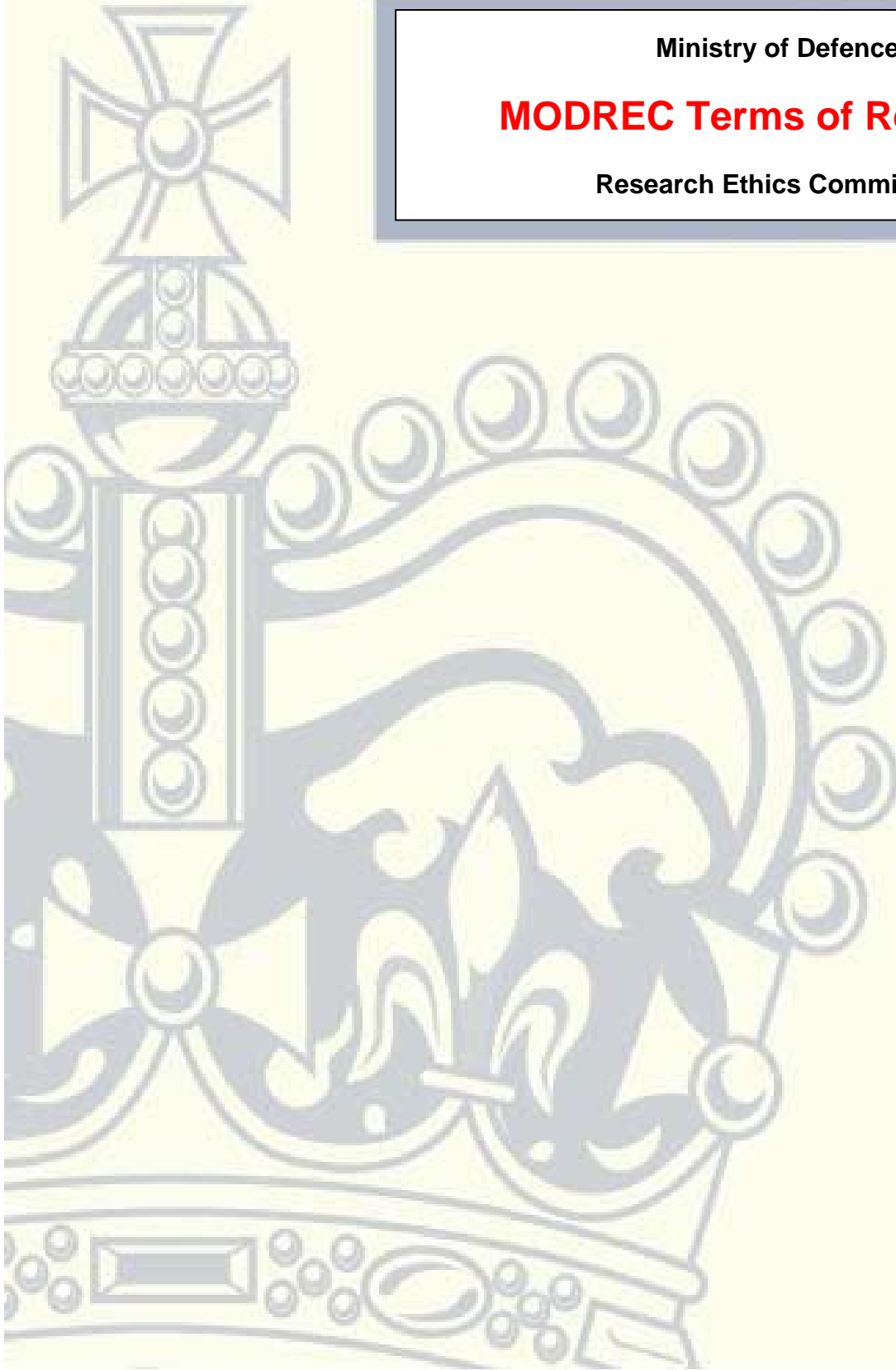


Ministry of Defence

MODREC Terms of Reference

Research Ethics Committees



Document Description:

The Ministry of Defence Research Ethics Committees (MODREC) should scrutinise the ethical implications of all submitted protocols for all research involving human participants, undertaken, funded or sponsored by the MOD. It should ensure that all policies, considerations, standards and safeguards as described or intended by JSP 536 and associated guidelines are applied appropriately, for the purpose of safeguarding the rights, dignity and welfare of people participating in research.

This document sets out the Terms of Reference of the MOD Research Ethics Committees (MODREC)

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1.0	24 Mar 2006	First issue
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MOD Research Ethics Committees - Terms of Reference

Objectives

1. The objective of MODREC is to ensure that all research involving human participants undertaken, funded or sponsored by the Ministry of Defence (MOD) meets nationally and internationally accepted ethical standards. It should ensure that all policies, considerations, standards and safeguards as described or intended by JSP 536 and associated guidelines are applied appropriately, for the purpose of safeguarding the rights, dignity, welfare and safety of people participating in research.

Composition

2. MODREC will have enough members to 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. MODREC may seek the advice of outside experts on any aspects of an application that are relevant to the forming of an ethical opinion.

3. MODREC will be constituted to contain a mixture of expert and lay members. MODREC will act independently, with the majority of voting members to be independent of the MOD (not MOD civil servants or serving members of the regular Armed Forces) and will be supported by a MOD Secretariat.

The Appointing Authority

4. Appointment to MODREC will be made by the Appointing Authority (Surgeon General (SG)), with the involvement of the Chairman of MODREC. Membership vacancies will be publicly advertised. Candidates will be interviewed by a panel including the Chairman of MODREC and at least one person who is independent of the MOD.

Chairman, vice-chairman and alternate vice-chairman

5. The Appointing Authority shall appoint:
- a. One of the members of each ethics committee to be chairman of the committee;
 - b. Another member to be vice-chairman; and
 - c. Another member to be alternate vice-chairman.

Expert Members

6. The 'expert' members of each committee will be chosen to provide the following expertise:
- a. Relevant methodological and ethical expertise in:

- i. applied physiological and psychological research
 - ii. clinical research
 - iii. non-clinical research
 - iv. qualitative or other research methods applicable to human sciences, including medicine and the social sciences.
- b. Relevant clinical practice.
 - c. Experimental design.
 - d. Statistics relevant to research.

Lay Members

7. At least one third of the membership should act as 'lay' members. These lay members should be independent of the MOD, as employees, and their primary personal or professional interest should not be in biomedical or human sciences research or other aspects covered in above Para 6. At least half the lay members should comprise people who have never been health professionals, clinical researchers, or chairs, members or directors of a health service body or organisation providing health care.

8. Ideally, lay members should include those with:

- a. professional ethical involvement (e.g. ministers of religion);
- b. specialist legal experience (e.g. practising or academic lawyers).

Non-Representative Role

9. Despite being drawn from groups identified with particular interests or responsibilities in connection with human and health sciences issues, MODREC is not in any way representative of those groups. Members are appointed in their own right, to participate in the work of MODREC as equal individuals of sound judgement and relevant experience.

Terms of Appointment

10. The length of appointment will be no longer than 3 years without review. Re-appointment will be a matter for discussion between the individual Independent member, the Chairman of MODREC and the Appointing Authority. The Appointing Authority reports the management of the ethical scrutiny process to the Defence Audit Committee when required. All appointments are subject to the conditions set out in personal terms of reference and appointment letters.

Quorum

11. For meetings at which research ethical review is undertaken, a quorum shall be at least 7, including the Chairman and/or Vice Chairman, at least one expert member and at least two 'lay' members. At least one lay member must be a person who is not, and never has been, a health care professional or a chair, member, director or employee of a health service body or organisation providing health care.

Education and Training for MODREC Members

12. MODREC members have a need for initial and continued education and training regarding research ethics. The MOD will be responsible for funding the necessary education and training. Members of MODREC should be encouraged to visit the facilities where the research is conducted.

The Annual Report

13. Within 6 months of the end of each financial year, MODREC will submit an Annual Report to the Appointing Authority.

14. The report will include:

- a. the names, affiliations and occupations of committee members ;
- b. the number and dates of meetings held;
- c. the attendance of members;
- d. the training undertaken by the ethics committee members;
- e. a list of proposals considered¹, and the decisions reached on each;
- f. the time taken from submission to MODREC to a final decision for each proposal;
- g. a list of projects completed or terminated during the year;
- h. the number of participants involved and, where appropriate, the number of exposures, etc. (information often required for Parliamentary Questions);
- i. any adverse or unexpected reactions.

15. The annual report should be produced as an unclassified document to allow publication.

Administrative Support

16. The MOD Secretariat will provide secretarial support and provide suitable and discrete facilities in which the work of MODREC and its administrators can be undertaken and its meetings held in a confidential manner. The handling and storage of all documents should comply with JSP 440 and MOD will provide appropriate facilities where practical.

Research Protocol Register

17. The MODREC Secretariat will keep an electronic register of all proposals that come before it. The register should form the basis of the MODREC Annual Report to the Appointing Authority. Provision must also be made for long term retention of

¹ Listing must respect confidentiality.

research protocols in case of future enquiries. Full records should be kept permanently by MOD in accordance with JSP 441.

Legal Liability

18. The arrangements for legal liabilities are outlined in members' letters of appointment.

Procedure

19. MODREC should consider valid applications in a timely manner. A valid application is one that has been submitted by the Chief Investigator to the MODREC Secretariat, is complete, with all the necessary documents attached, including approval from the relevant scientific advisory committee. The Chief Investigator will normally be expected to attend if the protocol is being considered at a committee meeting. In the absence of the Chief Investigator a decision should be reached and communicated to the applicant within 7 working days of the MODREC meeting at which it is considered.

20. After an initial review, further written information or clarification may be requested from the applicant. The further information may be considered by the Chairman of MODREC, by a sub-committee or at the next scheduled meeting of MODREC as appropriate. The Chairman may be given delegated authority to issue the final opinion following the initial review. In the case of a Clinical Trial of an Investigational Medicinal Product (CTIMP), a final opinion shall be given within 60 calendar days of the date on which a valid application was received. This excludes any time taken by the applicant to respond fully to one request for further information or clarification.

21. Amendments submitted once the research has started shall be considered at the next scheduled meeting of MODREC or out of committee as appropriate. A response should be given to the applicant within a total of 20 working days from receipt of the resubmission. However, where the amendment is very far-reaching, e.g. involving a change in its primary purpose, a significant change of methodology or new types of investigation or intervention with research participants, it may be treated by MODREC at their discretion as a new application requiring full ethical review within the standard 60 calendar days timeframe.

22. MODREC should meet with sufficient frequency to complete all its business in a timely manner. It is anticipated that this should be every two months.

23. To expedite review, protocols which fall within the limits of the Schedule of Approved Procedures (SAPs) (see paragraph 45), namely those of recurring and straightforward nature, should be reviewed by the Chairman/Vice Chairman where appropriate.

24. MODREC should not be expected to accept a workload that compromises the quality of ethical review. When this is likely, the Appointing Authority should establish additional sub-committees of MODREC.

25. If MODREC does not provide favourable ethical opinion of a protocol, the investigators may request an appeal (see Para 63-67).

Confidentiality of proceedings

26. MODREC 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 MODREC meetings will be held in private. The Chief Investigator may be invited and other observers may attend, at the discretion of the Committee. A summary of details of the application shall be made available, through the Minutes, once the final decision on the application is ratified by MODREC. These shall include:

- a. the names of the Chief Investigator and sponsor;
- b. the name of the research site;
- c. a summary of the research proposal comprehensible to a lay person;
- d. the issues discussed by the committee and the committee's conclusions;
- e. its overall opinion.

Following up and reports

27. Once MODREC has given approval, the Chief Investigator is required to notify the committee, in advance, of any proposed deviation from the original research protocol. The committee may then wish to review its decision.

28. No deviation from, or change to, the research protocol shall be initiated by the Chief Investigator without the prior written approval of MODREC, save where this is necessary to eliminate immediate hazards to research participants ('urgent safety measures') or when the change involves only logistical or administrative aspects of the research. In these cases, the changes may be implemented immediately. MODREC must be informed no later than 3 calendar days from the date any urgent safety measures are taken.

29. 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 MODREC and approval obtained before implementation (except when there are immediate hazards to research participants).

30. MODREC should indicate at the time of approval any progress reports it requires from the applicant. It shall request a final report, to be delivered within 3 months of completion of the study. This need not be onerous and it should be possible to submit it electronically to the Secretariat.

31. Where the research is terminated prematurely, a report indicating the reasons for early termination should be submitted within 15 working days to the Secretariat and relevant MODREC chairman.

32. Reports to the committee are also required if there are any unusual or unexpected results that raise questions about the safety of the research. Where any serious untoward effects occur in any research study except a CTIMP, then research MUST cease immediately and the event reported to the Chairman of MODREC as well as to line management and/or the customer sponsoring the protocol. Research must not recommence until cleared by MODREC after full discussion. In the case of a CTIMP, MODREC will refer any concerns about safety to the Medicines and Healthcare products Regulatory Agency (MHRA) for further advice. Responsibility for suspending or terminating the clinical trial authorisation for a CTIMP lies with the MHRA.

33. Reports on success (or difficulties) in recruiting participants provide MODREC with useful feedback on perceptions of the acceptability of the project among potential research participants. MODREC may wish to request such reports where they anticipate potential difficulties.

34. On the basis of any such reports MODREC may wish to review its decision. Failure to produce such required reports without a reason acceptable to MODREC in the case of a non-CTIMP may result in suspension of the Committee's favourable opinion, in which case the research must cease.

35. Other than by means of these required progress reports, MODREC has no responsibility for pro-active monitoring of research, the accountability for which lies with the sponsor and the employing organisation. MODREC may, however, wish to be reassured of the process for such monitoring in certain specific cases.

36. A member of MODREC who becomes aware of a possible breach of good practice in research should report this initially to the Chairman of MODREC, who shall inform the Appointing Authority. The Appointing Authority's officers (in the Defence Medical Services Department) shall be accountable for taking appropriate action.

The Review

37. MODREC shall meet as required (see para 22), to ensure that it has sufficient flexibility to deal with applications in a reasonable time. Meetings should be planned in accordance with the needs of the workload, but MODREC should aim to meet the time standards for review.

38. MODREC members should be given at least 15 working days, in advance of the meeting to review the relevant documents.

39. Minutes shall be taken at the meetings by the MODREC Secretariat. There should be an approval procedure for the minutes. In order to ensure free discussion and a true record of meetings, the minutes must be confidential to the members of MODREC and held under such understanding by the MODREC secretariat. They will be made available to SG, as the Appointing Authority, and his staff upon request for the purposes of an Appointing Authority.

40. The applicant (and if appropriate, the sponsor and/or other investigators) shall be invited to be available to elaborate on or clarify specific issues if required by MODREC at its meeting. MODREC 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.

41. 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

42. The primary task of MODREC lies in the ethical review of all research involving human participants as defined within JSP 536. The review should cover all 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 research protocol. This must meet national and international standards.

43. The quality of the science is the prime responsibility of the organisation sponsoring the project (often MOD) and must be validated by line management, and undergo appropriate scientific peer review (i.e. relevant SAC), prior to submission for ethical review. This will precede formal submission to MODREC. It is not the task of MODREC to undertake additional scientific review, nor is it constituted to do so, but it should be satisfied that the review already undertaken is adequate for the nature of the proposal under consideration. The quality of the proposed science, however, should be open to challenge by experts on MODREC.

44. In addition to considering prior scientific review, MODREC needs to take into account any relevant laws and regulations. It is not the role of MODREC to offer a legal opinion, but it may advise the applicant to seek such advice.

45. For some types of research, particularly those involving minimal risk, the use of the Schedule of Approved Procedures (SAPs) may be appropriate. This Schedule lists experimental procedures that have been approved by MODREC for the purpose of allowing ex-committee review of research within those limits.

46. Specified business areas may be granted tightly bounded Generic Protocols to cover repetitive, non-contentious, minimal risk work performed within specified facilities. A Generic Protocol must be approved by MODREC. Once approved, a Generic Protocol allows the named management area to undertake the specified research, after scientific peer review, without seeking further approval from MODREC.

Requirements for Approval

47. Before approving a research protocol, MODREC should be satisfied that the following issues have been addressed, as applicable:

- a. *Scientific design and conduct of the study:*

- i. 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;
 - ii. the justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants, other present and future personnel and the communities concerned;
 - iii. the justification for use of control arms in trials, and the randomisation process to be used;
 - iv. criteria for prematurely withdrawing research participants;
 - v. criteria for suspending or terminating the research as a whole;
 - vi. the adequacy of provisions made for monitoring and auditing the conduct of the research;
 - vii. the adequacy of the research site, including the supporting staff, available facilities and emergency procedures.
- b. Recruitment of research participants:
- i. the characteristics of the population from which the research participants will be drawn (e.g. gender, age, ethnicity) and the justification for any decisions made in this respect;
 - ii. the means by which initial contact and recruitment is to be conducted;
 - iii. the means by which full information is to be conveyed to potential research participants or their representatives;
 - iv. inclusion criteria for research participants;
 - v. exclusion criteria for research participants.
- c. Care and protection of research participants:
- i. the safety of any intervention to be used in the proposed research;
 - ii. the suitability of the investigator's qualification and experience for ensuring good conduct of the proposed study;
 - iii. any plans to withdraw or withhold standard therapies and the justification for such action;
 - iv. the health and social care to be provided to research participants during and after the course of the research;

- v. the adequacy of health and social supervision and psychosocial support for the research participants;
- vi. steps to be taken by research participants who voluntarily withdraw during the course of the research;
- vii. the arrangements, if appropriate, for communicating with the research participant's general practitioner, including procedures for seeking the participant's consent to do so;
- viii. a description of any plans to make the study product available to the research participants following the research;
- ix. a description of any financial costs to research participants;
- x. the payments and compensations (if any) for research participants (including money, services and/or gifts);
- xi. when research is carried out by organisations other than MOD, that the insurance and indemnity arrangements provide for treatment and/or compensation in the event of injury, disability or death to the research participant arising from participation in the research (note when research is carried out by MOD, the Department accepts the liability to pay compensation to healthy volunteers);
- xii. the nature and size of any grants, payments or other reward to be made to any researchers or research hosts;
- xiii. circumstances that could lead to conflicts of interest which may affect the independent judgement of the researcher(s);
- xiv. if medical assessment or research gives rise to information of relevance to the current or future health and quality of life of research participants, this information must be offered to them. This shall be done within a framework of healthcare or counselling. In communication of such information, due care must be taken in order to protect confidentiality;
- xv. potential volunteers will be made aware, prior to signing a consent form, that the medical officer may, in some cases, have a legal responsibility to inform appropriate authorities if medical assessment or research gives rise to information relevant to their fitness for duty (e.g. fitness to fly, etc.) or identifies a notifiable disease;
- xvi. in the case of therapeutic research, that the patients' best interests will not be compromised by the research;
- xvii. in the case of studies on healthy volunteers, which may be undertaken by non-medical personnel, there is adequate medical supervision to ensure the safety and well-being of the participants;

- xviii. in the case of studies on medical records, that there is a data controller who can act in the best interests of those whose personal information is being employed.

- d. Protection of research participants' confidentiality:
 - i. a description of the persons who will have access to personal data of the research participants, including medical records and biological samples;
 - ii. the measures taken to ensure the confidentiality and security of personal information concerning research participants;
 - iii. the extent to which the information will be made anonymous;
 - iv. how the data/samples will be obtained, and the purposes for which they will be used;
 - v. how long the data/samples will be kept;
 - vi. the countries, if any, to which the data/samples will be sent;
 - vii. the adequacy of the process for obtaining consent for the above.

- e. Informed consent process:
 - i. 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;
 - ii. the adequacy, completeness and clarity of written and oral information to be given to the research participants;
 - iii. assurances that research participants will receive information that becomes available during the course of the research relevant to their participation (including their rights, safety and well-being);
 - iv. the provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project.

Expedited review

48. The MODREC Chairman or designated deputy may conduct expedited review of research proposals, in consultation with two expert members of MODREC, when the research concerns matters of urgent operational or business need. The requirement for expedited review in these circumstances must be formally certified by the research's MOD sponsor at senior management level (SCS or at least 1* equivalent). Scientific review by a scientific advisory committee is still required prior to ethical review.

49. The MODREC Chairman or designated deputy may conduct expedited review of research proposals, when the research is:

- a. within SAPs;
- b. minor modifications being made to a previously approved submission;
- c. the deadline for a previously approved research project is reached and minimal or no changes are requested or required.

50. Any such expedited decisions must be reported and endorsed at the next MODREC meeting.

Decision-making

51. In making decisions on applications for the ethical review of research, MODREC should take the following into consideration:

- a. In the case of a conflict of interest a member may be asked to withdraw from the meeting for the discussion and decision procedure concerning an application. The conflict of interest should be indicated to the Chairman prior to the review of the application and recorded in the minutes.
- b. If a member of MODREC has an interest in a protocol tabled for discussion (s)he must leave the meeting whilst that discussion takes place.
- c. By invitation of the Chairman, independent experts or others may take part in the discussion of the proposal at the MODREC meeting. At the Chairman's discretion, the applicant may attend discussion of the proposal to speed up decision-making and accurately design redrafting. The process should be seen as constructive collaboration between the Committee and the applicant, rather than adversarial.
- d. Decisions can only be made by full MODREC members and at meetings where a quorum is present.
- e. The documents required for a full review of the application shall be complete and the relevant elements mentioned above should be considered before a decision is made.
- f. Written comments from absent members shall be allowed to inform the discussion, but only those members who actually participate in the review by the committee at its meeting shall participate in the decision.
- g. It is recommended that decisions be arrived at through consensus where possible. However, where members differ on the decision despite adequate discussion, a vote may be taken to determine the majority opinion of those members present at the meeting. Where there is a division of opinion, the Chairman may obtain the views of any members of the Committee not present. He may also seek the opinion of additional outside experts. Final decision on a project may be carried on a vote with at least two-thirds of the Committee participating in the decision in agreement.

- h. Where the decision is not unanimous, minority reservations should be recorded formally, and also made known to the Chief Investigator.
52. Advice that is not binding may be appended to the decision.
53. In cases of conditional decisions, clear suggestions for revision and the procedure for having the application undergo further review should be specified.
54. An unfavourable opinion/rejection of an application should be supported, in writing, by clearly stated reasons.

Submission of applications

55. The application shall be submitted by the Chief Investigator who is the person designated as taking overall responsibility within the team of researchers for the design, conduct and reporting of the study. It follows that the applicant must be of adequate qualification and expertise to fulfil this important role. A current CV of the Chief Investigator should be submitted with the application.
56. Where a potential applicant is inexperienced, there should be an identified supervisor of adequate quality and experience who will take responsibility for the ethical and scientific conduct of the research. A current CV of the supervisor should be submitted with the application.
57. MODREC should ensure that its requirements for submitting an application for review are described in an application procedure that is readily available to prospective applicants.

Application Procedures

58. This will be published by the MODREC Secretariat and should include the following:
- a. Contact details of the MODREC Secretariat;
 - b. the application form;
 - c. any additional documentation;
 - d. the deadlines for submission of the application in relation to the review dates;
 - e. the means by which the application will be acknowledged ;
 - f. the expected time for notification of the decision following review;
 - g. the time frame to be followed in cases where MODREC requests supplementary information from the applicant, or changes to the documents;
 - h. the application procedure for amendments to the research protocol, the recruitment material, the information for participants, the consent form or procedure for obtaining consent.
 - i. the process for addressing any disputed decisions.

Documentation and archiving

59. All documentation and communication of MODREC should be dated, filed and archived, by the MODREC Secretariat, according to JSP 441. A statement is required defining the access and retrieval procedure (including authorised persons) for the various documents, files and archives.

60. The MODREC Secretariat should ensure documents are retained permanently. The Committee must recommend in its approval the retention period for medical documents relating to trial procedures and the participants' individual records. This must be guided by a 20 year minimum appropriate for non-invasive procedures and a 100 year expectation for procedures where long-term health effects could conceivably be manifest.

61. Documents that should be filed and archived include, but are not limited to:

- a. annual reports;
- b. the curriculum vitae of each MODREC member;
- c. a record of all income and expenses of MODREC including allowances and reimbursements made to the secretariat and MODREC members;
- d. the published guidelines for submission established by MODREC;
- e. the agendas of MODREC meetings;
- f. the minutes of MODREC meetings;
- g. one copy of all materials submitted by each applicant;
- h. the correspondence by MODREC with applicants or concerned parties regarding application, decision and follow-up;
- i. a copy of the decision and any advice or requirements sent to an applicant;
- j. all written documentation received during the follow-up;
- k. the notification of the completion, premature suspension, or premature termination of a study;
- l. the number of participants;
- m. the number of exposures, where appropriate;
- n. reports of adverse events, their investigation and any follow-up response or action by the committee;
- o. the final summary or final report of the study.

Complaints

62. Any complaints from applicants should be directed initially to the Chairman of MODREC and then, if necessary, to the Appointing Authority through the MODREC Secretariat.

Appeals

63. An applicant who has received an unfavourable ethical opinion may appeal against the decision. A notice of intention to appeal including the grounds for appeal should be provided to the MODREC Secretariat within 90 days of formal receipt of the MODREC decision. The MODREC Secretariat will staff the Appeal to the Surgeon General who will form the Appeals authority. The appeals authority may call upon the advice of experts not associated with the research protocol. If the appeals Authority allows the appeal, then it will be submitted to the second MODREC.
64. The application should be reviewed by the second MODREC in accordance with the standard procedures for review of any new application.
65. The second MODREC may consider the matters raised by the first MODREC in the course of the review but is not bound by them. It should consider carefully any representations made by the applicant.
66. There can be no appeal against the decision of the second MODREC.
67. If the second MODREC gives a favourable opinion, it will assume all further responsibility for monitoring the research and reviewing amendments.