In the UK, all proposals for research involving human subjects must be approved by a Research Ethics Committee (REC). The Department of Health requires that a National Health Service REC must be consulted about any research proposal involving NHS patients (i.e. subjects recruited by virtue of their past or present treatment by the NHS), including those treated under contracts with private sector providers, fetal material and IVF involving NHS patients, the recently dead in NHS premises, and access to the records of past or present NHS patients. It is common for research projects involving human subjects to be referred for approval by an NHS REC even if there is no NHS connection, but there are other RECs, for example in universities and research institutions.

Projects that are carried out by more than four UK centres are scrutinized by Multicentre Research Ethics Committees (MREC). One MREC has been set up in Scotland, one in Wales and one in each of the eight English health service regions. The protocol for the proposed research must be sent to the MREC in which the principal UK researcher works and a standard application form must be completed. If the application (possibly after revision) is approved, documentation is provided which must be sent to the Local Research Ethics Committee (LREC) in each centre in which the research is to be conducted. The LREC must then consider whether or not the subject information sheet is intelligible in that locality (it may need translating into other languages) and whether the proposed local researcher or group is suitable to undertake the study. Reasons for rejecting a local researcher might be: lack of suitable expertise; lack of facilities, including adequate resuscitation equipment for dealing with possible adverse effects; a bad ‘track-record’ of projects started and not completed; or it might be known that the subjects required for the project were being asked to participate in an unreasonable number of studies already. It should be appreciated that RECs do not have the authority to allow protocols to be implemented. They advise health authorities (or in practice NHS Trusts) that a study is ethically acceptable. It is for the authority to allow the study to proceed. However, health authorities are instructed that they must not allow any research which has not been found to be ethical by an REC.

Research in four or fewer UK centres must be approved by the LREC in each locality in which the research is proposed to take place. The Health Service Guidance document which formalized the establishment of LREC required that an Ethics Committee be set up by each health authority to advise about the ethical acceptability of research which is proposed to take place in its hospitals or other premises. The term ‘health authority’ is now sometimes interpreted as a purchasing authority and sometimes as a hospital trust. There are approximately 250 LREC in the UK. It is suggested that it would be desirable to reduce the number (probably to approximately 100) in order to introduce more uniformity in practice between LREC and more efficiency in terms of the time taken to review protocols.

Other countries have different administrative arrangements, but the need for ethical review of research proposals is widely accepted and reputable journals will not accept reports of research which has not received written ethical approval.

The principal function of an REC is to protect human subjects from unethical research. Recommendations to guide physicians in biomedical research involving human subjects have been formulated in the World Medical Association ‘Declaration of Helsinki’ adopted in 1964. It has subsequently been revised several times; the most recent edition was published in 1996. Sponsors of research frequently state in the protocol that the research will be conducted in accordance with the terms of the Declaration. Of particular concern is the matter of informed consent. The Nuremberg Code drawn up after the War Trials in 1949 states: ‘The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted, all inconveniences and hazards reasonably to be expected, and the effects upon his health or person which may possibly come from his participation in the experiment’.

This seminal document still provides a useful statement of the conditions necessary for consent in the majority of research studies in patients, although it did not envisage research in groups whose ability to give consent is impaired because they are children or are affected by illness or handicap. Issues of consent or assent in such groups are considered in publications by the Royal College of Physicians.

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of his relatives or general practitioner before signing the consent form.

The patient information sheet must include the title of the research project, perhaps paraphrased but not so as to distort the meaning, a clear statement that the project is research and that participation is voluntary, that refusal will not effect present or future treatment or the attitude of staff and that the subject may withdraw at any time and without giving reasons.

Possible hazards to the subject and any discomfort and distress likely to be caused must be described. These may be put in perspective but not minimized. For example, a drug for the treatment of irritable bowel syndrome caused small bowel cancer in mice but only when doses far greater than the clinically useful range had been given. The effect had not been observed in other species. The REC realized that provision of this information to the research subjects might seriously affect recruitment to the study, but after careful consideration it was decided that this information had to be provided, but the industrial doses and the absence of the effect in any other species were emphasized.

The discomfort and distress likely to be caused must be assessed and described to the subject. They must not be unreasonable or disproportionate to the potential value of the research. For example, a relatively high risk is acceptable in a study of a drug which may aid patients with inoperable pancreatic cancer, but the risk in an investigation of a treatment for dandruff must be small to vanishing. No one can consent to serious injury to himself or anyone else.

Expected benefits should be spelt out, and possible benefits to future patients should be distinguished from benefit to the research subject. If a placebo is used it must be explained that the patient may receive a treatment of no known benefit. Placebos may be used as comparators only in studies of conditions for which there is no known effective treatment with which the trial drug could be compared.

Inducements to recruitment such as money or the promise of special attention or facilities are undesirable, but it is recognized that it may be idealistic to rely on altruism to induce subjects to offer themselves for research which may not benefit them. It is probably inevitable that some small inducement may have to be offered, but not so much as would induce them to submit to a risk they would not otherwise take. Reasonable expenses may be paid, or compensation for inconvenience in healthy volunteers.

Ethics Committees have to be convinced of the scientific validity of a study. Badly planned, poorly designed research that causes inconvenience to subjects and may carry risk, without producing useful or valid results, is unethical. REC's often have an educational function in guiding inexperienced investigators in the formulation of a scientifically valid protocol. Ethics Committees subject protocols to rigorous statistical review. Studies must possess adequate power to confirm or reject the hypothesis under investigation. For the vast majority of researchers, the advice of a professional statistician in the preparation of a research protocol is an essential prerequisite for its ethical approval.

The ‘down side’ of ethical review of research is that it takes time. Researchers and their sponsors are frequently inconvenienced by what may seem to be, or may in fact be, unreasonable delay caused by the need to obtain ethical approval. To delay necessary research without good cause is itself unethical. Considerable pressure is being applied to compel RECs to review protocols within rigid time constraints. Desirable as this may be, thorough review of the ethics of research protocols must not be sacrificed in the interests of industrial economics and ‘timeliness’.

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