodies			
~~Para~~	SOP 7.3	Para	SOP 7.4
14.7	~~A Memorandum of Understanding (MoU) between the MHRA, RES, GTAC and AAPEC sets out the respective roles and responsibilities of MHRA and recognised RECs in relation to CTIMPs, and agreed procedures for collaboration and communication. The MoU is published on the HRA website and includes contact points for use by RECs and operational managers.~~	~~14.7~~	Text Deleted
Section 15: Storage and retention of documentation			
Para	SOP 7.3	Para	SOP 7.4

15.8	Signed final copies of the minutes of full REC meetings and sub-committee business should be retained for at least ~~30~~ years. ~~Where electronic versions are available, paper copies may be destroyed.~~ Draft versions of the minutes should be uploaded to HARP and ~~may~~ be deleted once the final version has been ratified and signed~~,~~ ~~together with any written comments submitted by members or manuscript notes taken during meetings.~~	15.8	Signed final copies of the minutes of full REC meetings and sub-committee business should be retained electronically for at least 20 years. Draft versions of the minutes should be uploaded to HARP and should be deleted once the final version has been ratified and signed.
~~15.11~~	~~Operational management guidance on archiving other historic paper files to CD or other electronic media is issued by the Head of RES.~~		Text deleted
~~15.18~~	~~RECs undertaking SSA for non-NHS sites should retain the SSI Form, accompanying documentation and any correspondence relating to the SSA until the retention date for the study.~~		Text deleted
~~15.19~~	~~RECs should also retain, until the retention date, documentation relating to SSA undertaken for NHS sites in CTIMPs prior to the transfer of responsibility to NHS R&D offices in April 2009. This includes "locality assessments" undertaken by Local Research Ethics Committees for CTIMPs reviewed by Multi-Centre Research Ethics Committees prior to the issue of version 1 of the SOPs in March 2004.~~		Text deleted
~~15.20~~	~~There is no requirement to retain any documentation relating to SSA or locality assessment undertaken for NHS sites in non-CTIMPs prior to April 2009.~~		Text deleted

Annex A: Index to standard letters and forms			
Para	SOP 7.3	Para	SOP 7.4
	~~SL1A Decision on SSA exemption for non-NHS site(s)~~ ~~SL9 Request for advice of referee following the meeting~~ ~~SL17 Valid application for SSA~~ ~~SL18 Invalid application for SSA~~ ~~SL23 Unfavourable opinion for site following objection from site-specific assessor~~ ~~SL23A Acknowledgement of notice of substantial amendment to add new non-NHS site or PI in a CTIMP~~ ~~SL23C Extension of favourable opinion to non-NHS site following SSA~~		SL2 Acknowledgement of a valid application

Annex G: Insurance, indemnity and compensation			
Para	SOP 7.3	Para	SOP 7.4
12.	GPs are usually independent practitioners who provide services under contract with the Clinical Commissioning Group (i.e. they are not salaried employees). As such, they are not covered by NHS indemnity and must have their own personal indemnity arrangements. Other independent	12.	<u>In England and Wales, GPs and practice staff (for example, practice nurses) are covered under the scope of the Clinical Negligence Scheme for General Practice (England) or the Clinical Negligence Scheme for Providers of Primary Medical Service (Wales).</u>

	practitioners to whom this applies include dentists, optometrists and community pharmacists. Independent practitioners will normally arrange indemnity cover for their clinical practice through their professional bodies or mutual defence organisations such as the Medical Defence Union. Cover will normally extend to private practice as well as NHS practice. NHS staff employed by independent practitioners (for example, practice nurses) are not covered by NHS indemnity but will normally be covered by the practitioner's professional indemnity arrangements.		In Scotland and Northern Ireland, GPs are usually independent practitioners who provide services under contract with the Clinical Commissioning Group (i.e. they are not salaried employees). As such, they are not covered by NHS indemnity and must have their own personal indemnity arrangements. Other independent practitioners (across the whole of the UK) to whom this applies include dentists, optometrists and community pharmacists. Independent practitioners will normally arrange indemnity cover for their clinical practice through their professional bodies or mutual defence organisations such as the Medical Defence Union. Cover will normally extend to private practice as well as NHS practice. NHS staff employed by these independent practitioners (for example, practice nurses) are not covered by NHS indemnity but will normally be covered by the practitioner's professional indemnity arrangements.
41.	~~*Site-specific assessment*~~ ~~The SSA~~ for a commercially sponsored Phase 1 trial does not need to check that the CRO or Principal Investigators, research nurses and other individuals have their own insurance or indemnity cover, as this does not affect the sponsor's undertaking to compensate the subject upfront. It is in the sponsor's own interest to check that other parties have appropriate insurance or indemnity so that the sponsor can recoup its own losses where the volunteer's claim was based on their negligence.	41.	Assessment of site suitability The site assessment for a commercially sponsored Phase 1 trial does not need to include a check that the CRO or Principal Investigators, research nurses and other individuals have their own insurance or indemnity cover, as this does not affect the sponsor's undertaking to compensate the subject upfront. It is in the sponsor's own interest to check that other parties have appropriate insurance or indemnity so that the sponsor can recoup its

			own losses where the volunteer's claim was based on their negligence.
42.	~~The Site-Specific Information Form for non-NHS sites in IRAS has therefore been modified so that~~, for commercial Phase 1 trials, it excludes the requirement to provide the REC with evidence of insurance and indemnity for the site.	42.	The non-NHS/HSC site assessment form excludes the requirement to provide the REC with evidence of insurance and indemnity for the site for commercial phase 1 trials
ANNEX J: The Gene Therapy Advisory Committee			
Para	SOP 7.3	Para	SOP 7.4
31.	~~Arranging the transfer~~ ~~The GTAC Manager will notify the applicant that GTAC plans to transfer the application. The applicant may indicate a preference for a particular flagged REC. The GTAC Manager will then contact the appropriate REC directly by phone or email to advise that it wishes to transfer an application. If an agenda slot is available at the next meeting, the second REC Manager should accept the transfer, book the application and allocate a REC reference number. If the agenda for the next meeting is full, the GTAC Manager should contact other flagged RECs. In case of any difficulty identifying a suitable agenda slot, the GTAC Manager /~~	31.	The transfer of the application should be undertaken by the Approvals Officer/REC Manager.

32.	~~Regional Manager should contact the Head of RES for further advice.~~ ~~Once a booking has been made, the GTAC Manager will notify the applicant and make arrangements to transfer the application to the relevant REC ("the second REC") within HARP.~~		
37.	The second REC has the discretion to seek the advice of GTAC on the application if required~~. If so, the REC Manager should contact the GTAC Manager by phone or email to discuss the advice required and the options for providing it. These include:~~ ~~• Written advice from the GTAC Manager or from a member of GTAC, acting as a referee~~ ~~• Co-opting a GTAC member to attend either the full Committee meeting or a sub-committee meeting.~~	36.	The second REC has the discretion to seek the advice of GTAC on the application if required either in writing or by co-opting a GTAC Member.