- delivering clinical interventions within a research study, where those interventions are accepted examples of normal care within their clinical practice (e.g. licensed medicines or CE Marked medical devices being used within their normal intended purpose).

3.58H However, professional indemnity would not normally cover the following research activities:

(i) Chief Investigator

Chief Investigators have a range of responsibilities that go beyond normal clinical care, for example protocol design, applying for ethical review, management of the research, data analysis and writing up the results. Independent practitioners will not be covered by personal professional indemnity for their role as Chief Investigator in any study.

(ii) Research procedures outside normal care

This would include any clinical interventions, tests or investigations that are not accepted examples of normal care within the practitioner's clinical practice. Examples include unlicensed medicines, non-CE marked medical devices, or licensed medicines or CE marked devices administered outside the normal conditions of use.

3.58J In the above circumstances, the practitioner may need to take out additional cover with their insurer.

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Further review following an unfavourable opinion

3.59 Where a REC has given an unfavourable opinion on an application, the applicant may seek further review as follows:

- A new application may be submitted, taking due account of the REC's concerns. This should be processed and reviewed in the same way as any other new application.
- A second review of the same application may be obtained from another REC by giving notice of appeal to NRES Head Office.

3.60 Procedures relating to further review are set out in Section 7.

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Communication with other bodies

Progress of applications

3.61 It is generally the responsibility of the Chief Investigator to inform other interested bodies of the progress of the ethical review. The REC system is not accountable for ensuring that bodies such as the sponsor, funder and relevant care organisations are kept informed and provided with copies of any documentation required. However, the policy from NRES Head Office s that the REC system should take reasonable steps to facilitate good communication between those concerned.

3.62 Standard procedures for the copying of correspondence are as follows:

(i) The main REC should send the sponsor (or the sponsor's representative) a copy of all letters to the Chief Investigator about the progress of the application, and any subsequent correspondence about the study following issue of a favourable opinion. Where more than one sponsor has been named on the application, correspondence will be sent only to the sponsor nominated to take responsibility for communications with the REC.

(ii) Where the main REC is also the local REC for the lead NHS site, it should send copies of correspondence to the R&D Department for the care organisation or consortium. 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 main REC confirming the favourable opinion for the study and for the site.

(iii) RECs undertaking site-specific assessment should send a copy of the letter validating the SSA (SL17) to the research governance contact for the care organisation or consortium. The Chief Investigator and sponsor will be expected to arrange for care organisations to be notified of the decision of the main REC following SSA.

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Communication with MHRA on CTIMPs – general policy

3.63 The MHRA has primary responsibility for the safety of medicinal trials. The MHRA Clinical Trials Unit assesses the safety of all proposed CTIMPs, drawing on expertise in pharmacology, toxicology and clinical medicine. The ethics committee may generally rely on the MHRA to assess the safety of medicinal trials. It is not required to undertake its own expert scientific or safety assessment or seek advice on safety issues from scientific referees. However, the committee should have sufficient understanding of the scientific background and the safety issues to be able to give an ethical opinion. In particular, the committee should make an ethical assessment of the information provided in the application about the potential risks and benefits to participants and any measures in place to minimise the risks (e.g. rescue medication, stopping rules, emergency procedures, intensive care facilities). The ethical review must also ensure that the potential risks and benefits of the trial are fully and clearly explained in the participant information sheet.

3.63A The Chief Investigator together with the sponsor is responsible for ensuring that the documentation submitted to the ethics committee fully and accurately describes the safety profile of the IMP and the potential risks to participants. The ethics committee may generally rely on the accuracy of this information.

3.63B The Clinical Trials Regulations provide for sharing of relevant information on CTIMPs between ethics committees and the MHRA. Where, exceptionally, the main REC requires further information or clarification from an independent source on safety issues that are relevant to the ethical review, it may seek advice directly from the MHRA Clinical Trials Unit (CTU). Requests should be sent to the Head of the CTU. SL16 may be used. Communications should be emailed to clintrialhelpline@mhra.gsi.gov.uk with the following subject line:

"URGENT: REC correspondence for Head of CTU".

3.63C Where significant changes are made to a trial as a result of either the ethical review or CTA process, it is the responsibility of the sponsor to ensure that both the MHRA and main REC are informed. Although substantial amendments are not normally submitted until a trial has started (see Section 5), it may exceptionally be necessary for the sponsor to submit a substantial amendment during the process of initial application to ensure that both agencies are aware of all relevant information before final decisions on applications are made. The MHRA will alert sponsors where it considers that substantial amendments should be submitted or any other communication with the ethics committee is necessary in the light of the safety assessment made for the purpose of the CTA. (This is of particular importance in relation to Phase 1 trials subject to special precautions by the MHRA – see paragraph 3.63F). The main REC should similarly advise applicants to submit substantial amendments where significant changes are made to the protocol which could impact on the MHRA's assessment of the trial.

3.63D The Chief Investigator should provide the main REC with a copy of the letter from the MHRA confirming the CTA. Any remarks made by the MHRA should be noted by the main REC. Where the main REC receives the letter after the issue of a favourable opinion, the Co-ordinator should ensure that the letter is reviewed at the next available sub-committee or committee meeting so that any remarks made by the MHRA can be noted. If necessary, the committee may seek further information or clarification from the Head of CTU (see paragraph 3.63B). Exceptionally, it may review its opinion in the light of any new scientific or safety issues arising from the MHRA assessment that have a bearing on the ethical acceptability of the trial (see paragraph 9.83-9.84). For further guidance about communication with MHRA on safety issues arising after the trial has started, see paragraph 9.56.

3.63E The main REC is required by the Clinical Trials Regulations to notify the MHRA of the final opinion, whether favourable or unfavourable, so that it can be entered on EudraCT. A copy of the final opinion letter should be sent by email[2] to clintrialhelpline@mhra.gsi.gov.uk with the following subject line:

"REC opinion for EudraCT".

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[2] It is planned to provide the MHRA Clinical Trials Unit with confidential access to RED so that it will be automatically notified of the issue of opinions on new applications and substantial amendments in CTIMPs. There will no longer be a requirement for the main REC to send notification by email. RECs will be notified when these arrangements are in place.

Phase 1 trials under precautionary measures

3.63F Special procedures apply to Phase 1 trials involving molecular antibodies or other novel molecules targeting the immune system, acting via a novel mechanism. Such trials are under precautionary measures by the MHRA. It is expected that protocols will be revised as a result of additional expert opinion obtained by the MHRA from the Commission on Human Medicine (CHM). It is essential for the ethics committee to be informed about the preliminary MHRA assessment of these trials, incorporating the additional expert opinion, and to understand how the protocol has been designed to minimise the risks to participants.

3.63G Applicants should provide a covering letter for the ethics committee summarising preliminary discussions with the MHRA and explaining, if applicable, how the protocol has been revised in line with the additional expert opinion from CHM. A copy of the correspondence with MHRA should be enclosed.

3.63H If such discussion has not yet taken place, or is still underway, applicants are advised not to submit the application for ethical review at this point. If an applicant proceeds with the application against this advice, the ethics committee is required to proceed with the review. It should request further information about the preliminary discussions with MHRA and a copy of relevant correspondence when issuing a provisional opinion. If this is not provided, along with evidence that the trial documentation has been appropriately modified, the committee could issue an unfavourable opinion.

3.63J The ethics committee may write to the CTU (see paragraph 3.63B above) to seek independent confirmation of whether a proposed trial is under precautionary measures and if so what stage the preliminary review by MHRA has reached.

3.63K These procedures apply routinely to trials under precautionary measures. In the case of other CTIMPs, the need to seek additional information or clarification about the MHRA safety assessment is at the discretion of the committee.

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Communication with MHRA on medical devices

3.63L When reviewing a medical device study requiring regulatory approval (see paragraph 3.47), the main REC may seek advice from the Medical Devices Division at the MHRA if appropriate. Clarification may be sought on issues relating to the safety or performance of the device that may be relevant to the ethical review, for example the description of risk in the participant information sheet. Requests for information should be sent to the Medical Director of MHRA (Devices) by emailing susanne.ludgate@mhra.gsi.gov.uk.

3.63M Where significant changes are made to a clinical investigation of a medical device as a result of either the ethical review or regulatory approval process, it is the responsibility of the sponsor to ensure that both MHRA (Devices) and the main REC are informed. Substantial amendments should be notified where appropriate (see section 5).

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Statements of compliance

3.64 Sponsors of CTIMPs are required under International Conference for Harmonisation (ICH) Guidelines for Good Clinical Practice (GCP) to obtain a statement from the ethics committee issuing the ethical opinion on the trial that it is organised and operates according to GCP. All the REC standard letters issuing ethical opinions on a CTIMP include an appropriate statement of compliance with the Clinical Trials Regulations as they apply to ethics committees and the conditions and principles of GCP, and should include or enclose a list of members involved in the ethical review indicating lay members and stating the profession of expert members. The statement of compliance also explains that the constitution of a NHS REC is as defined in GAfREC and its operating procedures are defined by the national SOPs issued by NRES Head Office. No additional documentation needs to be provided to sponsors. In particular, there is no requirement to provide details of local REC members or other individuals involved in site-specific assessments.

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Publication of opinions

3.65 Guidance on the publication of decisions in the REC's annual report is set out in GAfREC.

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Approval to proceed with research

3.66 A favourable opinion from a REC does not imply management (i.e. research governance) approval from relevant care organisation(s) to proceed with the research. Applicants should be informed of the requirement to apply separately to each care organisation for research governance approval. The R&D Departments of NHS care organisations may indicate approval in principle prior to the ethical review, but will not give final approval to proceed until a favourable ethical opinion and, where applicable, regulatory approval have been confirmed.

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Section 4: Site-specific assessment

Summary

Under the EU Directive and the Clinical Trials Regulations there can be one ethical review only for any CTIMP in the UK. The policy of the UK Health Departments is that this should apply to the ethical review of all research in the NHS.

The single ethical opinion includes an opinion on each site and investigator taking part in the research (unless it is "SSA-exempt"). The REC undertaking the ethical review (the "main REC") is responsible for all aspects of the review, taking advice on the suitability of sites and investigators from other relevant RECs. The process of site-specific assessment (SSA) by RECs may take place in parallel with the main review.

Guidance is given to applicants and RECs on the definition of a research site. Normally this will be a single NHS organisation but could also be a discrete operating unit within a NHS organisation, or a network of researchers, or a research unit outside the NHS. Each site should have a single Principal Investigator, who is responsible for the management and conduct of the research at the site.

"SSA-exempt" studies are those involving routine or low risk research procedures (defined in this section) that do not require the appointment of Principal Investigators at each site. The applicant may declare a study as SSA-exempt. This must be confirmed by the main REC when giving the ethical opinion. Studies designated as SSA-exempt do not require SSA by local RECs or approval of individual sites by the main REC.

Local Principal Investigators may submit applications for SSA as soon as the main application for ethical review has been validated. The application comprises the SSI form and the PI's CV. Additional documentation is required for non-NHS sites.

Guidance is given on issues relevant to the SSA. The local REC is not responsible for wider ethical issues raised by the research. It may draw wider concerns to the attention of the main REC but should not raise formal objections except on site-specific grounds. The main REC may over-rule objections if satisfied that they are not valid.

SSAs may be considered at Committee or sub-committee meetings, or in correspondence involving at least 2 members including the Chair. The PI may be invited to attend a meeting. Clarification of issues relevant to the SSA may be sought.

The SSA may be delegated to another assessor such as local R&D but the local REC remains responsible for communicating decisions to the main REC using RED. The OREC Manager is responsible for drawing up a written agreement with the assessor.

The local REC has 25 days from receipt of a valid application to notify the main REC of the decision. The main REC then informs the Chief Investigator whether it has given a favourable opinion for the site. Form SF1 is used to list approved sites. The CI is responsible for notifying each PI when the site has been approved.

Neither the main REC nor the local REC is responsible for proactive monitoring of the conduct of the research at the site. However, if concerns arise the main REC may request a new SSA and review the favourable opinion for the site. The local REC may itself instigate a new SSA and should report any new concerns to the main REC.

Section 4 Site-specific assessment

General policy on multi-site studies

4.1 In the case of a clinical trial of an investigational medicinal product, the Clinical Trials Regulations provide that a single ethical opinion should be given on any trial, regardless of the number of sites at which the research is to be conducted.

4.2 The policy of the Department of Health and the devolved administrations is that the requirement for a single ethical opinion should apply to all multi-site research within the UK.

4.3 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. The REC that reviews the application is referred to in this section as the "main REC". The main REC is responsible for all aspects of the ethical review.

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Site-specific assessment

4.4 Where a study involves certain types of research procedure, the suitability of each site or sites at which the research is to be conducted requires "site-specific assessment" (SSA). The SSA is not a separate ethical review, but forms part of the single ethical review of the research. Where there is no objection on site-specific grounds, a site may be approved as part of the favourable ethical opinion given by the main REC.

4.5 SSAs will be undertaken either by the local REC for the relevant geographical area or by another local assessor appointed by the OREC Manager. In the case of single-site or multi-site research studies where the main REC is also a relevant local REC for a site, it may undertake the SSA itself alongside its consideration of the application. In all other cases, the SSA for each site will be undertaken separately, and the outcome notified as advice to the main REC from the local REC. As far as possible, SSAs should be undertaken in parallel with the consideration of the application by the main REC and within the 60 day time period, so that the approved

sites can be listed when issuing a favourable opinion. In certain circumstances, however, SSAs may be carried out subsequently, and the list of approved sites for the study updated by the main REC.

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The Principal Investigator

4.6 In the case of any single or multi-site research requiring SSA, the investigator responsible for the conduct of the research at an individual research site will be known as the Principal Investigator for that site. There should only be one Principal Investigator at each site.

4.7 A "single site study" is a study that the Chief Investigator plans to conduct at one site only in the United Kingdom. If the study requires SSA, the Chief Investigator will in most cases also be the Principal Investigator for the site.

4.8 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 if the research procedures require SSA (see paragraphs 4.19-4.32). 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).

4.9 Principal Investigators are responsible to the Chief Investigator for complying with the terms of the REC application and the protocol.

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Definition of a research site

4.10 Under the Clinical Trials Regulations, a "trial site" means a hospital, health centre, surgery or other establishment or facility 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. The guidance should be taken into account by applicants and RECs in relation to:

- identifying the individual sites at which the research is to be conducted
- appointing a Principal Investigator (where SSA is required)
- applying for SSA (entering the name of the site on the SSI form)
- giving an ethical opinion for each site.

4.11 In general, the research site should be identified as the single organisation responsible for conducting the research at a particular locality.

4.12 In the case of research conducted within the NHS, the site will in most cases be one of the following:

- A NHS Trust (in England or Wales)
- A NHS Health Board (in Scotland)
- A Health and Personal Social Services Trust (in Northern Ireland)
- A GP practice.

4.13 Where the research will be conducted at more than one location within the same 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.

4.14 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 operating divisions or community health partnerships established by NHS Health Boards in Scotland.

4.15 For research conducted by GPs, the Primary Care Trust (England), Health Board (Scotland), Local Health Board (Wales) or Central Services Agency (Northern Ireland) is the "organisation providing care" as defined in the NHS Research Governance Framework. However, the GP 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 are conducting a study within the same GP practice, the practice should be regarded as a single site and one of the GPs should be appointed as the Principal Investigator.
- In some cases, two or more independent GP 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 GP 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 Investigator for the site. Researchers other than GPs may also be involved in the network/consortium.

4.16 A Primary Care Trust, Health Board, Local Health Board or the Central Services Agency 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.

4.17 A Strategic Health Authority in England could be identified as the research site for some research, for example studies in public health, epidemiology or needs assessment.

4.18 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)
- a private hospital or private clinical practice.

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), the name of the site should be clearly distinguished from the NHS organisation concerned.

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Exemption from site-specific assessment

Responsibilities of the main REC

4.19 The need for site-specific assessments to be carried out in the case of multi-site studies is a matter for the discretion of the main REC, taking into account the guidance in paragraphs 4.24-4.32. The guidance applies to both single- and multi-site studies.

4.20 When submitting an application, the Chief Investigator should declare (at A6 on the application form) if in his/her opinion the research does not require SSA at any research site. Where such a declaration is made, this should be considered by the main REC at the meeting at which the application is ethically reviewed. The REC should consider the procedures to be carried out and decide whether SSA is required. The decision should be one of the following:

(a) SSA-exempt. All sites in the study are exempt. There is no requirement for Principal Investigators to be appointed at individual sites or for any SSI form to be submitted as part of the application. No research site requires specific approval as part of the ethical opinion for the study. The main REC will assess the suitability of the Chief Investigator, and his/her research facilities, as part of the main ethical review. The information provided in Parts A and B of the application form and supporting documentation should normally be sufficient for this purpose. Aggregated information about recruitment of local research sites should be

provided to the main REC in annual progress reports.

(b) Non-exempt. In general no sites are exempt. A Principal Investigator should be appointed at each site and an application made for SSA. Specific approval for each site should be given by the main REC as part of the ethical opinion. (Exceptionally, individual sites in a non-exempt study may be specially exempted from SSA by decision of the main REC – see paragraph 4.32.)

4.21 After the meeting the Co-ordinator should notify the Chief Investigator of the decision of the REC. The outcome should be entered on RED.

4.22 In the case of SSA-exempt studies, no information about the study needs to be provided to other RECs. However, local collaborators should still seek research governance approval from the R&D Department for the care organisation. Where the Chief Investigator is conducting the research directly at a number of sites, he/she also requires research governance approval from the R&D Department for each care organisation.

4.23 The main REC may review SSA exemption at any time. In particular, it may be appropriate to review the designation of some multi-site studies that received ethical approval prior to 1 March 2004 in the light of the guidance in paragraph 4.24-4.32. A decision to change the designation of a study should be taken at a sub-committee or Committee meeting. The Chief Investigator may seek a review of the designation of the study by writing to the main REC.

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Research procedures requiring SSA

4.24 In deciding on the need for site-specific assessment at particular sites, the main REC should consider:

(a) whether the site has direct involvement with participants, and
(b) whether participants may be placed at more than minimal risk of physical or emotional harm as a result of the research procedures.

The following guidance should be taken into account. If in doubt, the main REC should require SSA to be carried out.

4.25 It is mandatory for Principal Investigators to be appointed, and SSA carried out, in the case of any research sites conducting one or more of the following procedures:

(a) Novel clinical interventions

This includes the administration of any investigational medicinal product or any other physically invasive clinical intervention, such as surgery, which is not already established as routine clinical practice.

It also includes the use of any novel mental health intervention.

(b) Novel clinical assessments

This includes any physically invasive procedure carried out for the purpose of assessment or diagnosis that is not within the routine professional competence of the health care staff that will be involved in the research at the site.

It also includes the administration of any novel mental health assessment tool by a trained mental health professional.

(c) Medical devices

This includes any use, in a clinical investigation, of a non-CE marked medical device or a CE marked device that has been substantially modified or is being used outside the use for which it was intended.

(d) Additional clinical monitoring

This includes procedures for monitoring the subject and providing data to investigators, which would be additional to the collaborator's normal clinical responsibilities for monitoring their patients and involve the analysis and interpretation of clinical data in accordance with the protocol.

4.26 Where any of the above procedures are to be carried out at local sites directly by the Chief Investigator's team, a Principal Investigator should be appointed for each site

and an application for SSA submitted. The Chief Investigator or another member of his/her team may act as the Principal Investigator for a number of different sites. Where a regional unit has clinical responsibility for the conduct of trials at "shared care" centres, the regional clinical lead should be named as the Principal Investigator and apply for SSA at each centre as a separate site.

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Research procedures not requiring SSA

4.27 SSA should not normally be required where the procedures to be carried out at research sites by local collaborators or by members of the Chief Investigator's team are limited to one or more of the following:

(a) Routine investigations or assessments

This includes any physical investigations, such as taking blood or urine samples, which would be within the routine professional competence of the local collaborator or researcher.

It also includes any routine mental health assessments to be carried out by a trained mental health professional, for example the administration of a validated depression scale.

(b) Questionnaires and surveys

Members of the Chief Investigator's team should normally be permitted to undertake questionnaires and surveys at all sites without the need for SSA. The information provided in Parts A and B should be sufficient to assess the competence of the Chief Investigator to undertake the research at any site.

In multi-site studies, local collaborators may also administer simple questionnaires or surveys on behalf of the Chief Investigator without the need for SSA. The main REC should be assured about the arrangements for selecting and training collaborators and for the oversight of the research by the Chief Investigator.

(c) Qualitative research methods

SSA is not normally required but the main REC should consider the general arrangements proposed for the conduct of the study at local sites, taking into account any risk of significant harm to participants.

Members of the Chief Investigator's team should normally be permitted to undertake qualitative research directly at all sites without the need for SSA. The information provided in Parts A and B should be sufficient to assess the competence of the Chief Investigator to undertake the research at any site.

Where significant responsibilities are delegated to local collaborators, however, and there is concern about their suitability or the local arrangements for supporting the research, the main REC may require the appointment of Principal Investigators and application for SSA at each site.

(d) Collection of data or human tissue

This includes any release of personal data or tissue samples in accordance with procedures described in the protocol and/or Parts A and B of the main application form.

(e) Routine clinical monitoring

This includes any monitoring of participants and provision of clinical data to investigators, which would be within the collaborator's normal clinical responsibilities. For example, care professionals may provide additional data in the follow-up phase of a clinical trial with long-term efficacy endpoints.

It does not include additional clinical monitoring or assessment in accordance with a protocol.

(f) Laboratory tests and analysis

Scientific laboratories undertaking tests or analyses in support of the investigators do not require SSA.

(g) Facilitating the recruitment of participants

Local collaborators may carry out ethically approved procedures to bring the research to the attention of potential participants and facilitate their recruitment by the Chief Investigator's team. This includes the forwarding of information sheets or recruitment packs, display of advertising material, or promotion of the research in the media. Postal consent forms may be returned via local collaborators.

Where such procedures are delegated to local collaborators, the Chief Investigator's team or other approved Principal Investigators should normally retain full responsibility for the informed consent process, in particular for answering participants' questions about the research and taking written consent whether in person or by post (see paragraphs 4.29-4.31).

4.28 Any procedures to be undertaken at local sites without SSA must still have a favourable ethical opinion from the main REC, and should be fully described in the protocol or the terms of the application. The main REC may attach specific approval conditions to the ethical opinion, relating to the conduct of the research at local sites. Research governance approval should also be obtained from the relevant NHS care organisation before any research procedures are undertaken at a site, whether by local collaborators or by members of the Chief Investigator's team.

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Informed consent

4.29 It is recommended that Principal Investigators should normally be appointed, and SSA carried out, where there is delegation of responsibility to local collaborators to give information about the research to potential participants (other than forwarding information provided by the Chief Investigator), to answer their questions, or to take written consent from them. Any actions that fall directly within the informed consent process normally require the appointment of a Principal Investigator.

4.30 However, the degree of responsibility assumed by local collaborators may vary significantly according to the nature of the study, and it is for the main REC to evaluate whether SSA is necessary in these cases.

4.31 The requirement for SSA may also be waived where informed consent is to be carried out at other sites directly by the Chief Investigator's team or other approved Principal Investigators without involvement of local research collaborators and, in the judgement of the main REC, no site-specific issues are likely to arise.

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Exemption of individual sites

4.32 There may be cases in which the procedures to be carried out vary between sites according to their level of involvement in the research. In a study designated as generally "non-exempt", the Chief Investigator or sponsor may ask the main REC to exempt particular sites from SSA if the procedures to be conducted fall within the criteria in paragraph 4.27. For example, 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 procedures such as scans, blood tests and follow-up monitoring to be carried out at other hospitals or GP practices in support of the research. (This may also be more convenient for patients.) If the procedures are within the protocol, these centres are technically research sites involved in the conduct of the research. Research governance approval from relevant care organisations will be required. However, the main REC may individually exempt such sites from SSA. A letter recording the decision should be sent to the Chief Investigator and sponsor. The sites concerned should be listed as approved on form SF1 (see paragraph 4.64) with a note to the effect that SSA is not required.

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Application for site-specific assessment

4.33 Applications for SSA may be made by local Principal Investigators at other sites as soon as – but not before - the Chief Investigator for the study has been notified by the main REC that the application for ethical review is valid. It is not necessary to wait for the issue of a favourable ethical opinion. The ethical review and the site-specific assessments should normally proceed in parallel, so that the outcome of the assessments can be included in the ethical opinion given by the main REC within the time limit of 60 days.

4.34 The Principal Investigator should send the application for SSA to the relevant Research Ethics Committee with area responsibility for the site ("the SSA REC"). OREC Managers are responsible for ensuring that all research sites within their areas, including sites outside the NHS (see paragraph 4.38), are allocated to a particular REC for the purposes of SSA.

4.35 The SSA REC Co-ordinator should enter all SSA applications on RED. The SSA will be allocated a local reference number in addition to the main REC reference number for the study.

4.36 It is not necessary for the Principal Investigator to book a meeting agenda slot for a SSA application. Such applications may be submitted at any time. However, Principal Investigators may be encouraged to contact the REC office beforehand so that advice can be given about local arrangements for SSAs.

4.37 In the case of CTIMPs, all RECs are authorised to carry out site-specific assessments. As the SSA is advice to the main REC, rather than an ethical review, there is no need for the SSA REC to be recognised by UKECA.

4.38 If a CTIMP is to be conducted at one or more sites outside the NHS, the recognised REC that reviews the application has a statutory duty to give an ethical opinion for each site. The SSA REC should carry out the SSA on such sites where this applies. In the case of other types of research, the NHS REC system is not obliged to give an ethical opinion on the suitability of sites outside the NHS. However, if the application has been accepted for ethical review, an opinion on all sites should normally be given. SSA RECs should therefore carry out SSAs on sites outside the NHS if requested.

4.39 Where the main REC is also the SSA REC for the lead site, it should carry out the SSA for this site alongside the ethical review.

4.40 A site-specific assessment may be made either by the SSA REC itself or by another assessor that is approved for this purpose by the OREC Manager (see paragraphs 4.58-4.61). However, even where the SSA is delegated to another assessor, the SSA REC remains responsible for the process. The application for SSA should be submitted to the SSA REC in all cases.