

Promoting and facilitating ethical research

John Saunders and Janet Wisely

PROMOTING ETHICAL RESEARCH

Is medical research a moral obligation or an option? The relief of suffering is medicine's noble goal and none would dispute its value. Research is the key to progress in achieving that ideal, the means to that desirable end. Of course, not everything that can be done to achieve that ideal should be done: there are other pressing needs and other ways to improve the human condition. The philosopher Hans Jonas memorably wrote:

Let us not forget that progress is an optional goal, not an unconditional commitment, and that its tempo in particular, compulsive as it may become, has nothing sacred about it. Let us also remember that a slower progress in the conquest of disease would not threaten society, grievous as it is to those who have to deplore that their particular disease be not conquered, but that society would indeed be threatened by the erosion of those moral values whose loss, possibly caused by too ruthless a pursuit of scientific progress, would make its most dazzling triumphs not worth having.¹

Jonas reminds us that the desire to pursue medical research must not come at the cost of moral values. Ethical medical research is an obligation, but we need to understand the implications of that word, 'ethical', both in the immediate sense of what is planned and in the wider context of society's needs.

These reflections are the background to the routine work of the research ethics committee (REC), a body of volunteers dedicated to the ethical review of research proposals. When reconsidering the REC's work in the course of revising its *Guidelines*, it was thought important that the Royal College of Physicians (RCP) should make its recommendations from the perspective of a firm belief in the desirability of ethical research – the pursuit of ethical research as an obligation, not merely as an option.

The story of unregulated research remains instructive.² Even after the Doctors' Trials, it appeared that many investigators in Britain and the USA did not see the recommendations as applying to them. In the UK, it was the RCP's 1967 Rosenheim Report³ that brought RECs into existence. The report was widely circulated by the then Department of Health and Social Security (HM(68)33) for action. The RCP made further recommendations in 1973,⁴ leading to another circular (HSC(IS)153) in which the

Secretary of State accepted the RCP proposals and asked:

Area Health Authorities and Boards of Governors to review...the composition of ethical committees and to arrange for any changes which may be needed to put these recommendations into effect.

By 1984 it was clear that further guidance was needed and the first *Guidelines on the practice of ethics committees in medical research* were published. This modest document of 25 pages was prepared by Desmond Laurence, an eminent pharmacologist, and was an obvious success. A second expanded edition was published in 1990 and a third in 1996.⁵ The *Guidelines* were highly influential. They were widely quoted, used by large numbers of those involved in the ethical review of research and sold more copies than almost any other RCP publication.

The late 1990s saw a series of developments that led some to question the value of such guidance. By the mid-1990s there seemed to be an excess of documents from a variety of research bodies, international organisations, royal colleges and specialist societies, all offering advice on ethical review. The organisational structure itself became subject to directives from the Department of Health, most notably those establishing local RECs,⁶ to be followed by the creation of Multi-centre Research Ethics Committees.⁷ The establishment of a Central Office for RECs (COREC) in 2000 then led to the publication of Governance Arrangements and Standard Operating Procedures. Even more recently, the Medicines for Human Use (Clinical Trials) Regulations of 2004 translated the EC Clinical Trials Directive of 2001 into UK law.⁸ For the first time in the UK, ethics committees were established on a legal basis. A UK Ethics Committee Authority (UKECA) was established as a

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legal entity, consisting of the health ministers of the four UK constituent countries. It was in the light of these developments that the RCP's Ethical Issues in Medicine Committee made its decision to re-write the *Guidelines*. Firstly, it was plain that there was still – astonishingly – a demand for the badly outdated 1996 document which was still quoted by authoritative bodies such as the General Medicine Council. Secondly, the extent of organisational change, the volume of relevant new law, such as the EC Directive, the Human Tissue Act 2004 and the Mental Capacity Act 2005, as well as the widening international interest, suggested a need for a concise summary to guide practice. Research ethics committee members lacked an accessible single-volume guide to their role and many in the research community were puzzled by issues raised by RECs. Thirdly, it was thought that less emphasis on organisational matters and more on highlighting the variety of ethical issues themselves would be helpful, especially coming from a professional body such as the RCP. Fourthly, there was a belief that a body such as the RCP should recommend standards from its standpoint of a continuing and firm belief in advancing medical science ethically.

Increasing complexity led to the formation of a working group with half its membership drawn from outside the RCP and with good lay representation. The result was circulated to a selection of interested experts before it was finalised. No one would pretend that the outcome will be free of controversy – indeed there were some strong disagreements even within the working group – but it is hoped that the *Guidelines*, above all, will be useful. For this reason, we have preserved the accessible layout of the third edition and the index remains a key part. The new *Guidelines* are extensively referenced with a comprehensive list of further authoritative documentation and summary information on drug development, audit, REC application and terminology in a series of appendices.

The consideration of the ethics of research requires some understanding of ethics. It also requires some understanding of research. A section of the *Guidelines* has therefore attempted to offer a simple outline of the varieties of research, a need that may not be recognised by many medical or other professional readers and seems to be assumed in almost all other guidance. A further section describes the legal basis of ethical review, along with a brief summary of some key items of legislation. Those fundamentals are followed by guidance on ethics, setting out a simplified scheme of equipoise/uncertainty as the first key principle, followed by the secondary one of consent. It is easily forgotten that in no case is informed consent sufficient for ethical clinical research and in many cases it is not even necessary. That rather bald sentence does not fly in the face of current concerns or recent abuses, but highlights the need for other requirements to make research ethical.⁹ Consideration of principles and their application leads to issues such as sensory impairments, language, capacity, cluster trials and so on. Research using placebos, research on tissues and on records follows. Perhaps the next two sections are the most novel. One covers research in special groups of participants such as children, prisoners, refugees, older people and the terminally ill. The next is about special classes of research: the ethical considerations of research on medical devices, practical procedures (such as surgery), genetics, the internet and complementary

medicine. Finally, the *Guidelines* cover the contentious area of payment for investigators, institutions and participants. This has been an ambitious and comprehensive project. The aim has been to create a tool that can be used by all those reviewing research around the REC table and guide those who do research or wish to understand its ethical practice. Alongside the governance arrangements for RECs, now undergoing revision, and the standard operating procedures, the *Guidelines* should be seen as a key document.

We believe they represent good value from the training budget to be supplied to REC members and researchers. Coming shortly after the launch of the new National Research Ethics Service (NRES) that replaces COREC, we are grateful to Sir John Lilleyman – who as medical director of the National Patient Safety Agency brought NRES to its launch – for his support in the foreword. Members of the College's Ethical Issues in Medicine Committee and of the Working Party hope this will be a significant contribution to encouraging efficient, high-quality ethical review throughout the UK and also of interest to colleagues in Europe. The result, we hope, will be the furthering of human welfare and of the understanding that the best medical science offers.

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FACILITATING ETHICAL RESEARCH

The role of any research ethics committee (REC) in the protection of the rights, safety, dignity and well-being of actual and potential research participants is well established and embedded within the principles of the Declaration of Helsinki,¹ Department of Health (DH) policy² and statute.^{3,4} Some challenge that the actions of the present day committees may be harmful rather than beneficial, interpreting protection as an infringement of individual choice and protesting at what they see as bureaucratic processes and the appropriateness of these for some less ethically challenging studies that are presented to ethics committees. Yet few would disagree that in striving to improve clinical care the end may not always justify the means. Ethics committees are in the unique position of being able to step back and consider the research proposal from the perspective of the research participant. This independent view is achieved in the UK by having a volunteer-based service, where membership is drawn from the clinical professions and lay members and where the lay member view must be considered for the opinion to be valid.

The challenge for the National Research Ethics Service (NRES) is to provide a robust and efficient service that protects the research participants but that is also able to promote and facilitate ethical research. Much has been done to improve the operational process for ethical review. Within the UK there is now an operational framework delivering one decision for the whole of the UK, removing the previous requirement for duplicate application and review. There are defined timelines against which committees are held to account, and correspondence with applicants is managed in an efficient manner. This operational framework is described in published standard operating procedures and the NRES quality assurance framework accredits committees against these standards. Delivery is demonstrated in published management information.⁵ Significant improvements to the operation of RECs are now being acknowledged.^{6–8}

The remit of the NHS ethics committees as described in DH policy encompasses some studies that would seem to be distant from those envisaged when the Declaration of Helsinki was agreed, and also from the described remit of RECs outside the UK. This presents a further challenge for NRES as it works towards greater consistency of the interpretation of what is research and therefore requires review.⁹ The service is, however, still left with the review of studies for which the ethical dimensions are minimal. For those submitting these low-risk studies even the more efficient process that has evolved may seem unwieldy and unjustifiable. Two things are therefore needed. The first is a revision of DH guidance to define more tightly the remit of RECs. The second is the need to develop a more

proportionate process for review of less ethically challenging studies that are nevertheless research and so therefore require independent review. In pursuit of these two aims, the DH will shortly issue revised guidance for consultation and it is expected that this will go some way to redefining the remit of ethics committees. NRES is currently developing an operational process and ethical framework for fast track review of low-risk studies.

The other major challenge that NRES faces is tackling inherent inconsistency of decision making between committees. The requirements in terms of quorum and structure can be prescribed but the decision reached will, rightly, be that of the diverse membership around the table. It is therefore a fine balancing act to maintain the independence of opinion while ensuring some degree of consistency within the REC service. NRES is approaching this challenge by continuing to invest in training for REC members and is establishing a quality assurance agenda that should improve the consistency of review through a number of initiatives including appraisal schemes for REC members and ethical debate exercises.

Finally, there is much potential for greater efficiency within the service if NRES is able to support applicants in understanding the expectation of RECs and in the development of ethically robust research protocols. We therefore welcome the publication of these *Guidelines* which provide an accessible and concise summary of the issues that the REC will consider as part of its review. They will become a frequently referenced source of advice and will make a significant contribution to the continued improvement to the NRES and the encouragement of ethical research.

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