

3 The remit of an NHS REC

- 3.1 Ethical advice from the appropriate NHS REC is required for any research proposal involving:
- a. patients and users of the NHS. This includes all potential research participants recruited by virtue of the patient or user's past or present treatment by, or use of, the NHS. It includes NHS patients treated under contracts with private sector institutions
 - b. individuals identified as potential research participants because of their status as relatives or carers of patients and users of the NHS, as defined above
 - c. access to data, organs or other bodily material of past and present NHS patients
 - d. fetal material and IVF involving NHS patients
 - e. the recently dead in NHS premises
 - f. the use of, or potential access to, NHS premises or facilities
 - g. NHS staff – recruited as research participants by virtue of their professional role.
- 3.2 If requested to do so, an NHS REC may also provide an opinion on the ethics of similar research studies not involving the categories listed above in section 3.1, carried out for example by private sector companies, the Medical Research Council (or other public sector organisations), charities or universities.
- 3.3 The appropriate REC in each case is one recognised for this purpose by the Health Authority within the area of which the research is planned to take place.
- 3.4 This will normally be one established by the Health Authority itself within its geographical area – currently called a Local Research Ethics Committee (LREC).
- 3.5 For the purposes of ethical review of the research proposal, a research “site” is defined as the geographical area covered by one Health Authority, whether the research is based in institution(s) or in the community. Even when the research may physically take place at several locations within that geographical boundary, a favourable ethical opinion on the research protocol is required from only one NHS REC within that Health Authority boundary.
- 3.6 Where the research is planned to take place at more than one “site” as defined above, different arrangements apply. (*See Chapter 8*).

- 3.7 For research involving gene therapy, application should be made to the Gene Therapy Advisory Committee (GTAC). *(Further details are given in Section B).*
- 3.8 For clinical research that involves xenotransplantation, application should be made to the United Kingdom Xenotransplantation Interim Regulatory Authority (UKXIRA). *(Further details are given in Section B).*
- 3.9 Certain types of research specified under the Human Fertilisation and Embryology Act, 1990, may not proceed without a licence from the Human Fertilisation and Embryology Authority, from whom further information may be obtained. Research Ethics Committee approval is also required. *(See Section B).*
- 3.10 Specific arrangements are in place for ethical review of research on prisoners. *(See Section B).*
- 3.11 Research on clients of Social Services (i.e. participants recruited by virtue of their past or present status as clients of Social Services), including those cared for under contracts with private sector care providers, should have the favourable opinion of a Research Ethics Committee which meets the same general standards as NHS RECs in respect of composition, review process and general operating procedures. *(Details of the arrangements for ethical review of research in Social Care taking place outside the NHS are under review, and will be published at a later date).*

4 Establishment and support of NHS RECs

- 4.1 Research Ethics Committees with the authority to offer an opinion on research within the NHS may only be established and governed by Health Authorities or the Department of Health.
- 4.2 Health Authorities are accountable for the establishment, support, training and monitoring of all NHS Local Research Ethics Committees (LRECs) within their boundary. Each Health Authority should identify a named officer who is not otherwise directly involved in REC administration who will have lead responsibility for the governance of Research Ethics Committees on behalf of the Chief Executive (who has overall accountability).
- 4.3 It is the responsibility of the appointing Authority to set an annual budget for the adequate support of the REC(s) for which it is accountable, irrespective of any income received from charges made for review in cases where this is appropriate.
- 4.4 The Department of Health is responsible for these functions for Multi-centre Research Ethics Committees (MRECs), for the Gene Therapy Advisory Committee (GTAC), and for the United Kingdom Xenotransplantation Interim Regulatory Authority (UKXIRA).
- 4.5 RECs are not accountable in any way to NHS Trusts, and in particular are separate from Trust R&D Departments in respect of the accountability for their operational processes and decision-making.
- 4.6 RECs are not in any way management arms of any NHS organisation, and have no management role. They are advisory committees to, not sub-committees of, NHS organisations.
- 4.7 A Health Authority is responsible for identifying the REC (or RECs) that routinely provides ethical advice on research proposals arising within its own boundaries. This will usually be an LREC or LRECs that it has itself established.
- 4.8 A Health Authority shall establish sufficient LRECs within its boundary to cope with the workload, and must provide adequate administrative support for their business. The RECs within a Health Authority boundary should work collaboratively, and a common administrative structure or network should be established, so that applications can be directed to the most appropriate committee.
- 4.9 Similarly, for practical management purposes neighbouring Health Authorities may agree to collaborate on the establishment, maintenance and administration of one or more shared LRECs, but the accountability of each Health Authority remains.

Education and Training of REC Members and Administrators

- 4.10 REC members have a need for initial and continuing education and training regarding research ethics, research methodology and research governance.
- 4.11 Appointing Authorities shall provide, within the annual budget for its REC(s), resources for such training, guidance on which will be issued by the Department of Health.

Office operation and support

- 4.12 The appointing Authority is responsible for providing suitable and discrete facilities in which the work of the REC officers and administrators can be undertaken in a confidential manner. These facilities should include adequate provision for handling and storing confidential documents.
- 4.13 Administrative staffing of the REC office should be sufficient to provide a comprehensive service to the REC, to researchers and, where appropriate, to the NHS. The administrator should have a sound knowledge of the Research Governance Framework, be trained in the work of RECs, and be of sufficient seniority to provide detailed operational advice to the REC officers and to researchers.

Legal Liability

- 4.14 The appointing Authority will take full responsibility for all the actions of a member in the course of their performance of his or her duties as a member of the REC other than those involving bad faith, wilful default or gross negligence. A member should, however, notify the appointing Authority if any action or claim is threatened or made, and in such an event be ready to assist the Authority as required.

5 Membership requirements and process

- 5.1 RECs should be constituted to ensure the competent review and evaluation of all ethical aspects of the research projects they receive, and to ensure that their tasks can be executed free from bias and influence that could affect their independence in reaching their decision.
- 5.2 The Health Authority is responsible for appointment of LREC members. The Department of Health or its appointed agent is responsible for the appointment of members of MRECs, GTAC and UKXIRA.
- 5.3 Appointment of members shall be by an open process, compatible with the Nolan standards. Vacancies should be filled following public advertisement in the press, and/or by advertisement via local professional and other networks as most appropriate to the vacancy to be filled. Potential candidates shall be required to complete an application form. The process for selection of members shall be laid down in Standard Operating Procedures.
- 5.4 An appointed member must be prepared to have published his/her full name, profession and affiliation. When making appointments, conflicts of interest should be avoided if at all possible. Where unavoidable there should be transparency with regard to such interests, and they should be recorded and published with the above personal details.
- 5.5 Normally an appointed member shall be required to attend in full at least two thirds of all scheduled REC meetings in each year, barring exceptional circumstances. (*See 6.15 below*).
- 5.6 As a condition of appointment, a member must agree to take part in initial and continued education appropriate to his or her role as an REC member.
- 5.7 An appointed member shall be expected to maintain confidentiality regarding meeting deliberations, applications, information on research participants, and related matters.
- 5.8 The appointed member shall be informed in writing of the terms of the appointment, including its duration, the policy for renewal, the disqualification procedure and the resignation procedure, the policy concerning declaration of interests, and details of allowable expenses.
- 5.9 The appointing Authority shall provide each appointed member with a personal statement regarding the indemnity provided, and its conditions.
- 5.10 Members should be appointed for fixed terms, normally five years. Terms of appointment may be renewed, but not normally more than two consecutive terms should be served on the same REC. A member may however subsequently serve on another REC. Simultaneous service on both an MREC and LREC is permitted.

5.11 The appointing Authority shall ensure that a rotation system for membership is in place that allows for continuity, the development and maintenance of expertise within the REC, and the regular input of fresh ideas.

6 **Composition of an REC**

- 6.1 An REC should have sufficient members to guarantee the presence of a quorum (*see 6.11*) at each meeting. The maximum should be 18 members. This should allow for a sufficiently broad range of experience and expertise, so that the scientific, clinical and methodological aspects of a research proposal can be reconciled with the welfare of research participants, and with broader ethical implications.
- 6.2 Overall the REC should have a balanced age and gender distribution. Members should be drawn from both sexes and from a wide range of age groups. Every effort should also be made to recruit members from black and ethnic minority backgrounds, as well as people with disabilities. This should apply to both expert and lay members.
- 6.3 RECs should be constituted to contain a mixture of “expert” and “lay” members. At least three members must be independent of any organisation where research under ethical review is likely to take place.

Expert members

- 6.4 The “expert” members of the committee shall be chosen to ensure that the REC has the following expertise:
- relevant methodological and ethical expertise in:
 - clinical research
 - non-clinical research
 - qualitative or other research methods applicable to health services, social science and social care research.
 - clinical practice including:
 - hospital and community staff (medical, nursing and other)
 - general practice
 - statistics relevant to research
 - pharmacy

Lay members

- 6.5 At least one third of the membership shall be “lay” members who are independent of the NHS, either as employees or in a non-executive role, and whose primary personal or professional interest is not in a research area.
- 6.6 The “lay” membership can include non-medical clinical staff who have not practised their profession for a period of at least five years.
- 6.7 At least half of the “lay” members must be persons who are not, and never have been, either health or social care professionals, and who have never been involved in carrying out research involving human participants, their tissue or data.

Non-representative role

- 6.8 Despite being drawn from groups identified with particular interests or responsibilities in connection with health and social care issues, REC members are not in any way the representatives of those groups. They are appointed in their own right, to participate in the work of the REC as equal individuals of sound judgement, relevant experience and adequate training in ethical review.

NHS Staff as members

- 6.9 NHS organisations should provide encouragement to their staff who wish to serve as members of RECs. The time required for undertaking such service and the necessary training should be protected, and form a recognised part of the individual's job plan.

Specialist referees

- 6.10 The Chair and Administrator may seek the advice of specialist referees on any relevant aspects of a specific research proposal that lie beyond the expertise of the members. These referees may be specialists in ethical aspects, specific diseases or methodologies, or they may be representatives of communities, patients, or special interest groups. Such referees are not voting members of the committee, and should not be involved in the business of the committee other than that related to the specific research proposal in question. Terms of reference for independent referees should be established. Their advice should be recorded in the minutes.

Quorum requirements

- 6.11 For meetings at which research ethical review is undertaken, a quorum shall consist of seven members. It shall include the Chair and/or Vice-Chair, at least one "expert" member with the relevant clinical and/or methodological expertise, one "lay" member as defined in 6.7 above, and at least one *other* member who is independent of the institution or specific location where the research is to take place.

Committee Officers

- 6.12 The Chair and Vice-Chair shall be appointed as such by the appointing Authority after consultation with the REC Administrator and committee members. The appointees should have had at least one year's experience of the work of RECs. Those appointed should have received personal training in research ethics reviewing, and possess the relevant chairing skills. Potential candidates should be offered any necessary supplementary training prior to appointment.
- 6.13 To facilitate communication, the REC may wish to designate a suitably qualified individual as Scientific Officer, who will be the principal point of liaison with applicants for more detailed discussion of issues related to the

content of applications, and who can if necessary represent the committee at scientific management discussions. Depending on their background and personal expertise, this could be the Chair, Vice-Chair or Administrator, but need not necessarily be so. This work may be shared by other REC members.

- 6.14 The process for appointment of all officers shall be laid down in the standard operating procedures.

Deputies

- 6.15 Where a member provides unique expertise to the REC (e.g. pharmacy or statistical advice) the REC may, if necessary, make arrangements to appoint deputies for individual members of the committee. These deputies must have undergone the same recruitment, selection and appointment procedure as the named members, and must also have been trained in ethical review. When deputising, these members are considered full members of the committee. The names of deputies should be recorded in the Annual Report.
- 6.16 However, attendance of the member at the scheduled meetings must be of sufficient frequency to ensure their effective contribution to the work of the committee.

Observers

- 6.17 Observers, who shall play no part in the committee's deliberations, may be invited subject to the minuted agreement of the REC, and subject to written invitation giving the terms under which observer status is permitted. Such observers should have no vested interest in, or scientific or management responsibility for, any applications being considered. Observers should be allowed only if they accept in writing the same duty of confidentiality as REC members.

7 Working procedures

- 7.1 Good standard operating procedures and accurate record keeping are important. Standard operating procedures shall be drawn up in line with national guidance, and approved by the appointing Authority. These standard operating procedures should be publicly available.
- 7.2 RECs shall have standard operating procedures that state:
- the Authority under which the REC is established
 - the functions and duties of the REC
 - membership requirements
 - the terms and conditions of appointment
 - the officers and the structure of the secretariat
 - internal procedures
 - quorum requirements
 - procedures for considering applications
- 7.3 Standard operating procedures shall be compatible with European and UK law, and, where appropriate, to the relevant provisions in Good Clinical Practice.
- 7.4 RECs shall act in accordance with their written standard operating procedures. The appointing Authority is responsible for the governance of the REC in this respect, and should ensure that account is taken of all guidance issued by the Department of Health.
- 7.5 An REC shall make its decisions at scheduled meetings at which a quorum is present.
- 7.6 All reimbursement for work or expenses, if any, within or related to an REC should be recorded and made available, by the Authority, to the public on request.
- 7.7 The REC should keep a register of all the proposals that come before it. This register will be available for public consultation. Appropriate sections shall be shared with the relevant NHS bodies hosting the research, for the purposes of governance and management. The register should form the basis of the REC's Annual Report to its appointing Authority.
- 7.8 An REC should retain all relevant records for a period of at least three years after completion of a research project, and should make them available upon request to any regulatory authorities.
- 7.9 The REC should always be able to demonstrate that it has acted reasonably in reaching a particular decision. When research proposals are rejected by the REC, the reasons for that decision should be made available to the applicant.

- 7.10 RECs should consider valid applications in a timely manner. A decision should be reached and communicated to the applicant within 60 calendar days of the submission of a valid application.
- 7.11 After an initial review, any further written information or clarification may be requested from the applicant on one occasion only. During this period, the time-frame is suspended and does not recommence until a response satisfactory to the REC is received. A final decision should then be made and communicated to the applicant within the total of 60 days. For multi-centre research, this time frame includes consideration of the locality issues.
- 7.12 Amendments submitted once the research has started shall be considered at its next meeting by the REC that approved the original protocol, and an answer given to the applicant within a total of 35 days. However, where the amendment is substantial (for example requiring additional interventions to research participants), it may need to be treated by the REC as a new application requiring full ethical review within the standard 60-day timeframe.
- 7.13 It follows that there should be a sufficient frequency of REC meetings within a Health Authority “site” to complete the business in a timely manner. It is recommended that individual RECs meet monthly, but that the timing of meeting of the individual RECs within one Health Authority “site” should be staggered.
- 7.14 Any local procedures for expedited review (where appropriate) outside the normal committee cycle shall be described in the standard operating procedures. (*See Section B*).
- 7.15 The ethical review by the REC should occur in parallel with the consideration of the proposed research by NHS host organisations (usually by its R&D Directorate) and any relevant regulatory authorities, e.g. the Medicines Control Agency.
- 7.16 An REC should not be expected to accept a workload that compromises the quality of ethical review. When this is likely, the Authority should establish additional RECs, or make formal arrangements for other RECs (e.g. from neighbouring Health Authorities) to provide an opinion.

Confidentiality of proceedings

- 7.17 REC members do not sit on the committee in any representative capacity and need to be able to discuss freely the proposals that come before them. For these reasons REC meetings will normally be held in private.
- 7.18 However, a summary of details of the application shall be made publicly available once the final decision on the application is ratified by the REC. These shall include:
- the names of the researcher and sponsor
 - and of the research site

- a simple summary of the research proposal comprehensible to a lay person
- the issues discussed by the committee and the committee's conclusions
- and its overall opinion.

Producing an Annual Report

- 7.19 Within six months of the end of each financial year, an LREC should submit its Annual Report to the appointing Authority, which shall consider it at a scheduled open meeting of the Authority to which the REC members are invited. In the case of LRECs, copies should be sent to all the NHS bodies within the Authority's boundaries.
- 7.20 The report, which should be available for public inspection, should include:
- the names, affiliations and occupations of committee members and of deputies (if used)
 - number and dates of meetings held
 - attendance of members
 - a list of proposals considered, and the decisions reached on each
 - the time taken from acceptance of application to final decision on each proposal
 - a list of projects completed or terminated during the year
 - the training undertaken by the committee and by its members
- 7.21 Similarly, each MREC shall produce its Annual Report (to include the same category items) for presentation to the Department of Health, and for publication.

Advice to non-NHS bodies

- 7.22 Not all medical, other health-related or social care research takes place within the NHS or public sector Social Services. All those conducting such external research should be encouraged to submit their research proposals to an NHS REC for advice, and the REC should accept for consideration all such valid applications that meet the relevant standards. In such cases, the REC should report to the appointing Authority the cost of its work so that the cost can be recovered from the outside body conducting the research, if appropriate.

Following up and reports

- 7.23 Once the REC has given a favourable opinion, the researcher is required to notify the committee, in advance, of any proposed deviation from the original protocol. The committee may then wish to review its decision.
- 7.24 No deviation from, or changes to, the protocol shall be initiated by the researcher without the prior written approval of the REC, save where this is necessary to eliminate immediate hazards to research participants or when the change involves only logistical or administrative aspects of the research. In

these cases, the changes may be implemented immediately, but the REC must be informed within seven days. The REC may then reconsider its opinion.

- 7.25 The research sponsor is responsible for ensuring that arrangements are in place to review significant developments as the research proceeds (particularly those which put the safety of individuals at risk) and to approve any modifications to the design of the research protocol. These modifications must be submitted to the REC and a favourable opinion obtained before implementation (except when there are immediate hazards to research participants, when the process laid out in 7.24 above shall apply).
- 7.26 The REC should indicate at the time of approval any progress reports it requires from time to time from the applicant. It shall request a final report to be delivered within three months of completion.
- 7.27 The REC shall require, as a minimum, an annual report from the researcher, and shall reconsider its opinion at that stage. Where the REC considers the degree of risk demands it, more frequent reports and subsequent interim review shall be required.
- 7.28 Where the research is terminated prematurely, a report shall be required within 15 days, indicating the reasons for early termination.
- 7.29 RECs may also ask to receive reports of inspections by other authorities.
- 7.30 Reports to the committee should also be required if there are any other unusual or unexpected results which raise questions about the safety of the research. *(See Section B for further details).*
- 7.31 Reports on success (or difficulties) in recruiting participants provide the REC with useful feedback on perceptions of the acceptability of the project among potential research participants. RECs may wish to request such reports where they anticipate potential difficulties.
- 7.32 On the basis of any such reports, the REC may wish to review its decision. Failure to produce such required reports without a reason acceptable to the REC may result in suspension of the REC's favourable opinion, in which case the research must cease.
- 7.33 Other than by means of these required progress reports, the REC has no responsibility for pro-active monitoring of research, the accountability for which lies with the host NHS institution, but the REC may wish to be reassured of the process for such monitoring in certain specific cases.
- 7.34 A member of an REC who becomes aware of a possible breach of good practice in research should report this initially to the Chair and Administrator of the REC, who shall inform the appointing Authority. The Authority's officers shall be accountable for taking appropriate action.

Second ethical review when an REC declines to give a favourable opinion

- 7.35 Exceptionally, a further review of the protocol may be undertaken by a second REC. *(Details of the procedure for a second REC review are given in Section B).*

8 Multi-centre Research

- 8.1 For the purpose of ethical review of research, a research “site” is defined as the geographical area covered by a single Health Authority, and includes all the research institutions and localities within it. *(See also paragraph 3.5).*
- 8.2 For the present, multi-centre research will continue to be defined as research carried out within five or more “sites”, i.e. the area covered by five or more Health Authority boundaries, irrespective of the number of LRECs within each Authority.
- 8.3 For research taking place in from two to four sites, application should be made to one LREC within each of the Health Authority boundaries. However, when a favourable opinion has been obtained from the first Health Authority’s LREC, the second, third and fourth Health Authorities may, on the advice of their own LRECs, accept that opinion with further review by their own LREC only of the “locality issues”. *(Further details of this process, which is similar to that which currently operates with MRECs, are provided in Section B).*
- 8.4 If recruitment is planned in five (or more) sites, irrespective of whether existing LREC approval in up to four sites has been already given, application is then required to a Multi-centre Research Ethics Committee (MREC). A favourable opinion of an MREC then covers the whole of the United Kingdom.
- 8.5 If the MREC declines to give a favourable opinion on the application, any existing approval by LRECs still stands, but those LRECs shall be informed of the MREC’s decision (and its reasons).
- 8.6 Once an MREC has declined approval, no further application using the same proposal may be made to any LREC.

Consideration of “locality” issues

- 8.7 The MREC (or “lead” LREC – see 8.3 above) undertakes the review of the ethics of the research protocol, including the content of the patient information sheet and consent form. No further ethical review of these items shall be undertaken by other RECs (except in the process of a “second review” described in 7.35 above).
- 8.8 The “locality issues” are limited to:
- the suitability of the local researcher
 - the appropriateness of the local research environment and facilities
 - specific issues relating to the local community, including the need for provision of information in languages other than English
- 8.9 The LREC should satisfy itself that the “locality issues” have been adequately considered, and that it can approve them. In undertaking consideration of the

“locality issues” the REC should work closely with the NHS host organisation, which also has a responsibility for research conduct and safety.

- 8.10 LRECs and local NHS trusts should set up administrative mechanisms to facilitate such joint working. The detailed assessment of the “locality issues” may be undertaken on behalf of the NHS either directly by an LREC itself (or its officers), or by the NHS host (if it is a Trust) with the prior agreement of the LREC. In the latter case the Trust shall inform the LREC of the outcome of the process. The LREC shall consider the advice of the Trust and, if accepted, shall record its approval in LREC minutes. For multi-centre research, the research may not proceed until the LREC has informed the approving MREC of its lack of objection with respect to the “locality issues”. *(Further details of this process are described in Section B).*
- 8.11 The consideration of “locality issues” should occur in parallel with the consideration of ethical review of the research protocol by the MREC or “lead” LREC.
- 8.12 The decision on the “locality issues” should be made and communicated within 60 days of receipt of a valid application for this purpose.

Multi-centre research where there is no “local” researcher

- 8.13 For multi-centre research where there is no “local” researcher, and where this is confirmed by the MREC (or “lead” LREC – see 8.3 above) during its review of the research protocol, no specific consideration of “locality” issues by an LREC may be needed and the overall process of review may thus be expedited. Approval by the host NHS organisation is still required before the research may proceed. *(Details of the operational process are given in Section B).*

9 The Process of Ethical Review of a Research Protocol

The Review

- 9.1 All properly submitted and valid applications shall be reviewed in a timely fashion and according to an established review procedure described in the REC's standard operating procedures. A valid application is one which has been submitted by an appropriate investigator, is complete, with all the necessary documents attached, and is signed and dated.
- 9.2 RECs shall meet regularly on scheduled dates that are announced in advance. Meetings should be planned in accordance with the needs of the workload, but RECs must meet the time standards for review.
- 9.3 REC members should be given enough time in advance of the meeting to review the relevant documents.
- 9.4 Meetings shall be minuted. There should be an approval procedure for the minutes.
- 9.5 The applicant (and if appropriate, the sponsor and/or other investigators) shall be invited to be available to elaborate on or clarify specific issues as required by the REC at its meeting. An REC should not cause unnecessary delay by deferring consideration of an application when the necessary further information it requires could have been obtained from the applicant at the first review meeting.
- 9.6 Independent expert referees may be invited by the Chairman to attend the meeting or to provide written comments, subject to applicable confidentiality agreements.

Elements of the review

- 9.7 The primary task of an REC lies in the ethical review of research proposals and their supporting documents, with special attention given to the nature of any intervention and its safety for participants, to the informed consent process, documentation, and to the suitability and feasibility of the protocol.
- 9.8 The Research Governance Framework makes it clear that the sponsor is responsible for ensuring the quality of the science. Paragraphs 2.3.1 and 2.3.2 state that:
 - “It is essential that existing sources of evidence, especially systematic reviews, are considered carefully prior to undertaking research. Research which duplicates other work unnecessarily or which is not of sufficient quality to contribute something useful to existing knowledge is in itself unethical.
 - All proposals for health and social care research must be subjected to review by experts in the relevant fields able to offer independent advice on

its quality. Arrangements for peer review must be commensurate with the scale of the research.”

- 9.9 Thus, protocols submitted for ethical review should already have had prior critique by experts in the relevant research methodology, who should also comment on the originality of the research. It is not the task of an REC to undertake additional scientific review, nor is it constituted to do so, but it should satisfy itself that the review already undertaken is adequate for the nature of the proposal under consideration.
- 9.10 If the committee is of the opinion that the prior scientific review commensurate with the scale of the research is not adequate (including adequate statistical analysis), it should require the applicant to re-submit the application having obtained further expert review.
- 9.11 In addition to considering prior scientific review, RECs need to take into account the potential relevance of applicable laws and regulations. It is not the role of the REC to offer a legal opinion, but it may advise the applicant and the host NHS body whenever it is of the opinion that further expert legal advice might be helpful to them.

Requirements for a favourable opinion

- 9.12 Before giving a favourable opinion, the REC should be adequately reassured about the following issues, as applicable:
- 9.13 *Scientific design and conduct of the study:*
- a. the appropriateness of the study design in relation to the objectives of the study, the statistical methodology (including sample size calculation where appropriate), and the potential for reaching sound conclusions with the smallest number of research participants
 - b. the justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants, other present and future patients, and the concerned communities
 - c. the justification for use of control arms in trials, (whether placebo or active comparator), and the randomisation process to be used
 - d. criteria for prematurely withdrawing research participants
 - e. criteria for suspending or terminating the research as a whole
 - f. the adequacy of provisions made for monitoring and auditing the conduct of the research, including the constitution of a data safety monitoring committee (DSMC)
 - g. the adequacy of the research site, including the supporting staff, available facilities, and emergency procedures. For multi-centre research, these

locality issues will be considered separately from the ethical review of the research proposal itself

- h. the manner in which the results of the research will be reported and published.

9.14 *Recruitment of research participants*

- a. the characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status and ethnicity) and the justification for any decisions made in this respect
- b. the means by which initial contact and recruitment is to be conducted
- c. the means by which full information is to be conveyed to potential research participants or their representatives
- d. inclusion criteria for research participants
- e. exclusion criteria for research participants.

9.15 *Care and protection of research participants*

- a. the safety of any intervention to be used in the proposed research
- b. the suitability of the investigator(s)'s qualifications and experience for ensuring good conduct of the proposed study
- c. any plans to withdraw or withhold standard therapies or clinical management protocols for the purpose of the research, and the justification for such action
- d. the health and social care to be provided to research participants during and after the course of the research
- e. the adequacy of health and social supervision and psychosocial support for the research participants
- f. steps to be taken if research participants voluntarily withdraw during the course of the research
- g. the criteria for extended access to, the emergency use of, and/or the compassionate use of study products
- h. the arrangements, if appropriate, for informing the research participant's general practitioner, including procedures for seeking the participant's consent to do so
- i. a description of any plans to make the study product available to the research participants following the research

- j. a description of any financial costs to research participants
- k. the rewards and compensations (if any) for research participants (including money, services and/or gifts)
- l. whether there is provision in proportion to the risk for compensation/treatment in the case of injury/disability/death of a research participant attributable to participation in the research; the insurance and indemnity arrangements
- m. the nature and size of any grants, payments or other reward to be made to any researchers or research hosts
- n. circumstances that might be lead to conflicts of interest that may affect the independent judgement of the researcher(s).

9.16 *Protection of research participants' confidentiality*

- a. a description of the persons who will have access to personal data of the research participants, including medical records and biological samples
- b. the measures taken to ensure the confidentiality and security of personal information concerning research participants
- c. the extent to which the information will be anonymised
- d. how the data/samples will be obtained, and the purposes for which they will be used
- e. how long the data/samples will be kept
- f. to which countries, if any, the data/samples will be sent
- g. the adequacy of the process for obtaining consent for the above.

9.17 *Informed consent process*

- a. a full description of the process for obtaining informed consent, including the identification of those responsible for obtaining consent, the time-frame in which it will occur, and the process for ensuring consent has not been withdrawn
- b. the adequacy, completeness and understandability of written and oral information to be given to the research participants, and, when appropriate, their legally acceptable representatives
- c. clear justification for the intention to include in the research individuals who cannot consent, and a full account of the arrangements for obtaining consent or authorization for the participation of such individuals