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OPERATIONAL PROCEDURES FOR  
RESEARCH ETHICS COMMITTEES:  
GUIDANCE 2004

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Published by



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Guidance on Operational Procedures for Research Ethics Committees

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## Introduction

In the last number of years the expansion of scientific knowledge has resulted in the development of new treatments and technologies. As Research Ethics Committees are among those at the forefront of ensuring that the scope and nature of such advances occur in a safe and ethical manner, it is imperative that a formalised, exemplary process of ethical review be in place. The development of codes of ethics related to research involving humans is comparatively recent. The first international code of ethics for research involving human participants, the Nuremberg Code, was issued in 1947 and laid down standards for carrying out human experimentation, emphasising the subjects' voluntary consent. In 1964 the World Medical Association took an important additional step by adopting the Declaration of Helsinki, most recently revised in 2000, requiring that proposed experimentation on humans be approved by a committee independent from the investigators conducting the research. The Belmont report was published in the United States in 1979 and forms the basis of all US human research regulation. The report sets forth the basic ethical principles underlying the acceptable conduct of research involving human participants. Those principles, respect for persons, beneficence, and justice, are now accepted as three essential requirements for the ethical conduct of research involving human participants. Most recently, the Council for International Organisations of Medical Sciences (CIOMS), working with the World Health Organisation, issued a third edition of biomedical research ethical guidelines in 2002 which feature recommendations on ethical review committees and the issue of safeguarding confidentiality. These documents demonstrate a trend towards making more explicit the ethical standards that must be met if research on human beings is to be ethically acceptable.

The regulations and recommendations contained within these international codes need to be adapted into institutional operational guidance to be used at the local level to guide the planning, review, approval and conduct of human research. In Ireland, the recent Regulations made by the Minister for Health and Children (Clinical Trials on Medicinal Products for Human Use, S.I. No. 190 of 2004), the report of the Irish College of General Practitioners entitled "Ethical questions to be considered by a research ethics committee when approving clinical trials which involve genetic testing" (2003) and the Health Research Board's report "Genetic Research and Human Biological Samples: The Legal and Ethical Considerations" (2002) provide useful guidance in relation to ethical review of clinical trials. However, Ireland currently lacks comprehensive guidance with respect to ethical review of research involving human participants outside the remit of clinical trials.

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This document is the result of systematic evaluation and analysis of international best practice (see list of Supporting Documents) and comprehensive discussion undertaken by a working group of the Irish Council for Bioethics. It is based on requirements for ethical review established in international guidelines and provides guidance on general standards and principles that should be considered by Research Ethics Committees when reviewing research proposals. This guidance is intended to facilitate and support efficient and effective ethical review of proposals. This document should be viewed as a basis upon which Research Ethics Committees can establish and develop their standard operating procedures.

Impartial ethical review is designed to maintain ethical standards of practice in research, to protect participants in research and research workers from harm or exploitation, to preserve the subject's rights, including the right to privacy and to provide reassurance to the public that all of this is being done. In promoting these goals Research Ethics Committees should be mindful that appropriately regulated, ethically acceptable, rigorous research benefits society as a whole. The primary task of Research Ethics Committees is the protection of the welfare and the rights of participants in research. Another important role is to facilitate and support the progress that the research community seeks to achieve.

The Council is hopeful that the guidance contained in this document will facilitate Research Ethics Committees in conducting independent, comprehensive, ethical review of research proposals, which will serve investigators and the public alike.

## Section 1 : Principles of Ethical Review

Research involving human participants should be based on a fundamental moral commitment to the individuals concerned and to advancing human welfare, knowledge and understanding. A number of guiding moral principles govern the ethical review of research proposals, which aim to protect the well-being and rights of research participants/volunteers.

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### 1.1 Respect for Persons

Respect for persons is expressed as regard for the welfare, rights, beliefs, perceptions, and customs, both individual and collective, of individuals involved in research. Respect for persons is most commonly manifested through the exercise of informed consent, which requires that people's beliefs and opinions be respected, and that they be allowed to choose for themselves whether or not they wish to participate in research. In order to choose they must be informed of their options, including the possible risks and benefits of those options. They must be assured of the necessity of the research, including the fact that all possible risks have been minimised, and, where significant risk is involved, that no other method of research is possible. They must be asked to make their choice in circumstances, which are free of coercion or undue pressure, and they must be free to withdraw from the research process at any time. This decision must not affect their health care in any way. Ethical review should focus on the entire process of obtaining consent, not just on the written consent documents, but on how participants are informed of the study, who discusses it with them, and in what circumstances. The requirement for free and informed consent presumes that adequate information is provided to obtain an informed judgement, that information provided is in a form and delivered in a manner that will enable it to be understood and that the consent is voluntary in nature.

In the research context, respect for persons requires that limitations to an individual's autonomy are recognised and that appropriate mechanisms are in place to protect against abuse, exploitation or discrimination. Of particular concern here are children, individuals with an intellectual disability or with short or long-term unconsciousness. Parental or guardian's consent must be sought, but such consent can only be accepted where the research in question is clearly in the best interests of the subject concerned, or where the research concerned carries minimal risk or impact on the subject concerned.

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## 1.2 Privacy and Confidentiality

Privacy and confidentiality are an integral part of the protection and promotion of human dignity and help to protect and maintain a person's mental or psychological well-being. The need for research should be weighed against infringements of privacy and steps must be taken to ensure that individuals are protected from any harm that might be caused as the result of access to their personal information.

## 1.3 Validity of Research Proposals

The scientific merit of a study is itself an ethical issue. The essential features of ethically justified research involving human participants are that the research offers a means of developing information, not otherwise obtainable, that the design of the research is scientifically sound, that the investigators and other research personnel are qualified and capable and that the methods to be used should be appropriate to the objectives of the research and the field of study.

## 1.4 Risks

As research involves advancing the frontiers of knowledge, its undertaking usually involves a degree of uncertainty about the precise magnitude of and kind of benefits and harms that attend proposed research. The principle of beneficence requires that researchers maximise the potential benefits to the participants and minimise the potential risks of harm. If there are any risks resulting from participation in the research, then there must be benefits, either to the subject, or to humanity or society in general. The principle of non-maleficence requires that researchers ensure that predictable injury, either through acts of commission or omission, will be prevented.

## 1.5 Justice

Justice imposes duties to neither neglect nor discriminate against individuals or groups who may benefit from advances in research, to avoid imposing on a particular group an unfair burden of participation in research and to design research so that the selection and recruitment of research participants/volunteers is fair. Justice requires also that the research be responsive to the health conditions or needs of vulnerable participants. In such cases there must be clear and unambiguous justification for the research and for its application to such participants, and normally there should be potential for direct health-related benefit to the subject, or the absence of any significant risk or discomfort.



## Section 2 : Research Requiring Ethics Review

All Research involving or impacting upon human participants requires ethics review by a research ethics committee, before the research is started, except as stipulated below.

For the purposes of this guidance, Research is defined as a systematic investigation to establish facts, principles or knowledge and a study of some matter with the objective of obtaining or confirming knowledge.

### 2.1 Specific activities that may require REC review

Specific activities that may require REC review include, but are not necessarily limited to the following:

- (a) Clinical trials involving human participants
- (b) New treatment or interventions
- (c) Research involving human remains, cadavers, tissues, discarded tissue (e.g. placenta), biological fluids
- (d) Physiological studies
- (e) Comparing an established procedure, whether therapeutic, non-therapeutic or diagnostic, with other procedures which are not recognised as established by virtue of their recent development, discovery or use in a new or unfamiliar way
- (f) Innovative practices in health and disability services
- (g) Research conducted by students, which includes all activities that meet the definition of research with human participants
- (h) Observational clinical research
- (i) Access to personal information by means of questionnaires, interviews or other techniques of information gathering
- (j) Research involving the secondary use of data (use of data not collected for that research purpose), if any form of identifier is involved and/or if health information pertaining to individuals is involved
- (k) Case studies, when a series of subject observations allow possible extrapolation of generalisation of the results from the reported cases and when there is an intent to publish or disseminate the data

Note to item 2.1(g) above: As supervised student research is conducted primarily for the purpose of educating students on research techniques and methodologies, REC should review research protocols with a view to contributing to the students' education concerning scientific and ethical principles governing research.

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## 2.2 Activities that may not require REC review

Review by REC may not be required for:

- (a) Research utilising existing publicly available documents or data
- (b) Observational studies in public places in which the identity of the participants remains anonymous
- (c) Case study of one patient with the proviso that written informed consent has been obtained from the relevant subject
- (d) Quality assurance studies
- (e) Audits

The opinion of the REC should be sought whenever there is any doubt about the applicability of this guidance to a particular research project.

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## Section 3 : Research Ethics Committees

### 3.1 Constituting a Research Ethics Committee

A REC should be constituted to ensure competent ethical review of research proposals submitted to the committee and an independent and just review of any such proposals. The REC must define its mandate and authority and must make clear the jurisdiction of the REC and its relationship to other relevant bodies or institutions. Institutions/ organisations under whose authority RECs are established must ensure that RECs have appropriate financial (including indemnity arrangements for members of the committee) and administrative support to fulfil their function. A publicly available standard operating procedure should be produced and RECs should act in accordance with their operating procedures.

### 3.2 Composition of a Research Ethics Committee

The guiding principle for appointing members to a REC is to ensure that the committee has the appropriate expertise, skills, knowledge and perspectives to ensure an adequate and thorough ethics review. RECs should be multidisciplinary and multi-sectoral in composition. Attention should be paid to age and gender balance. One third of the total membership should be lay members. The qualifications for lay members are independence from the institution/organisation under whose authority the REC is established and their non-involvement in scientific, clinical practice and legal work. Those who have no experience in professions associated with research on human beings are more likely to bring a truly lay perspective. Committee members should elect a chairperson and a vice-chairperson.

In general it would be advisable for a committee's membership to include but not be restricted to the following:

- (a) member(s) with knowledge of and current experience in the areas of research which are regularly considered by the REC (e.g. scientist).
- (b) member(s) with knowledge of and current experience in the professional care, counselling or treatment of people (e.g. nurse, medical practitioner, clinical psychologist, as appropriate)
- (c) member(s) with training in ethics (e.g. ethicist, philosopher, theologian)
- (d) member(s) with a qualification in law
- (e) member(s) with training in statistics
- (f) lay member(s)

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A minimum of seven members of the REC is required to be present at a meeting held to determine an opinion in relation to an application to the REC. There should be a reasonable representation of members, which must include the chairperson, or in his/her absence the vice-chairperson; a member with relevant clinical and/or methodological expertise; a lay member and a member who is independent of the institution/organisation under whose authority the REC is established.

A REC should have sufficient members to secure the minimum number of members required to determine an opinion on an application.

A REC may appoint a person to act as an alternate for each member of the committee, where the alternate satisfies the same membership criteria as the member. The standard operating procedure of the REC should identify the primary member for whom each alternate member may substitute. When alternates substitute for a primary member, the alternate member should have received and reviewed the same material that the primary member received or would have received. An alternate can only vote if the member for whom he/she acts as an alternate is absent.

Where a chairperson or members of a REC believe there is insufficient expertise on the committee to assess an application or an issue, the committee should seek additional expert advice. Experts may have specialist knowledge in particular fields of science or medicine or they may be representatives of communities or special interest groups. Co-opted expert members are not entitled to vote.

### **3.3 Appointment of Members of a Research Ethics Committee**

Clear procedures should be formulated to identify and appoint members to RECs. These should include:

- (a) procedures for selecting candidates
- (b) procedures for appointing members
- (c) name or description of person or institution responsible for making appointments
- (d) duration of an appointment
- (e) policy for renewal of an appointment
- (f) procedure for replacing members
- (g) procedure for resignation of a member
- (h) procedure for the disqualification of a member
- (i) training of members

Note to item 3.3(a) above: When selecting candidates, the committee should take into account whether or not by virtue of employment, profession or relationship, the candidate could be construed to have a potential conflict of interest with respect to a majority of proposals reviewed.

Note to item 3.3(b) above: appointing members should be by an open process. Vacancies should be advertised publicly in the press and/or via local professional networks.

Note to item 3.3(d) above: Members should be appointed for a fixed term, which may be renewed, but should not normally exceed two consecutive terms on the same REC. The benefit of maintaining some continuity of membership by overlapping terms of office should be considered.

### **3.4 Duties and responsibilities of a Research Ethics Committee Member**

- (a) Committee members have a commitment to protect and safeguard the rights and interests of human participants participating in research, while promoting and facilitating research excellence.
- (b) A member should be prepared to have his/her name, profession and affiliation published.
- (c) Members are expected to treat as confidential all applications, meeting deliberations, information on research participants/volunteers and related matters.
- (d) When a committee member believes they have a conflict of interest on a subject which will compromise their ability to make an impartial decision, they should declare that conflict of interest and withdraw themselves from the discussion and/or activity.
- (e) A member is expected to attend at least two-thirds of all scheduled REC meetings in each year. Should a member fail to do so, the chairperson should address this with the member concerned.
- (f) A member must agree to take part in education and ongoing training appropriate to his or her role as a REC member.

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## Section 4 : Submitting an application

RECs have the responsibility of establishing well-defined submission procedures for research proposals, which are readily available to prospective applicants.

### 4.1 Application Procedure

An application for ethics committee review in respect of proposed research must be made in writing and signed by a qualified researcher responsible for the conduct of the study. This will usually be the chief investigator. Material to be submitted as part of an application may include but is not restricted to:

- (a) the name(s) and address(es) of the REC members to whom the application is to be submitted.
- (b) the application forms
- (c) the documentation required
- (d) the format for submission
- (e) the number of copies to be submitted
- (f) the deadline for submission of the application
- (g) the means by which applications will be acknowledged, including the communication of an incomplete application
- (h) the expected time for notification of the decision following review
- (i) the fee structure, if any, for reviewing an application
- (j) the application procedure for amendments to the proposal, the recruitment material, the potential research participation information, or the informed consent form
- (k) the information given to research participants/volunteers and the appropriate safeguards for the protection of personal data

### 4.2 Documentation

The applicant should submit all documentation required for a thorough and complete ethical review of the proposed research. The applicant should be aware of the elements of the review process (see 5.2) and submit the necessary documentation to conduct this review. The REC should advise all applicants on documentation required for review.

This may include but is not restricted to:

- (a) a signed and dated application form
- (b) the protocol of the proposed research (clearly identified and dated), together with supporting documents and appendices
- (c) a summary, synopsis or diagram ('flowchart') in non-technical language
- (d) a description of the ethical considerations involved in the research
- (e) case report forms, diary cards, and other questionnaires intended for research participants/volunteers
- (f) when the research involves the study of a product (such as a pharmaceutical or device under investigation) an adequate summary of all pharmacological and toxicological data available on the product, together with a summary of clinical experience with the product to date (e.g. recent investigator's brochure, a summary of the product's characteristics) should be included
- (g) current curriculum vitae of the applicant(s) (updated, signed and dated)
- (h) material used (including advertisements) for participant/volunteer recruitment
- (i) patient/volunteer information
- (j) a full description of the process to obtain and document consent
- (k) suitable arrangements for indemnifying participants/volunteers and investigators
- (l) all significant previous decisions (e.g. those leading to a negative decision or modified proposal) by other RECs or regulatory authorities for the proposed research (whether in the same location or elsewhere) and an indication of the modification(s) to the protocol made on that account. The reasons for previous negative decisions should be provided.

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## Section 5 : Review procedure

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.

*Under the Clinical Trials on Medicinal Products for Human Use Regulations 2004 RECs are required to give an opinion on research protocols involving standard products, no more than 60 days after acknowledgement of receipt of a "valid" application has been received. Where research involves gene therapy, somatic cell therapy or genetically modified organisms RECs are required to make a decision no more than 90 days after acknowledging that a "valid" application has been received. Where external consultation is deemed necessary RECs are permitted a total of 180 days to make a decision following acknowledgement of receipt of a "valid" application. There are no time limits imposed on RECs making a decision on research involving xenogenic cell therapy.*

### 5.1 Meeting Requirements

RECs should meet in accordance with regularly scheduled dates. Meeting requirements should include the following:

- (a) meetings should follow a previously scheduled agenda
- (b) members should be given sufficient time to review relevant documentation
- (c) meetings should be minuted. There should be an approval procedure for the minutes
- (d) when appropriate, the sponsor and/or investigator may be invited to present the proposal to the members and answer any questions a committee may have
- (e) when appropriate, independent experts (e.g. researchers with specific competence, ethicists, statisticians) may be invited to attend



## 5.2 Elements of Review

When reviewing research proposals a REC should consider the following:

### 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) and the potential for reaching reliable conclusions with the smallest number of research participants/volunteers
- (b) the justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants/volunteers and the concerned communities
- (c) the justification for use of control arms in trials (whether placebo or active comparator), and the randomisation programme to be used
- (d) criteria for withdrawing participants/volunteers prematurely
- (e) criteria for suspending or terminating research
- (f) the adequacy of conditions made for the monitoring and auditing the conduct of the research
- (g) the adequacy of the site including the supporting staff, facilities and emergency procedures
- (h) the form in which the results will be reported and published

### Recruitment of research participants/volunteers

- (a) the characteristics of the population from which the participants/volunteers will be drawn (including gender, age, ethnicity) and the justification for any decisions made in this regard
- (b) the method by which initial contact and recruitment are to be conducted
- (c) the method by which information is to be conveyed to participants/volunteers or their representatives and by which means consent is to be obtained
- (d) inclusion and exclusion criteria for research participants/volunteers

### Care and protection of research participants/volunteers

- (a) the safety of any intervention to be used in the proposed research
- (b) the suitability of the investigator for the proposed research in relation to his/her qualifications and experience
- (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

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- (d) the adequacy of health and social supervision and psychological support for the research participants/volunteers
  - (e) the adequacy of medical supervision and follow-up concerning the participants/volunteers
  - (f) steps to be followed if participants/volunteers decide to withdraw during the course of the research
  - (g) the arrangements, if appropriate, for informing the participant's/volunteer's GP, including procedure for seeking consent to do so
  - (h) a description of any scheme to make the study product available to the participants/volunteers following the research
  - (i) a report of the expenses (if any) payable to participants/volunteers
  - (j) the provisions for compensation/treatment in the case of the injury/disability/death of a participant/volunteer connected to participation in the study
  - (k) the provisions made for receiving and responding to queries and complaints of participants/volunteers throughout the course of the study
    - (i) the insurance and indemnity agreements covering the liability of the investigator by the sponsor
    - (l) a description of any grants, payments or other reward to be made to any researchers or research hosts
  - (m) a description of possible conflicts of interest which might affect the independent judgement of the researcher(s)

#### **Protection of confidentiality of participants/volunteers**

- (a) a description of the persons who will have access to personal data of the participant/volunteer including medical records and biological samples
- (b) a description of provisions to ensure the confidentiality and security of personal information concerning participants/volunteers
- (c) the extent to which the information will be anonymised
- (d) how samples/data will be obtained, and the purposes for which they will be used
- (e) how long samples/data will be kept
- (f) to which countries (if any) the samples/data will be sent

Both REC members and investigators should be aware of the provisions of the Data Protection Acts 1988 and 2003 and their obligations as set out in those Acts.

### **Informed consent process**

- (a) description of the procedures for obtaining informed consent, including the identification of those responsible for obtaining consent and the time frame in which it will occur
- (b) the adequacy, comprehensiveness and understandability of written and oral information given to the participants/volunteers, their relatives/guardians and, if necessary, their legal guardians
- (c) the content and wording of the informed consent form and, when applicable, the provisions made for participants incapable of giving consent personally
- (d) clear justification for the intention to include participants/volunteers who cannot consent and a full account of the arrangements for obtaining consent or authorisation for the participation of such individuals
- (e) description of the procedures for disclosure, if appropriate, of relevant information to participants/volunteers which may become available during the study

### **Community considerations**

- (a) the impact and relevance of the research on the local community and on the concerned communities from which the participants/volunteers are drawn
- (b) a description of procedures to consult with the concerned communities during the course of designing the research
- (c) the extent to which the research contributes to e.g. the enhancement of local healthcare, research and the ability to respond to public health needs
- (d) a description of the availability and affordability of any successful study product to the concerned communities following the research
- (e) the manner in which the results of the research will be made available to participants/volunteers and the concerned communities

## **5.3 Expedited Review**

Where a REC wishes to incorporate expedited review into its standard operating procedures the following specifications should be taken into account:

- (a) the research should present minimal risk to participants/volunteers e.g. risks related to invasion of privacy and/or breach of confidentiality

- (b) expedited review should be undertaken by the chairperson of the REC or by one or more experienced reviewers i.e. REC members designated by the chairperson
- (c) reviewers may not disapprove research using expedited review. Research may only be disapproved in accordance with non-expedited operational procedures
- (d) each REC which uses expedited review must adopt a method for keeping all members informed of research proposals which have been approved under this procedure

## 5.4 Decision-making

A REC should ensure that all supporting documentation for an application is complete before coming to a decision on a research proposal. A REC should comply with a pre-defined method for arriving at a decision. It is recommended that REC use the consensus model where the process of discussion and debate will lead to a decision, rather than a formal vote-casting process. Under the consensus model, the proposal will be approved when all members present are willing to allow the proposal to proceed. In cases in which consensus seems unlikely, the chairperson may call for a vote with a two-thirds majority required for approval. Dissenting members should be afforded the opportunity to append an opinion to the REC decision.

The REC should accommodate reasonable requests from investigators to participate in discussions about their proposal, but may not be present when the REC is making its decision.

It is desirable to adopt a consistent approach to granting or declining approval of a proposal. It is recommended that the following terminology be used in communicating the decision of the REC to an applicant:

- i. **Approved**, the applicant may conduct the research as outlined in the research proposal submitted to the REC
- ii. **Provisionally approved**, subject to recommended revisions to the proposal or answers to questions posed to the applicant. The revisions and/or answers must be resubmitted to the REC before receiving final approval. No research may be conducted prior to receiving final approval.
- iii. **Approval declined** detailed reasons for declining approval should be forwarded to the applicant, with or without an invitation to resubmit a substantially altered proposal for reconsideration.

The REC decision should be communicated to the applicant in writing within two weeks of the meeting at which the decision was taken. The chairperson should sign and date all such communications. The decision is to include, but is not limited to the following:

- (a) project identification number and/or date of the proposal that the decision is based on
- (b) exact title of proposal reviewed
- (c) name and title of applicant
- (d) name of REC taking the decision
- (e) date and place of the decision
- (f) chairperson and list of members present when decision was taken
- (g) clear statement of the decision taken

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- (h) terms and conditions, if any, of approval of proposal, with clearly defined reasons for such terms and conditions
  - (i) clearly stated reasons if approval has been declined
  - (j) whether approval was by expedited review

## Section 6 : Procedures for monitoring ongoing research

REC should establish a review procedure for following the progress of all studies for which approval has been granted. The review procedure should be specified in the standard operating procedure and should be clearly communicated to investigators.

### 6.1 Status report from investigators

On-going research should be subject to continuing ethics review. The frequency of such review should reflect the degree of risk to participants in the research project. As a minimum the REC should require an annual report from investigators on matters including:

- (a) progress to date or outcome in the case of a completed project
- (b) a statement of compliance with the approved proposal and/or amendments to the proposal
- (c) a description of measures taken to maintain and secure personal information/records pertaining to the research

### 6.2 Amendments

Any significant alteration to a previously approved proposal must receive prior approval from the REC before implementation. Significant alterations include changes to:

- (a) personnel (including where work has been subcontracted to another investigator) any changes to named researchers responsible for the conduct of the research; any change to the personnel involved in obtaining informed consent or having access to personal information about research participants/volunteers
- (b) method
- (c) design of the study
- (d) duration of the study
- (e) informed consent procedures
- (f) patient information leaflets
- (g) method of recruitment

Under the Clinical Trials on Medicinal Products for Human Use Regulations 2004, the REC must, within a period of 35 days from the day of receipt of a valid notice of an amendment, furnish the applicant with an opinion.

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### 6.3 Adverse Event

As a condition of approval of the research proposal the REC should require investigators to immediately report any serious or unexpected adverse events on participants or unforeseen events that might affect the benefits/risks ratio of the proposal.

A serious adverse event is defined as any untoward medical occurrence that:

- (a) results in death
- (b) is life threatening
- (c) requires in-patient hospitalisation or prolongation of existing hospitalisation
- (d) results in persistent or significant disability/incapacity
- (e) results in a congenital anomaly/birth defect

An unexpected event is an adverse reaction, the nature and severity of which is not consistent with the applicable product information.

Investigators may take urgent safety measures to eliminate immediate jeopardy to the research participants/volunteers prior to approval by the REC. However, investigators should provide the REC with a written report of any action taken at the earliest possible opportunity. The REC should review any new material and decide whether there are sufficient grounds for changing its initial decision to grant approval to the proposal.

*Under the Clinical Trials on Medicinal Products for Human Use Regulations 2004, a written report of any urgent safety measures taken should be submitted to the REC no later than three days from the date the measures were taken.*

### 6.4 Suspension or Termination of a Project

In the case of a premature suspension/termination of a study, the REC should require the investigator to inform the REC of the reasons for premature suspension/termination. This should be accompanied by a summary of the results obtained in the study up to the point of suspension/termination. The REC should require investigators to notify the committee once a study has been completed. The REC should receive a final study report, summarising the main findings.



*Under the Clinical Trials on Medicinal Products for Human Use Regulations 2004, the REC must be provided with a detailed written explanation of the reasons for suspension or premature termination of a clinical trial within 15 days of the trial being halted. The REC must be provided with a written declaration of the end of the trial within 90 days. End of the trial is defined as the date of the last visit of the last patient undergoing the trial. Suspension, termination or end of trial notification to the REC should be done using the Annex 3 form of the Community “Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial” (ENTR/CT 1). The REC must receive within one year of the end of the trial a summary of the clinical trial report. The format of this summary should comply as closely as possible with Annex 1 of the Community guideline on the Structure and Content of Clinical Study Reports (CPMP/ICH/137/95).*

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## Section 7 : Documentation & archiving

All documentation and communications of a REC should be dated, filed and archived according to provisions set out in the standard operating procedures. Documents must be stored in a secure place where there is adequate protection against fire. A statement is required in the standard operating procedures defining the access and retrieval procedures for documents, including details of who is authorised to access and/or retrieve REC documents.

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

- (a) written standard operating procedure
- (b) annual reports
- (c) curriculum vitae of each REC member
- (d) record of all income and expenses of the REC, including expenses paid to REC members and co-optees
- (e) guidelines on application procedures
- (f) agendas of REC meetings
- (g) minutes of REC meetings
- (h) copies of all materials submitted by applicants
- (i) correspondence by the REC concerning applicants, decisions and follow-up
- (j) copies of decisions and any advice and/or requirements issued to applicants
- (k) all written documentation received during follow-up
- (l) notification of completion or premature suspension/termination of studies
- (m) final study reports

Documents should be kept for a minimum of three years following notification of completion or premature suspension/termination of a study.

## Section 8 : Research ethics committee annual report

The REC should produce an annual report containing information relevant to its procedures including, but not limited to:

- (a) membership/membership changes
- (b) number and dates of meetings held
- (c) attendance of members; confirmation of participation by required categories of members
- (d) substantive changes to the standard operating procedures
- (e) list of training undertaken by members
- (f) a list of proposals considered, the decision reached on each
- (g) time taken from acceptance of application to final decision on each proposal
- (h) list of projects completed or terminated during the year

Annual reports are public documents and should be available upon request.

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## Section 9 : Multi-centre studies

Multi-centre studies may include research conducted at more than one institution or organisation, in one more countries, either by the same or different investigators or research conducted jointly by investigators working with different institutions or organisations. RECs should require investigators to indicate on application forms if a study is being or has been reviewed by another REC and if so, the identity and decision of the REC.

In order to facilitate prompt and efficient review of multi-centre studies:

- (a) An investigator may wish to distinguish between core elements of the research that cannot be altered without invalidating the pooling of research data and those elements which can be altered to comply with local requirements
- (b) RECs may wish to communicate with, give or receive advice from other RECs reviewing the proposal
- (c) RECs may wish to accept a scientific assessment of the proposal from another REC
- (d) RECs may agree to accept the conclusions of a single review committee

Note to item 9(c) above: A common scientific assessment could be produced by qualified members of a number of RECs involved or by one REC which has accepted the role.

Note to item 9(d) above: A single committee could review the scientific and ethical aspects of a proposal. Individual committees could verify the practicability of the proposal in the institution/ organisation and that the proposal conforms to the ethos of the institution/organisation in which the research will be carried out.

*Under the Clinical Trials on Medicinal Products for Human Use Regulations 2004 in the case of multi-centre clinical trials, either limited to sites in Ireland, or to sites located in more than one EU member state, a single ethics committee opinion must be given by a recognised ethics committee and this opinion must prevail at all centres where the trial is to be conducted.*

## Supporting Documents

CIOMS (Council for International Organisations of Medical Sciences). *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (1993;2002).

CIOMS (Council for International Organisations of Medical Sciences). *International Guidelines for Ethical Review of Epidemiological Studies* (1991).

Council of Europe. *Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine* (1997).

Department of Health & Children. *Clinical Trials on Medicinal Products for Human Use Regulations* (2004).

European Forum for Good Clinical Practice. *Guidelines and Recommendations for European Ethics Committees* (1995; 1997)

Health Research Board. *Genetic Research and Human Biological Samples: The Legal and Ethical Considerations* (2002)

International Conference on Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH). *Note for Guidance on Good Clinical Practice* (1996).

Irish College of General Practitioners. *Ethical questions to be considered by a research ethics committee when approving clinical trials which involve genetic testing* (2003).

Medical Research Council of Canada. *Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans* (1998).

Ministry of Health, New Zealand. *Operational Standard for Ethics Committees* (2001).

National Health & Medical Research Council. *Commentary on the National Statement on Ethical Conduct in Research involving Humans* (2001).

Nuremberg Code. *Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10, Vol. 2, pp. 181-182.* (1947).

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Report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *Belmont report: ethical principles and guidelines for the protection of human subjects of research* (1979)

UNESCO (United Nations Educational, Scientific, Cultural Organization. *Universal Declaration on the Human Genome and Human Rights* (1997).

World Health Organisation. *Draft Operational Guidelines for Ethics Committees Reviewing Biomedical Research* (2000).

World Medical Association. *Declaration of Helsinki: Recommendations Guiding Physicians in Biomedical Research Involving Subjects* (1964; 1975; 1983; 1989; 1996, 2000)

## Working Group on Research Ethics Committees

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Dept. of Public Health Medicine and Epidemiology, University College Dublin

**Dr. Margaret Fitzgerald** *Vice-Chairperson*

Dept. of Public Health, Eastern Regional Health Authority

**Mr. Dermot Gleeson**

Senior Counsel

**Mr. Kenneth Kearon**

Irish School of Ecumenics

**Mr. Dan Lynch**

Secretary to the Research Ethics Committee of St. James's Hospital and the Federated Dublin Voluntary Hospitals

**Professor Anne Scott**

School of Nursing, Dublin City University

**Dr. Siobhán O'Sullivan**

Irish Council for Bioethics

### Terms of reference

1. To review in depth, the existing practices of Ethics Committees in the Republic of Ireland, with particular reference to Research Ethics Committees.
2. To identify best practice in the area internationally and across the island of Ireland.
3. To produce guidance on the composition and operation of Ethics Committees and to suggest a national structure for such organisations in the Republic of Ireland.
4. To report to Council on all aspects of the deliberations and conclusions of the working group on Ethics Committees.

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# The Irish Council for Bioethics

## Comhairle Bitheitice na hÉireann

**Mr Dermot Gleeson SC, MRIA Chairperson**

**Professor Peter Whittaker** (Vice Chair) Institute of Environment, Philosophy and Public Policy at Lancaster University

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**Mr Matt Dempsey**, Irish Farmers' Journal

**Dr Dolores Dooley**, Department of Philosophy, National University of Ireland, Cork

**Dr Margaret Fitzgerald**, Department of Public Health, Eastern Regional Health Authority

**Dr Patrick Flanagan**, formerly of Environmental Protection Agency

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**Mr Asim Sheikh**, BL, Division of Legal Medicine, University College Dublin

**Professor Seán Strain**, School of Biomedical Sciences, University of Ulster

### Secretariat

Dr Siobhán O'Sullivan, Scientific Director

Mr Pauric Dempsey

Ms Emily de Grae

### Terms of Reference

1. To identify and interpret the ethical questions raised by biological and medical research in order to respond to and anticipate questions of substantive concern.
2. To investigate and report on such questions in the interests of promoting public understanding informed discussion and education.
3. In the light of the outcome of its work, to stimulate discussion through conferences, workshops, lectures, published reports and, where appropriate, suggest guidelines.