contribute to standing sub-committee business as appropriate.

(ii) The REC may appoint members of a sub-committee on an entirely *ad hoc* basis, depending on the particular business to be conducted. For example, meetings to consider further information provided by applicants and to confirm the REC's ethical opinion might be attended by the relevant lead reviewer. The Chair or vice-Chair (or, if neither is available, the alternate vice-Chair) should be present at all meetings.

6.9 The REC may establish more than one sub-committee and may operate a mix of standing and ad hoc sub-committees.

6.10 Deputy members should not be appointed to serve on sub-committees in their own right, but may attend sub-committee meetings or submit written comments in place of their lead member.

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Quorum for meetings

6.11 The quorum for any meeting of a sub-committee is at least the Chair or vice-Chair (or, if neither is available, the alternate vice-Chair) and at least one other member. The Chair and vice-Chair together constitute a quorum. The Chair is responsible for ensuring that appropriate expertise is available, depending on the business for the meeting. It is desirable but not essential for a lay member to be present.

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Distribution of papers

6.12 The agenda and papers for sub-committee meetings should normally be distributed no later than 3 days prior to the meeting. The local requirements for distribution of papers should be discussed and agreed by members of the sub-committee.

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Telephone meetings

6.13 It is recommended that face-to-face meetings take place where practicable. However, sub-committee meetings may be conducted over the telephone. Where available, teleconferencing facilities should be used. If such facilities are not available, it is acceptable for business to be conducted over a normal telephone line between the Chair and one other member.

6.14 Where a telephone meeting is necessary, the Co-ordinator 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 Co-ordinator. Where he/she is unable to follow the telephone discussion, the Chair should provide written notes for incorporation in the minutes.

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Submission of written comments prior to meetings

6.15 A member who is unavailable to attend a sub-committee meeting may submit comments in writing on any agenda item prior to the meeting. These may be tabled at the meeting at the discretion of the Chair. The minutes should record the submission of written comments.

6.16 A member who submits written comments but does not attend the meeting either in person or on the telephone does not count towards the quorum.

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Conduct of sub-committee business by correspondence

6.17 Sub-committee business may be conducted by correspondence, including e-mail, except as specified in paragraph 6.5.

6.18 Where business is conducted by correspondence, the Chair is responsible for reviewing any comments made by other members and for making decisions on behalf of the REC. Where there are differences 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 Co-ordinator should ensure that records are kept of the comments of all members concerned.

6.19 Matters considered by correspondence should be recorded in the Co-ordinator's next report for the REC (see paragraphs 2.15-2.20).

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Attendance of investigators

6.20 The REC may invite the Chief Investigator or the local Principal Investigator for a research study to attend a sub-committee meeting where matters relating to the study are to be discussed

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Co-opted members

6.21 A REC may co-opt one additional member at any sub-committee meeting. A person may be co-opted as a member only if he/she is or has been a member of a REC (see guidance on indemnity in paragraph 2.41-2.42).

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Referees

6.22 Specialist referees may be invited to submit written advice prior to a sub-committee meeting, or to attend the meeting in person, in the same way as for a REC meeting. The procedures set out in paragraph 2.47(iii) should be followed.

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Observers

6.23 The procedures for attendance of observers at REC meetings (see paragraphs 2.65-2.68) also apply to sub-committee meetings.

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Responsibilities of the Co-ordinator

6.24 The responsibilities of the Co-ordinator or assistant Co-ordinator in relation to sub-committee meetings are as follows:

(i) Preparing the agenda for meetings
(ii) Distributing the agenda and papers at least 3 days prior to a meeting
(iii) Preparing the venue
(iv) Recording apologies for absence prior to meetings
(v) Recording attendance by members and referees at meetings
(vi) Advising meetings as necessary on compliance with standard operating procedures
(vii) Making a written record of meetings
(viii) Preparing the minutes of the meeting (incorporating any notes made by the Chair in the case of telephone meetings).
(ix) Following up the decisions taken as appropriate.

6.25 The responsibilities of the Co-ordinator or Assistant Co-ordinator in relation to sub-committee business conducted in correspondence are:

(i) Distributing papers to members and specifying dates for written comments to be returned
(ii) Arranging for written comments to be reviewed by the Chair
(iii) Following up the decisions taken as appropriate
(iv) Recording the decisions taken and the members involved in the Co-ordinator's Report
(v) Keeping records of all comments submitted by members.

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Minutes of sub-committee meetings

6.26 The requirements of paragraphs 2.75-2.77 apply to the minutes of sub-committee meetings in the same way as for REC meetings.

6.27 Minutes of sub-committee meetings should be ratified by the members or deputy members who were present. This may be done by correspondence or at a subsequent meeting of the sub-committee. Following ratification, the minutes should be signed and dated by the Chair and by the Co-ordinator or assistant Co-ordinator.

6.28 The minutes of sub-committee meetings are confidential, and paragraph 2.79 applies in the same way as for REC meetings.

6.29 The REC should be notified of the decisions taken at sub-committee meetings (see paragraphs 2.15-2.20).

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Section 7: Further review of research given an unfavourable opinion

Summary

There are two options available to an applicant who has received an unfavourable opinion: *submission of a new application*; or *appeal against the unfavourable opinion*.

Both new applications and appeals are given a new REC reference number on RED.

New applications

The new application should take account of the ethical concerns raised previously. The form must declare that the research proposal has been reviewed before. If SSA is required, new SSI forms must be submitted and the SSA process repeated.

A locally allocated application should normally be booked for review with the same REC that reviewed the previous application. For applications allocated through CAS the normal allocation procedure will be followed.

When the application is being reviewed by a "second REC", the previous documentation should be obtained from the "first REC" and included with the papers for members.

In principle an applicant may continue to submit new applications relating to the same research project. Further evidence of scientific review may be requested before a new application is validated. An applicant may be considered "vexatious" by the Operations Director in consultation with the Chair and OREC Manager if a genuine attempt is not being made to address the concerns raised previously.

Appeals

The applicant can *appeal* against the decision of the "first REC" and seek another opinion of the same application from a "second REC".

The Clinical Trials Regulations make statutory provision for appeals relating to CTIMPs. The functions of UKECA relating to appeals are undertaken by NRES Head Office and the same system of appeal applies to CTIMPs and other research.

Notice of appeal should be sent in writing to the OREC Manager (if it is a locally allocated application) or to the Operations Director at NRES (if it is an application allocated through CAS). The notice must be sent within 90 days of the previous opinion. Appeals will normally be allowed though NRES Head Office reserves the right to disallow an appeal.

The application and supporting documentation should not be revised but further representations may be made relating to the opinion given by the first REC.

The OREC manager or Operations Director will appoint a second REC to review the application. Previous documentation should be obtained from the first REC and included with the papers for the members at the meeting. It is highly desirable that the Chief Investigator should attend the meeting if possible. Any SSAs underway should continue and will be transferred to the second REC for processing site approvals.

If the "second REC" also gives an unfavourable opinion there is no provision for further appeal but a new application may be submitted.

Section 7 Further review of research given an unfavourable opinion

Options available to the applicant

7.1 Where a REC has given an unfavourable opinion on an application for ethical review, the applicant has two options for seeking further review:

(i) He/she may submit another application, which should be reviewed as a new application.

(ii) He/she may appeal against the decision of the first REC and seek a second opinion from another REC on the same application ("the second REC").

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Submission of a new application

General procedures for review of new applications

7.2 It is open to the applicant to submit a new application relating to the same research proposal. The assumption should be that the applicant is attempting to address the concerns raised by the first REC when rejecting the previous application. It should be clearly indicated on the application form (at A55) that it relates to a research proposal that has been previously reviewed, and should cite the REC reference number. If it comes to light that an applicant has failed to declare this, the Chair should consider reporting the matter to the OREC Manager and the REC's appointing authority (see paragraphs 9.89-9.91).

7.3 A new application should be entered on RED by the Co-ordinator, 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 1.49):

- A covering letter has been provided, explaining how the new application addresses the reasons given for the unfavourable opinion.

- Any changes to study documents have been highlighted, and documents given revised version numbers and dates where applicable.

7.4 The application should be ethically reviewed according to normal procedures. In the case of studies requiring SSA, new applications for SSA should be submitted by Principal Investigators and processed by local RECs in the normal way.

7.5 Where the application is being reviewed by a different REC, the Co-ordinator of the second REC should contact the Co-ordinator of the first REC to request a copy of the correspondence relating to the previous review. This should be included with the documentation submitted to members at the meeting.

Applications submitted direct to local RECs

7.6 In the case of applications submitted direct to a REC, the applicant should book the application in the usual way with a REC within the domain. It is highly desirable that the new application is booked with the first REC, as the members will already be familiar with the issues relating to the research and well placed to evaluate the changes made to the application. However, the applicant is entitled to apply to another REC within the domain if he/she prefers.

7.7 The Co-ordinator of the first REC should offer the applicant the option of submitting to another REC in the domain (or if necessary another domain within the OREC area) where there is a significant risk that the first REC might not be able to give an opinion within 60 days, for example due to the following:

- The application is received, or is likely to be received, more than two weeks ahead of the REC's next closing date
- The agenda for the next meeting of the REC is full
- The next meeting of the REC will need to be cancelled due to a risk that it may not be attended by sufficient members.

Similarly, if the applicant submits the application direct to the first REC without prior booking, the Co-ordinator may offer the applicant the option of transferring it in these circumstances.

7.8 Review by a second REC should take place only with the Chief Investigator's agreement. If the Chief Investigator is content to wait for an agenda slot at the first REC, the validation date will be the closing date for submissions to the next available meeting.

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Applications allocated through CAS

7.9 Where the new application is booked through CAS, the applicant should be offered the first available meeting slot at an appropriate REC. If the applicant agrees, the application should be assigned to this meeting.

7.10 If the applicant declines the first available slot, the application should normally be allocated back to the first REC. If its next agenda is full, the applicant may opt to wait for the following meeting, or other options may be discussed.

7.11 If the applicant declines the first available agenda slot, the validation date will be the closing date of the meeting of the REC to which the application is assigned.

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Vexatious applicants

7.12 An applicant may in principle continue to submit new applications relating to the same research proposal. However, following review of three applications, the procedure for declaring an applicant to be vexatious may be invoked if:

- There is no reasonable possibility of the applicant being able to address the concerns raised by the committee(s) that gave an unfavourable opinion, or
- The applicant does not appear to be making a genuine attempt to understand or address the concerns, or his/her behaviour is in any other way vexatious, and
- Further review of the project would serve no useful purpose and would be a waste of members' time and public resources.

7.13 Procedures for declaring an applicant to be vexatious are as follows:

(i) The Chair of any REC that is in the process of reviewing, or has reviewed, an application may raise concerns with the OREC Manager based on the grounds in 7.12.

(ii) The OREC Manager should investigate the application history in consultation with the Chair and Co-ordinator of the REC most recently involved in review of the project and, if appropriate, with other RECs concerned.

(iii) If the OREC Manager considers that the criteria in paragraph 7.12 apply, a recommendation should be made to the Operations Director at NRES to declare the applicant vexatious.

(iv) If the Operations Director endorses the recommendation, notification should be sent to the CAS Co-ordinator and all RECs that no further applications related to the project in question should be accepted for review until further notice. Review of any outstanding application should cease. Any subsequent correspondence or enquiry from the applicant, or any further applications, should be redirected to the Operations Director.

(v) The Operations Director should inform the applicant in writing that any further correspondence or new applications should be sent direct to the Operations Director.

(vi) On receipt of any further correspondence or a new application, the Operations Director will consult the Chair of the REC that most recently rejected an application from the applicant ("the last REC"). A valid new application not related to the previous project should be accepted for review and centrally allocated to an appropriate REC. If the application relates to the same project, and it appears that the ethical issues raised previously may have been addressed, the application may be allocated to the last REC. If in the opinion of the Chair no attempt has been made to address the issues, the unfavourable opinion for the previous application should be re-issued and no further review will take place.

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Appeals: statutory provisions and general policy

7.14 Where a recognised REC has given an unfavourable opinion on a CTIMP, the Clinical Trials Regulations allow the Chief Investigator (except where paragraph 7.15 applies) to send a written notice to UKECA stating that he/she wishes to appeal against the opinion and making representations. Such notice must be given within 90 days of being notified of the unfavourable opinion of the first REC, but UKECA may extend this period in a particular case. UKECA may then direct that the application should be reviewed by another recognised REC. It may refuse to issue a direction if it considers that the grounds for appealing against the opinion are unfounded. If so, a notice should be sent to the Chief Investigator setting out the reasons for refusal.

7.15 The Clinical Trials Regulations specifically exclude provision for appeal where a CTIMP involving adults with incapacity in Scotland has been given an unfavourable opinion by the "designated committee" (Scotland A REC) under the Adults with Incapacity (Scotland) Act 2000.

7.16 The policy of the Department of Health and the devolved administrations is that NRES Head Office should exercise the functions of UKECA relating to appeals. The procedures for appeals should apply to any research reviewed by a REC in the UK, except where paragraph 7.15 applies.

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Notice of intention to appeal

7.17 When sending SL6 or SL15 giving an unfavourable opinion on an application, the REC should notify the applicant of the procedures for giving notice of an intention to appeal and the appropriate contact points.

7.18 Notice of intention to appeal should normally be given in writing within 90 days of the date of the letter confirming the unfavourable opinion of the first REC. The notice may include representations with respect to the opinion of the first REC. The applicant may not make changes to the application or supporting documentation. Appeals will normally be accepted, though NRES Head Office reserves the right to disallow an appeal.

7.19 In the case of any application allocated through the Central Allocation System, notice should be given by the applicant in writing to the Operations Director at NRES (or the OREC manager designated by the Operations Director to manage such appeals). The Operations Director or designated OREC manager should then allocate the application to another recognised REC for review, taking into account geographical proximity to the Chief Investigator's professional base, and book an agenda slot at its next meeting through CAS.

7.20 In the case of applications made locally, notice should be given in writing to the relevant OREC Manager, who should normally allocate the application to another REC within his/her area of responsibility and arrange for an agenda slot to be booked at the next meeting.

7.21 The operational manager responsible for managing the appeal (either the Operations Director or OREC Manager as applicable) is known as the "Appeal Manager".

7.21A The Appeal Manager has the discretion to accept a notice of intention to appeal given after 90 days has elapsed, taking account of any exceptional circumstances.

7.22 The Appeal Manager should notify the Chief Investigator in writing whether or not the appeal is allowed. Where the appeal is allowed, SL36 should be sent. The letter should state which REC has been allocated to review the application, the date of the meeting at which it has been booked, the new REC reference number and the closing date for submission. Copies should be sent to the Co-ordinators of both RECs. Where the appeal is disallowed, the Appeal Manager should send SL36A to the Chief Investigator giving reasons.

7.23 The validation date for the appeal will be the date of the letter to the applicant confirming that the appeal is allowed.

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Preparation for the appeal

7.24 The applicant is not permitted to make any revision to the application reviewed by the first REC. It is therefore the responsibility of the Co-ordinator of the first REC to send

the application form and all accompanying documentation to the second REC by the specified closing date, together with all correspondence relating to the application.

7.25 If the first REC gave an unfavourable opinion at the Committee meeting, without a request for further information, the documentation sent to the second REC should be that originally submitted to the first REC. If the unfavourable opinion was confirmed at a later stage of the process, and the documentation was revised in response to a request for further information, then the latest versions should be submitted to the second REC.

7.26 Once the second REC has accepted the appeal a copy of the application will be received on RED. The application does not need to be re-entered on RED. There is no requirement for the normal validation letter to be sent. The Chief Investigator should be notified of the arrangements for the appeal by the Co-ordinator of the second REC using SL36B.

7.27 The applicant may submit additional representations to the second REC by the specified closing date. In this context, "representations" means observations with respect to the opinion of the first REC, not changes to the application or supporting documentation.

7.28 When distributing the application documentation to members prior to the meeting, the Co-ordinator of the second REC should include a copy of the correspondence relating to the application and any representations submitted by the applicant.

7.29 The Co-ordinator of the second REC should invite the Chief Investigator to the meeting. It is particularly important that the Chief Investigator attends the meeting if at all possible so that a full discussion can take place on the main ethical issues.

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Review of applications on appeal

7.30 The application should be reviewed by the second REC in accordance with the standard procedures for review of any new application.

7.31 The second REC may consider the matters raised by the first REC in the course of the review but is not bound by them. It should consider carefully any representations made by the applicant.

7.32 In the case of studies requiring SSA, the second REC assumes all responsibilities relating to the approval of sites, taking account of advice received from site-specific assessors. The SSA process already underway should continue. There is no need for new applications to be submitted.

7.33 If the second REC gives a favourable opinion of the application, this supersedes the opinion given by the first REC. The second REC assumes all further responsibility for monitoring the research and reviewing substantial amendments.

7.34 If the second REC gives an unfavourable opinion, there is no provision for any further appeal relating to this application. The letter issuing an unfavourable opinion (either SL6 or SL15) should be amended to omit reference to any further appeal. The applicant may however submit a new application relating to the same research proposal (see paragraph 7.2), suitably revised to take account of the ethical concerns raised. If so, the application should normally be reviewed by one of the RECs that reviewed the previous application.

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Section 8: Expedited review

Summary

A REC has a total of 60 days to give an opinion on any valid application received. There is no statutory provision for expedited review. Co-ordinators and Chairs of RECs have no authority to expedite the usual procedure for ethical review.

In very exceptional circumstances, however, there may be a need to start a research project urgently for reasons of public policy, for example:

- A research field causing public anxiety
- An urgent threat to public health
- A unique opportunity for research that is likely to be temporary.

In these circumstances, the sponsor and/or Chief Investigator should contact the Operations Director at NRES Head Office directly for advice. The Operations Director of NRES will consult with UKECA and Ministers as necessary and, if appropriate, will authorise an expedited review.

If permission is given for expedited review, the sponsor or Chief Investigator should submit the standard NRES application form with all the usual documentation. The Operations Director at NRES will arrange for the application to be validated on the day of receipt.

NRES Head Office will allocate the application for review in one of the following ways:

- An existing REC may be appointed to review the application. Two members with relevant expertise could be co-opted from other RECs, and/or relevant experts may be specially appointed as members for review of this application.

- A new REC may be established for the review of the application. If it is a CTIMP, the REC will need to be legally recognised by UKECA.

The "appointed REC" should follow SOPs during review, except that NRES Head Office will specify the time periods required for processing the application.

Procedures for site-specific assessment by other RECs may be waived, but the Chief Investigator or sponsor should provide the appointed REC with evidence that the local sites, facilities and investigators involved are adequate. The appointed REC may consult relevant local RECs or care organisations directly for advice.

If a specially appointed REC issues a favourable opinion and is later abolished, NRES Head Office should re-assign monitoring and reviewing responsibilities to another recognised REC.

Section 8 Expedited review

General policy

8.1 There is no statutory provision for the expedited review of applications. The Clinical Trials Regulations provide only that a REC shall give an opinion on any valid application within a period of 60 days, which may be suspended once pending receipt of further information from the applicant.

8.2 There may however be wholly exceptional circumstances where as a matter of public policy, and in the national interest, it is essential that an application should be reviewed urgently to allow a health-related research study to commence as quickly as possible. Such circumstances could include the urgent need for research data in a field that is currently the subject of major public anxiety, or where there is an urgent threat to public health. There could also be a need to capitalise on a unique opportunity for significant research that is likely to prove temporary.

8.3 Where a research sponsor or Chief Investigator believes that such circumstances may apply, he/she should contact the Operations Director at NRES directly for advice. The Co-ordinators or Chairs of individual RECs have no authority to expedite the normal procedures for ethical review.

8.4 Where, after consultation with UKECA and Ministers as necessary, the Operations Director considers that the circumstances justify it, the sponsor or Chief Investigator may be given permission to submit an application for expedited review.

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Procedures for expedited review

8.5 An application for expedited review may be submitted by either the sponsor or the Chief Investigator of the proposed research. The standard NRES application form should be used and all the usual supporting documentation should be provided. The application should be submitted to the Operations Director at NRES. A decision on validation should be made on the day of receipt and notified to the applicant.

8.6 The Operations Director should then allocate the application for review in one of the following ways:

(i) An existing REC may be appointed to review the application. NRES Head Office may arrange for two members of other RECs with relevant expertise to be co-opted to the REC, and/or for other experts to be specially appointed as members of the REC for the review of this application.

(ii) A new REC may be established by NRES Head Office specifically for the review of this application. If the application relates to a clinical trial of an investigational medicinal product, the REC will need to be legally recognised by UKECA. The membership of the REC will be a matter for the discretion of NRES Head Office but should include both lay members and relevant experts. A Chair and Co-ordinator should be appointed by NRES. Head Office

8.7 The REC appointed to review the application ("the appointed REC") should do so following standard operating procedures, except that NRES Head Office may specify the time periods within which each stage of the process should be completed.

8.8 Where the application relates to a multi-site research study with Principal Investigators, the appointed REC is responsible for giving ethical approval for each site as part of a favourable ethical opinion, but the normal procedures for site-specific assessment may be waived at the discretion of NRES Head Office. The sponsor or Chief Investigator should provide the appointed REC with appropriate evidence of the adequacy of local sites, investigators and facilities. The Chair of the appointed REC may require that the SSI form is completed for each proposed site and submitted direct to the appointed REC for assessment together with the CV for each Principal Investigator. The Chair or Co-ordinator of the appointed REC may consult relevant RECs or care organisations for advice by telephone, e-mail or fax.

8.9 Where a favourable ethical opinion is given by a specially appointed REC under paragraph 8.6(ii), and that REC is later abolished, NRES Head Office should re-assign the responsibilities for monitoring the research and reviewing amendments to another REC.

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Section 9: Monitoring of research given a favourable opinion

Summary

The main REC is not required to monitor the conduct of the research proactively but should keep the ethical opinion under review in the light of progress and safety reports submitted by the sponsor or Chief Investigator, and any other developments in the study. Primary responsibility for monitoring lies with sponsors and employing organisations.

Research should normally start within 12 months of the final opinion letter. If no participant has been recruited within 12 months the Chief Investigator should give an explanation of the delay in the annual progress report. The Chair may allow a further 12 month period.

Progress reports on all studies should be sent to the main REC annually by the Chief Investigator using the NRES form. More frequent progress reports may be requested. Progress reports should be reviewed by the Chair or by another member. The Co-ordinator will issue a reminder letter if an annual report is not received.

Safety reporting for CTIMPs is subject to guidance from the European Commission. Sponsors are required to send the main REC expedited reports of Suspected Unexpected Serious Adverse Reactions (SUSARs) occurring in the UK and an annual safety report, including a global line listing and a safety assessment. Quarterly reports should also be provided where the sponsor is conducting trials of the product outside the UK.

When submitting safety reports, sponsors should complete the covering form issued by NRES. Reports should only be sent to the main REC.

The main REC is not required to review expedited reports of SUSARs. Quarterly and annual safety reports should be reviewed at least by the Chair and an expert member. Primary responsibility for safety lies with the sponsor. The MHRA has the main regulatory responsibility and will keep the main REC informed about any safety issues.

For other research, Serious Adverse Events (SAEs) that are research-related and unexpected should be notified within 15 days using a separate form issued by NRES.

The Chief Investigator may permit a minor "deviation" from the protocol without notifying the main REC. If the deviation meets the criteria for a "substantial amendment" then it requires ethical review. A significant protocol "violation" or breach of GCP resulting from error or misconduct must be reported.

The main REC should be notified of the conclusion of the study within 90 days, or within 15 days if it has terminated early. For CTIMPs the sponsor should submit the European Commission form. For other research the Chief Investigator should submit the NRES form.

The main REC may review the ethical opinion at any time. Guidance is given on circumstances that might justify suspension or termination of the favourable opinion. Such a decision should be taken at a full Committee meeting.

A summary of the final report on the research should be sent to the main REC within 12 months of its conclusion.

Any information relating to possible misconduct or criminal offences relating to research should be passed confidentially by the REC to the OREC Manager and its appointing authority. The REC should not undertake its own investigations.

Section 9 Monitoring of research given a favourable opinion

Statutory requirements

9.1 Under the Clinical Trials Regulations, the sponsor of a clinical trial of an investigational medicinal product has a variety of statutory responsibilities for notifying the main REC of developments in the research after it has started. These are set out in this section, with the exception of provisions relating to substantial amendments (see Section 5). Where there is more than one sponsor, "the sponsor" refers to the sponsor that has been designated to take responsibility for the function concerned. A single sponsor should take responsibility for each of the following:

- notification of urgent safety measures
- pharmacovigilance and safety reporting
- notification of the conclusion or early termination of the trial.

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General policy on monitoring of research

9.2 The general policy from NRES Head office is that the main REC should keep under review the favourable ethical opinion given to any research study in the light of regular progress reports and significant developments in the research. This applies equally to CTIMPs and to other types of research, except in relation to safety reporting where different provisions apply.

9.3 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 NRES Head Office to request that a single main REC is appointed to take responsibility for monitoring of the research (see paragraph 10.10).

9.4 Other than by means of the reports that the sponsor and investigators are required to submit, the main REC has no responsibility for proactive monitoring of research studies. The accountability for this lies with the sponsor and the employing

organisation. Similarly, those local RECs responsible for site-specific assessment have no responsibility for proactive monitoring of the local conduct of the research.

9.5 The Chief Investigator and representatives of the sponsor may be requested to attend a meeting of the main REC or sub-committee at any time to discuss any ethical or safety concerns about the research. Similarly, local Principal Investigators may be requested to attend a meeting of the relevant local REC or its sub-committee to discuss any new concerns relating to the suitability of the site.

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Commencement of the research

9.6 Research should normally commence within 12 months of the date on which a favourable ethical opinion is given by a REC. A study is generally considered to have commenced when any of the procedures set out in the protocol are initiated. The commencement date should be stated in the first annual progress report for the research.

9.7 Should the study not commence within 12 months, the Chief Investigator should give the main REC a written explanation for the delay in the first annual progress report (see paragraph 9.11). It is open to the Chair to allow a further period of 12 months within which the trial should commence.

9.8 Should the project not commence within 24 months, the matter should be discussed at a meeting of the REC. At the discretion of the REC, the favourable ethical opinion may be terminated and the Chief Investigator required to submit a new application once the problems relating to the delay of the study have been fully addressed. Alternatively, a further period may be allowed.

9.9 If a study is abandoned prior to commencement, the Chief Investigator or sponsor should notify the main REC (and, in the case of a CTIMP, the MHRA) using the appropriate form for declaring the conclusion or early termination of the study (see paragraphs 9.62-9.63). If a study is abandoned and it is later proposed to start it afresh, a new application should be made.

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