RESEARCH REPORT 13

Ethics and Health Care

The role of research ethics committees in the United Kingdom

Julia Neuberger

King's Fund Institute

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Julia Neuberger was a visiting fellow at the King's Fund Institute from 1989 to 1991. She serves on the Royal College of Nursing's Ethics Advisory Committee, the Human Fertilisation and Embryology Authority, and St. George's Hospital Medical School Council. She chaired the Patients Association from 1988 to 1991, and was recently a Harkness Fellow and a visiting fellow at Harvard Medical School, looking at ethics in the healthcare and other professions.

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Summary

This report examines the work of research ethics committees (RECs) in the United Kingdom. RECs examine proposals for research on human subjects largely within the NHS. Research on human subjects throws up a variety of ethical problems. The role of RECs is essentially that of a public watchdog: to try to protect subjects from harm, to ensure that they are adequately informed, to see that valid consent is given, and that no undue pressure to participate is exerted upon subjects, and to reassure the public that this is so.

The research was carried out by a postal survey of members of RECs in England and Wales, as well as visits to 25 RECs, observing them in action, and interviewing their chairmen and members. The report describes the present position, examines the history of ethical review in the UK, and compares practice with current guidelines from the Royal College of Physicians and the Department of Health.

Membership
Membership of RECs varied in size considerably, and was often larger than the suggested maximum of 12. It was also medically dominated. Many RECs fell short on the number of lay members required and many more failed to have either a pharmacist or a clinical pharmacologist, despite the fact that the bulk of the trials they were vetting were drug studies. There were often insufficient nurse members. Membership tended to be for too long a period, with members who were untrained, largely uninformed of recent thinking about ethical review, and too isolated from members of other RECs.

Chairmen of RECs raised large numbers of issues. A growing number of REC chairmen are now lay members, reflecting a sense that the public watchdog role is being seen as increasingly important. Lay chairmen were effective in ensuring that other non-scientific members understood the research proposed, and lay members in general were particularly concerned that information be made available research subjects. But there was no clear difference in attitude to information and consent issues between lay and medically qualified chairmen.

RECs were also chronically understaffed, leaving their chairmen with an enormous task to perform. Paperwork was considerable, but organisation was often chaotic, making cross-referral impossible. There is room for considerable improvement at a constitutional level, as well as in terms of organisation.

The ethical debate
Ethical debate centred around valid consent, because the major concern of REC members was that research subjects should be properly informed and be able to give valid consent, insofar as this was possible. They debated the issues relating to research on children without coming to an agreed conclusion about what was permissible and what not. They agonised about undue pressure being exerted upon research subjects, and were particularly concerned about the difficulty of explaining, and gaining valid consent for, randomised controlled trials.

There was clearly room for more debate on principles about consent, about research upon children, the mentally disordered, the frail and those in intensive care, as well as about local requirements of populations, be they specific religious and cultural concerns or language issues. There was also clearly room for major improvement in procedures for consent, with consent forms and information sheets and a consent checklist for investigators, to use while conducting interviews.

Policy issues
There were major concerns about the quality of research, and a confusion as to whether RECs are in fact research committees or research ethics committees. There are strong arguments for DHAs and other authorities – where there is a considerable amount of research involving human subjects taking place – to establish a separate research committee to vet the research for quality and the likelihood of its achieving its stated objectives.

Multicentre trials posed another problem, with RECs processing applications in a variety of different ways. There is probably a role for some form of national committee to vet such proposals in the future, leaving local RECs with the final approval role only.

A further policy issue is that of the insuring of research. Much research conducted within academic departments – other than that sponsored by the pharmaceutical industry which normally provides full indemnification – is uninsured. As a result, research subjects are unprotected. The question is whether it is legitimate to conduct this

research on human subjects if they have not been informed that it is uninsured, or whether all such research should stop. The DoH has made it clear that NHS institutions are not empowered to pre-indemnify on a general basis. This would leave research subjects with no alternative but to sue for negligence, a lengthy and often distressing procedure with an uncertain outcome. This was a major issue in several RECs, and led on to concerns about mishaps as a result of the research design, rather than as a result of negligence.

Conclusions

There is a large number of recommendations to be made which would strengthen RECs in their work, provide their members with training and support, ensure there is greater standardisation of practice, and give research subjects greater protection and further information. These proposals are listed in full at the end of the report. But over and above such recommendations is the clear recognition that there should be legislation on this subject. It is clear that RECs have not hitherto followed guidelines particularly closely. It is also clear that they lack power, being advisory to DHAs and other appointing authorities, and have no policing or monitoring role. However hard they work, however thorough their examination of research protocols on a case-by-case basis, however much better constituted and trained, and however well supported they may be administratively, unless they have the power to ensure that all research is submitted to them and to stop research that they regard as unethical, they will not be taken sufficiently seriously. For these reasons and others, this report, whilst making detailed recommendations for improvements to present practice, recommends that there should be proper legislation.

Introduction

1

Ethics and therapeutic trials

Medical research has always raised major moral questions, be they about the use of animals, or about cadavers and their decent burial, or about testing new procedures on human beings, often patients, for the furtherance of medical knowledge, rather than for the individual's personal and particular gain. Until the 1960s, despite the universal horror at the Nazi doctors' experiments and the codes emerging in the wake of the Nuremberg trials, there was little public involvement in decision-making about medical research. But the mood began to shift, and since the mid-1960s there have been committees all over the United Kingdom, set up in a somewhat haphazard way, to examine the ethics of medical research on a case-by-case basis.

To a large extent these were prompted by American influences. In 1966 Henry Beecher, Professor of Research in Anaesthesia at the Harvard Medical School, published 'Ethics and clinical research', an article that was to have far-reaching effects. He drew attention to twenty-two reports of unethical clinical research in which patients had been put at considerable risk. His article strengthened the US Surgeon-General's hand in his ruling requiring institutions that accepted federal funds to establish an independent review of research projects before they began.

Britain was quick to follow. The Royal College of Physicians set up a committee on the supervision of the ethics of clinical investigations, which in 1967 recommended that every institution where clinical research was undertaken should have a group of doctors to 'satisfy itself of the ethics of a proposed investigation'. In that year, Dr. Maurice Pappworth published his influential *Human Guinea Pigs*. It highlighted some of the dilemmas facing both the researchers and the general public. He proposed the creation of research committees in every region – with at least one lay member – to review the ethics of proposed research. He also suggested that they should be responsible to the General Medical Council by law, a suggestion still not put into effect.

The concerns which gave rise to research ethics committees (RECs) have become stronger over the last twenty-five years with an increasing numbers of clinical trials sponsored by the pharmaceutical companies and a growing demand by the public to be consulted and informed. The Department of Health (DoH) has issued guidelines on three occasions in that period, and the European Community is moving into the area of legislation as well. With new guidelines finally in place, and with increasing pressure upon the committees, the time is ripe for a thorough review of how the system operates and how it could be improved.

The role of the research ethics committees

The public interest issues

The issues the RECs have to address are complex. Many of them can only be described as public interest issues. It is, therefore, no coincidence that at the launch of the new DoH guidelines in August 1991 they were signalled as part of the Citizens' Charter. The committees are charged, for instance, with checking that adequate arrangements for seeking consent from research subjects are in place and that the principle of valid consent is acknowledged. This requires thinking about consent in general terms. Should patients be given full information about all research procedures? Will patients understand risk and benefit? Do the members of the committees themselves understand risk and benefit? Can children give consent? Or can parents or guardians on their behalf?

There are also issues of finance. Payment to healthy volunteers could be considered 'an inducement', and there are doubts over whether it is appropriate to give an inducement to take such risks. Patients, some might argue, should also be paid if the researchers are being paid. Running clinical trials can be a good way of generating income for research funds starved of cash in a time of tight budgetary control, but is it ethical to do so unless the research is worthwhile in its own right?

There are issues about protecting patients from unnecessary research at a time when all students of medicine and nursing are increasingly encouraged to do a research project as part of their training. Sick people should perhaps not be subjected to this. Research can be invasive physically, posing questions about pain, risk and benefit. But it can also be emotionally threatening, with questions which are too personal. Does the expected outcome justify the invasion of privacy? Will it be useful, giving patients or volunteers the sense that they have contributed to the furtherance of human knowledge? Or will it be purely to gain the researcher a qualification, or a publication needed for career advancement and be of little

long-term importance?

Although RECs have frequently been thought to be very small cogs in the NHS machine, these are some of the major public interest issues that arise from their work. Yet medical research does, in fact, throw up large numbers of other public interest issues which these committees do not begin to consider. The way that finances for research are allocated, by whom and for what conditions, for example, as well as the politics and fashions of medical research as a whole. There are issues about gender in the selection of research subjects; about protection for research subjects in case of accident; and about the level of public understanding of the nature of medical research as a whole. Except in very rare instances, these matters are not discussed. It could be argued that it is not appropriate for the committees to do so, yet they, more than any other body in a DHA, know what is going on in research terms. They could take a view as to whether the system of research funding as a whole furthers good and innovative research, whether the local population is sympathetic to the research, and whether there are genuine public concerns that go wider than individual protocols.

At present the committees are largely reactive to individual research protocols, rather than proactive, and rarely demand an account of how the financing of research came about, or how the decision was made to fund one project rather than another. Nor do they play what could be an important educative role within a DHA, discussing the nature of the research that comes before them, and their concerns about it.

The nature of clinical trials

The committees have a variety of objectives, including:

> *...to maintain ethical standards of practice in research, to protect research subjects from harm, to preserve the subjects' rights, and to provide reassurance to the public that this is being done* (RCP, 1990b)

Research protocols for clinical trials of a variety of kinds are the meat of RECs' discussions. By far the majority are those sponsored by the pharmaceutical industry, but there are also significant numbers of student research protocols in teaching authorities, comparative studies of compounds of drugs and other treatments sponsored by major research organisations, and other research carried out in individual departments. Surgical research is marked by its absence, as is nursing research in many DHAs.

Pharmaceutical company sponsored trials, and other drugs trials, are broadly divided into four main categories:

- Phase I studies are early toxicological studies, rarely encountered by a research ethics committee.
- Phase II studies include some 'first use in man' studies, as well as other early studies. They are usually conducted on healthy volunteers but are also occasionally conducted on patient volunteers where the patients are seriously ill and the preparation is very new.
- Phase III studies form by far the majority of the studies seen by RECs. Early safety testing has already been done and a study on a reasonably large scale, usually conducted on a multi-centre basis, is a requirement in order to obtain a product licence from the Medicines Control Agency.
- Phase IV studies are those which require the mass observation of patients using products which are already on the market and where side-effects need to be noted. They are usually conducted by GPs, sponsored by the pharmaceutical companies, on a very large scale. These studies, which are relatively commonplace, are frequently carried out without reference to a REC.

Most trials seen by RECs, particularly drugs trials, are randomised controlled trials, where some participants are taking the new preparation and some a placebo, without the patient or the doctor knowing who is in which group. They are usually conducted in a variety of different centres at the same time, both to allow for regional variations and in order to recruit enough research subjects into the trial.

These trials are usually described, somewhat loosely, as 'therapeutic', on the basis that they might be beneficial to the individual patient if the patient were randomly allocated to the right group. But although they might benefit individual patients, the motives behind the testing of most drugs at the Phase III stage are a mixture of commercial (acquiring a product licence in order to be able to market the drugs) and public good (checking that the drugs are safe for the wider public). These motives should not discount the genuine scientific and professional interest in the development of many drugs, but they do cast the trials in a rather different light from that of a wholly altruistic endeavour.

Amongst the other categories of studies which RECs address are a considerable amount of public health research, epidemiological research and psychological research. Some RECs, though by no means the majority, vet proposals from nurses and other healthcare workers which are less physically invasive than pharmaceutical trials, but often rest on detailed personal questionnaires. Most of this research is described as 'non-

therapeutic' since it is unlikely to benefit the patient concerned directly, although it is designed to benefit the population at large.

The other category of testing most commonly encountered at RECs are tests on healthy volunteers. These range from the very rare 'first use in man', where a drug is given to a human being for the first time after testing on animals, to exposure to certain conditions and then attempted treatments or cures, and to experiments on reactions, or to lengthy testing of the comparative efficacy of certain preparations. Healthy volunteers are paid by the companies or by university departments, and it is a key part of the REC's work to examine both the amounts paid and, in university medical schools, whether any pressure is applied to participants to enter the trial.

The borderlines between therapeutic and non-therapeutic trials, and between research on some categories of patients and on healthy volunteers, are far from clear. Different ethical issues are raised by each category, relating to risks and benefits, payment and information, as well as to the nature of the advantage to the individual as compared with the researcher or the pharmaceutical company. These issues will be addressed in detail later on, but it is significant that RECs spend proportionately more time discussing trials of no benefit to the individual and trials concerning healthy volunteers. Clearly, it is here that they feel their public watchdog role more strongly.

Surveys of Research Ethics Committees

Until recently, the major work on the subject of RECs was by Dr. Richard Nicholson, carried out while he was Deputy Director of the Institute of Medical Ethics in London. It was based largely on research involving children (Nicholson, 1986). Part of his task was to conduct a postal survey of ethics committees in England and Wales.

In 1982-3, when Nicholson conducted his survey, many of the RECs were still hospital or institution based. There were also the ethics committees of the Royal Colleges, two ethics committees which served regions rather than districts, and a number associated with a research institute alone. At that stage, 153 chairmen (88 per cent of respondents) said that it was compulsory for all proposals involving research on human subjects to be submitted to the committee for approval. Amongst those who did not require a submission, a third provided written guidelines to researchers about which types of research should be submitted. A summary of Nicholson's main findings is given in Box 1.

Nicholson's research demonstrates that there was a worrying variation in the practices of RECs, both in the requirements they made of researchers and in the way they were constituted. There was also some difficulty in acquiring the names of the REC chairmen, including one District administrator who refused to give the name on the advice of the members of the REC! Nicholson revealed that nurses played an important role in REC workings and that their presence reduced the percentage of protocols approved unamended. His research concluded that the RECs were unclear about the nature of their task, were variable in their practices, and needed to be more coherent in their approach.

Other more recent surveys of the work of RECs have usually been relatively small and largely conducted by post. Amongst them has been an examination of ethics committees, taking one teaching and one non-teaching district per region, conducted by Claire Gilbert *et al.*, published in the *BMJ* (Gilbert, 1989). Table 1 shows a remarkable variation in the number of members of committees, and the guidelines committee members were given to help them in their work. That survey prompted an editorial in the *BMJ*, warning the profession that it was time to get its house in order in this regard, and that time was not on its side (Lock, 1990). There was also a survey conducted by the joint university and district Southampton Research Ethics Committee in November 1988 (Southampton, 1988) of ethics committees in their region of Wessex. Table 2 illustrates the marked variation in practice, suggesting that little had changed since Nicholson's survey of 1982.

1

INSTITUTE OF MEDICAL ETHICS, 1982-83: MAIN FINDINGS

254 research ethics committees identified.

174 (69%) of research ethics committees returned questionnaire.

Eight (3%) refused to complete questionnaire.

153 (88%) said all proposals for research on human subjects had to be submitted for approval.

21 said not compulsory, but only seven provided written guidance to researchers on the categories of research that should be submitted.

Membership varied from one to 73 members.

49 committees (28%) had 10 or more members.

14 (8%) had no members who are other than doctors or nurses.

9 of those 14 had no nurse.

93 committees (53%) had only one lay member.

1 committee had 7 lay members.

Table 1 Characteristics of 28 RECs, 1989

Characteristics	All Committees	Committees in teaching districts	Committees in non-teaching districts
No. of members	4-22	5-22	4-15
No. of lay members	0-4	1-4	0-2
No. of applications received in 1988	8-400	140-400	8-250
No. of words in their printed guidelines	0-4250	250-4250	0-2500

Source: Gilbert *et al* (1989)

Table 2 Constitution and procedures of RECs in Wessex, 1988

District	Membership	Frequency of meeting	Ethical form
Bath	8 consultants, 2 general practitioners, 1 nurse, 2 health authority members, 1 university representative	Every 2 months	Standard
Basingstoke	3 consultant, 2 general practitioners, 1 chaplain	All done by correspondence	Not standard
East Dorset	5 consultants, 1 general practitioner, 1 nurse, 2 health authority members, 2 clinical tutors	Five times a year	Standard
West Dorset	6 consultants, 1 general practitioner, 1 health authority member, 1 dental representative	Once a year	Not standard
Isle of Wight	3 consultants, 1 general practitioner, 1 pharmacologist	Every 4 months	Not standard
Portsmouth	5 consultants, 1 general practitioner, 1 nurse, 1 health authority member, 1 community health council member	Monthly	Standard
Salisbury	1 consultant, 1 nurse, 1 health authority member, 1 community health council member, 1 chaplain, 1 clinical tutor	Every 6 weeks	Standard
Southampton	5 consultants, 1 junior doctor, 2 general practitioners, 1 nurse, 1 health authority member, 1 community health council member	Monthly	Standard
Swindon	1 consultant, 1 general practitioner, 1 nurse, district general manager, chairman of medical advisory committee, community health council chairman	Every 3 months	Standard
Winchester	4 consultants, 2 general practitioners, 1 senior registrar, 1 chaplain	Two or 3 times a year	Standard

Source: Southampton (1988).

Guidelines for Research Ethics Committees

The RECs are theoretically governed by a series of guidelines, though none can be enforced unless the DHA concerned chooses to do so through its own regulations.

The RCP Guidelines

In January 1990, the Royal College of Physicians published two volumes of guidelines to cover clinical trials, one entitled *Research involving patients*, (RCP 1990a) and the other *Guidelines for Ethics Committees* (1990b). These were tougher than others issued previously. They contained clear and detailed instructions about how research ethics committees ought to work, and who their members ought to be.

The DoH Guidelines

The Department of Health (DoH) Guidelines of August 1991, summarised in Box 2, replaced those

2

DoH GUIDELINES FOR RECs, 1991

The REC's task is to advise any NHS body on the ethics of proposed research projects which will involve human subjects. They are organised by district for convenience reasons, but it is the NHS body, be it DHA, NHS Trust, Family Health Service Authority (FHSA) or Special Health Authority (SHA) which decides whether the project should go ahead.

The REC must be consulted about any project involving NHS patients, fetal material and IVF involving NHS patients, the recently dead in NHS premises, access to records, and use of NHS premises or facilities.

The REC should have eight to 12 members.

They should include

- **hospital medical staff**
- **nursing staff**
- **general practitioners**
- **two or more lay persons**

At least one of the chairman or vice-chairman's posts should be filled by a lay person.

They should serve for three to five years.

They should keep a register of proposals.

Standing orders should be drawn up by the DHA covering working methods and frequency of meetings, and postal and telephone business should be discouraged.

The meetings should be private.

An annual report should be published, with copies made available to all NHS bodies advised, as well as the Community Health Council (CHC).

The REC will need to know:

- **Has the scientific merit been properly assessed?**
- **How will the health of the research subjects be affected?**
- **Are there possible hazards, and, if so, adequate facilities to deal with them?**
- **What degree of discomfort or distress is foreseen?**
- **Is the investigation adequately supervised, and is the supervisor responsible for the project adequately qualified and experienced?**
- **What monetary or other inducements are being offered to the NHS body, doctors, researchers, subjects, or anyone else involved?**
- **Are there proper procedures for obtaining consent from the subjects or where necessary their parents or guardians?**
- **Has an appropriate information sheet for the subjects been prepared?**

Written consent should be required for all research (except where the most trivial of procedures is concerned). For therapeutic research consent should be recorded in the patient's medical records.

Source: **DoH (1991)**

published in 1975. Whilst their tone is tougher than that of previous versions, they lack the detailed discussion of the RCP guidelines. They also differ somewhat on substance. For instance, the DoH requires an annual report, unlike the RCP, whilst the RCP assumes the chairman of the REC will be medically qualified, unlike the DoH. These differences exist despite the fact that there has been considerable consultation between the RCP and the DoH. The DoH guidelines do, however, express much more clearly than hitherto the duty of District Health Authorities (DHAs) to set up the committees with other NHS bodies who might consult them. It is likely that DHAs will be largely guided by the DoH guidelines, whilst the RCP guidelines will be used for further clarification, particularly by the medical profession.

Despite several attempts by those who have researched this field to press for the DoH guidelines to be made statutory, they remain advisory. The United Kingdom appears to be lagging behind other European countries in this respect.

European moves

The European Commission (EC) has already issued guidance on this subject, published in June 1990 and effective from July 1991. It is likely that the Commission will convert the guidelines into a directive in 1992, a move supported by the UK along with several other European states. The directive would govern clinical trials, and deal with a variety of issues relating to fraud as a result of the US Food and Drug Administration (FDA) discovery in 1989 of serious fraud in clinical trials in the United States. It would also monitor trials taking place in more than one country, and would probably suggest a confidential register of trials so that similar standards could be assured throughout the EC.

The original EC guidelines recommended obtaining the opinion of the relevant ethics committee before a trial could take place and insisted that subjects should not be entered into the trial until the committee had issued a favourable opinion. There followed a list of the issues which the ethics committee should consider in forming that opinion, such as the suitability and qualifications of the investigator to carry out the trial, the extent to which subjects and investigators were to be rewarded financially, and the way in which recruitment was to be conducted and consent obtained. The recommendations are similar to the DoH guidelines.

One member state, France, has already legislated on the subject of biomedical research. Consultative committees (which are similar to research ethics committees) have been set up in every region of France. Legislation also exists, though only for pharmaceutical trials, in the Irish

Republic. This followed the death of a healthy volunteer as a result of being involved in more than one trial. The National Drugs Advisory Board in Dublin has a team of inspectors which is empowered to inspect research in progress throughout Ireland. Similarly, in France, medical inspectors and pharmacist inspectors from the Ministry of Health have the power to see that the conditions specified under the French legislation are adhered to (France, 1990).

Other influences

One other series of guidelines which have had some influence on the way RECs function are those originally published by the Voluntary Licensing Authority (VLA) for IVF and other assisted reproduction issues. Although this was not, on the whole, a series of guidelines for RECs, much of the supervision of IVF in its early stages when carried out in NHS premises was undertaken by the existing REC. It then had to conform to the VLA requirements, particularly in the matter of genuine lay members, hitherto often people who had a financial or professional interest in the institution.

Aims and objectives of the project

In 1986 Richard Nicholson argued in *Medical Research with Children* that 'the types of information that can be obtained by the use of a questionnaire are necessarily limited', and lamented the fact that money was not available to conduct a substantial survey in person by interviewing chairmen and members. This report is an attempt to begin to rectify that situation.

The committees are now largely, but not entirely, District Health Authority (DHA) and Scottish Health Board based. There are, however, a considerable number of RECs which are shared by a university and a DHA, whilst Northern Ireland has only university-based RECs. Scotland has had a mixture of systems, and is gradually reducing the number of committees, following a similar pattern to that of England and Wales.

The primary method of research was through a two-year programme of interviewing the members of 28 committees (three of which were sub-committees of the 25 RECs in the sample) as well as observing the committees in action. The sample shown in Box 3 was chosen to represent a good geographical spread, both teaching and non-teaching DHAs, and also some Special Health Authorities (SHAs). In-depth interviews were carried out with all chairmen and some members. In all, there were 96 interviews.

The primary data source was a postal questionnaire sent to 241 RECs in England and Wales in the autumn of 1990, other than those

3

LIST OF COMMITTEES VISITED

SCOTLAND:

Aberdeen

Tayside

Lothian Area (central committee with seven sub-committees)

Lothian Medicine and Oncology Sub-committee

WALES:

Pembroke

South Glamorgan Joint Ethics Committee (with 14 sub-committees

Velindre Hospital (oncology) sub-committee

Medicine Sub-committee

NORTHERN IRELAND:

Queen's University Belfast

University of Ulster

ENGLAND:

Special Health Authorities:

The Maudsley and Bethlem

The Royal Marsden

District Health Authorities:

Camberwell

Cambridge

Cornwall and Isles of Scilly

Durham

East Birmingham

Islington (although the Health Authority is now merged with Bloomsbury, the research ethics committee still exists as a northern branch of the research ethics committee in Bloomsbury)

North Bedfordshire

North Lincolnshire

Redbridge

Salisbury

Southampton (joint with university)

Southmead

Wandsworth

West Lambeth

West Somerset

York

Of these, all the Scottish authorities are in fact teaching authorities, as is South Glamorgan in Wales. Both Northern Ireland committees are in teaching authorities, obviously, as university based, but only Queens has a medical school. Both special health authorities have post-graduate teaching and a high research involvement. Of the district health authorities, five are teaching authorities, and one is not a teaching authority as such, Southmead in Bristol, but is closely involved with the medical school.

which formed the small sample for visiting. The questionnaire covered the numbers of members, their gender and their disciplines. Of the 241, 19 (8 per cent) did not respond and four responded later, informing us that the committees were undergoing major changes and that data could be supplied at a later date.

Issues covered by the questionnaire were also raised at interviews and the responses in the small sample were statistically indistinguishable from these to the questionnaire, confirming that the sample of committees visited formed a reasonable cross-section of the entire population. The geographical coverage of the survey and the interviews was slightly different: the questionnaire was restricted to England and Wales while the interviews included both committees in Northern Ireland and four in Scotland. At the time the questionnaire was sent out, RECs in Scotland were undergoing drastic change and the Scottish Home and Health Department was involved in carrying out a survey itself.

The research focused on two main areas:

- The formal constitution of each committee, the number of members, how they are appointed, the length of their appointment, the mix of members, the appointment and powers of the chairman.
- The way the committees operate in practice.

It was with the interviews that the work became most exciting and, ultimately, most fruitful. For although issues of constitution would seem to be relatively easy and accessible, the composition of the membership and the interaction between members make for a vigorous or less vigorous committee. It is how members view each other, as well as the task in hand, that will at least partially govern the thoroughness with which they tackle their tasks.

It was also possible to find out the specific concerns of REC members by proceeding in this way. Some have major concerns about the finances of the research projects. They worry that clinical research is being increasingly driven by the needs of the pharmaceutical industry (that is to say, by what can get funded) rather than by the potential benefit of specific individual projects. Though their role is not to take an overview, they are charged with examining the financial implications of proposals before them, as far as researchers and institutions are concerned, and worry about whether research that is largely being conducted in order to generate further research funds for the department is strictly ethical.

Others are extremely worried about indemnity. They may be concerned about indemnity of lay members of research ethics committees themselves, or they may worry about the much larger, and much more important, question of whether the research itself is adequately insured. That could be by cover in accordance with the ABPI guidelines (ABPI, 1990) for pharmaceutical industry sponsored research, or by other types of indemnity for non-sponsored studies. This turned out to be one of the major recurrent concerns of many RECs. Still others worry about the role of the ethics committees themselves, and whether they are in fact ethics committees or research committees which assess the value of the research concerned. This has been a fruitful area of discussion, as has been observing the committees in action.

Although having a 'silent observer' at meetings must have been disquieting at first, it became increasingly clear that if the meetings were long enough – and few are under two hours – members gradually forgot the interloper and became involved in heated discussion, if that was their normal practice. It was also possible to observe how the committees used their members from different backgrounds and disciplines in different ways, to see how the role of the chairman was so crucial in these mixed groups of people, and how the chairman's ability to encourage members to voice their concerns was of paramount importance.

There were no overriding regional differences between RECs and remarks in the text should be interpreted as applying to the whole of the UK except where indicated to the contrary. The objectives of the research were to show variation and to illustrate good practice, to point out failures of energy and failures in debate, as well as failures to recognise the prime purpose of RECs, and to demonstrate that there are problems inherent in the task the committees are being asked to address. This leads to some suggested remedies, especially those that came from members of RECs themselves, followed by policy options and a number of recommendations for future action.

2 The Committees and their work

This chapter reviews the membership of the committees, their method of appointment and how they function. It discusses how far current practice conforms with the guidelines established by the Department of Health in 1991, and by the Royal College of Physicians in 1990. It examines how they are set up and their independence from the District Health Authorities. It also looks at how they are serviced and the way that records are kept.

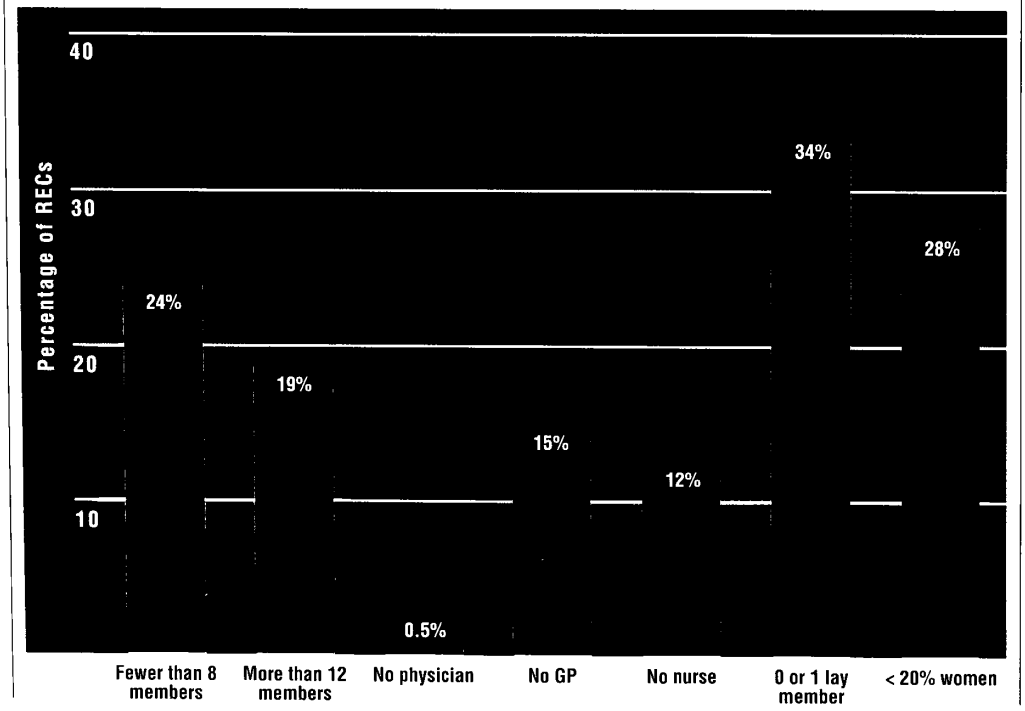
Membership

The purpose of an REC is to consider the ethics of proposed research projects which will involve human subjects and to offer informed and independent advice. The issues involved are important and delicate and are not the exclusive province of any one professional background or discipline. If an REC is to perform its function effectively, and if it is to be seen as authoritative, it must be small enough to act as a single cohesive body and yet contain a broad enough spectrum of expertise and experience to be able to address the full range of issues which come before it.

The Department of Health in its guidelines for RECs, published in August 1991, stipulates that they should have between eight and 12 members, that membership should be drawn from both sexes and from a wide range of age groups, should include hospital medical staff, nursing staff, and general practitioners and two or more lay persons. The RCP guidelines are broadly similar, although they mention scientists as well as hospital doctors working with patients, besides making provisos about the kinds of nurses who should be on the committees, namely those who are 'hands on' in current practice with patients.

Figure 1 shows the extent to which these guidelines are breached. While the majority of committees did conform to the guidelines, a substantial minority fell short in at least one or more respects – by having too many or too few members, or by having no GP member, no nurse member or insufficient lay members. Although the

Figure 1 Breaches of DoH guidelines



guidelines are not specific on the number of women members of the committee, they do stipulate that membership should be drawn from both sexes. Yet in 28 per cent of committees women constituted less than one-fifth of the membership, and in only 7 per cent were they either equally represented or in a majority.

How much does the formal composition of the committee matter? The calibre of a REC depends heavily on the personal qualities of individual members, which is not, of course, revealed in a survey of this nature. But evidence from observing RECs in action and interviewing members does suggest that the guidelines are sensible and should be observed. Committees which were larger than the suggested maximum functioned without using all the members. In three cases, there were members who were obviously excluded from the debate and remained silent throughout. Committees which were very small seemed to lack specific expertise, particularly if they had neither a clinical pharmacologist nor a pharmacist, and tended to have a large number of questions about the trials at the end of the meeting which the chairman was then charged to address by consulting other people. The smaller committees also tended to be more medically dominated than the larger ones.

Figure 2 casts further light on the composition of the committees. It shows the breakdown of the total membership of 2185 of the 222 responding committees by professional background. The dominance of hospital doctors, who account for just over half the total membership, is striking. The contribution of hospital doctors of a variety of kinds is of course essential, but it is questionable whether it is necessary to have so many on an REC.

Figure 2 Membership of RECs

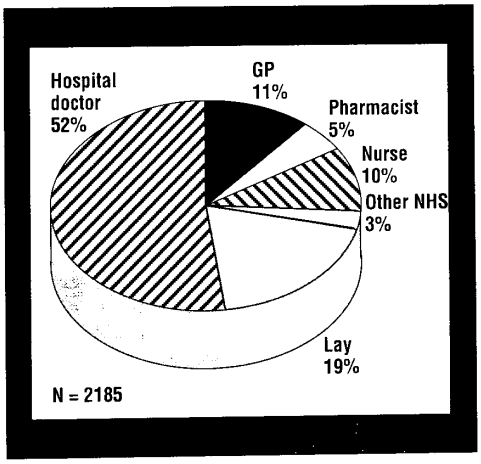
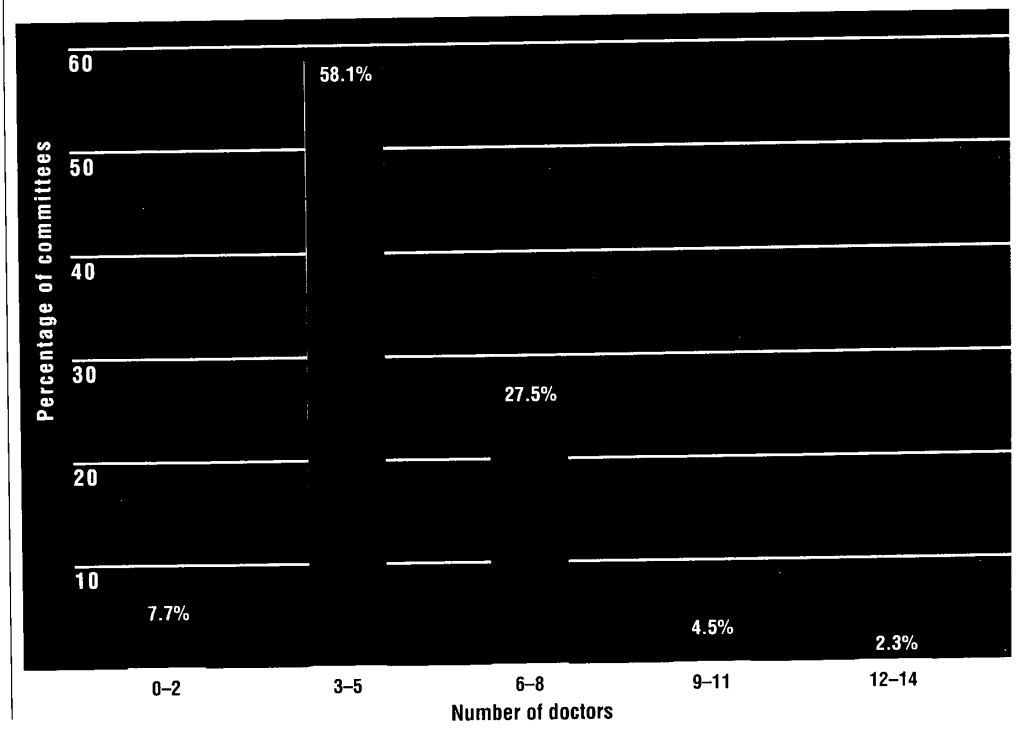


Figure 3 Hospital doctors on RECs (Excluding clinical pharmacologists)



As can be seen from Figure 3, 34 per cent of the committees surveyed had six or more hospital doctors on them. Indeed, in the sample of committees visited, more than half had six or more hospital doctors, of whom the overwhelming majority were physicians. Unless the chairman stopped discussion that was of interest only to them, it was clear that their dominance could exclude others on the committee, including GPs.

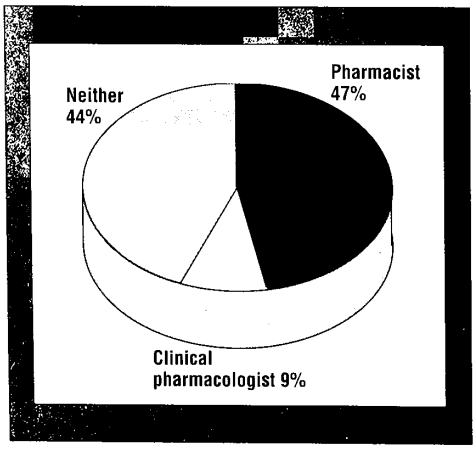
It was also remarkable that only half the committees visited had surgeons as members; this statistic may help to explain the dearth of surgical research that comes to the RECs. Only twenty psychiatrists were on the committees visited, and since one had eight most had none at all. Nevertheless, there were a significant number of protocols discussed which were clinical trials of drugs to be used for psychiatric patients.

In the course of my interviews, a number of interesting points came out concerning the role and contributions of members with particular backgrounds.

Basic scientists

The DoH guidelines make no specific mention of the advantages of having basic scientists of any kind on the committees. Whilst the RCP guidelines mention scientific members, they do not single out clinical pharmacologists or pharmacists as being particularly important. Figure 4 shows that 47 per cent of the committees had a pharmacist member, while 9 per cent had a clinical pharmacologist. The rest (44 per cent) had neither a pharmacist nor a pharmacologist. Yet much of the research which is being vetted involves the use of drugs. Many of the chairmen interviewed argued that clinical pharmacologists were amongst the most useful members of their committee. My own impressions from attending meetings of RECs confirmed this, since they were the members who always checked the randomisation codes, made comments about the batching of drugs, and commented when they thought that the trial was clearly one that was 'me too', the term they used to describe the trial of a preparation that was an imitation of something already on the market from another company, and which was very successful. Pharmacists made similar contributions and also looked for the availability of the coding of randomisation in case of a need to break it, something that was never mentioned at a committee where no pharmacist or clinical pharmacologist was present.

Figure 4 RECs with pharmacists and clinical pharmacologists



GPs

As already noted, a substantial number of committees (15 per cent) had no GP member, despite the DoH guidelines. The case for having a GP member is made by the Royal College of Physicians on the basis that virtually all research subjects are patients of a GP. There are two aspects to this. First, most committees insist that the subject's GP be informed of their participation in a trial. Since RECs generally tend to do little monitoring, GP members of the committee provide useful feedback on the degree to which they are informed in practice. Second, and more significantly, GPs are well-positioned to contribute to the debate, having the technical knowledge and the experience with patients while being totally independent of the hospital department promoting the study. It is noticeable, however, that virtually no studies being carried out by GPs came to the RECs, even though GPs are involved in a large number of Phase IV studies. Only one country-wide GP study carried out came to more than one REC observed.

From my observation, GP members played a very important role in forcing the committees to take account of the ease with which patients could be persuaded to give consent to relatively risky procedures. Two committees visited which had no GP member did not raise this issue at all, whilst all the others, in different ways, were concerned about how patients were recruited and whether they were truly aware of risks involved. These were not always issues raised by the GPs, however, which may suggest that their very presence has an influence on the debate.

The committees without GPs felt their lack, but had found it difficult to recruit them. Part of the problem lay in the need to pay a locum if committee meetings were held during normal surgery hours. Nevertheless, in most cases this problem had been overcome.

Nurses

Most committees had just one nurse member; 12 per cent had none at all and 7 per cent had two or

more. Typically, the nurse member would be a senior nurse rather than one currently operating on the wards; only three of the nurses on the committees visited were in active practice with patients. Nurse members argued that they had a special role to play on the RECs since nurses tend to get closer to the patient than do medically qualified professions.

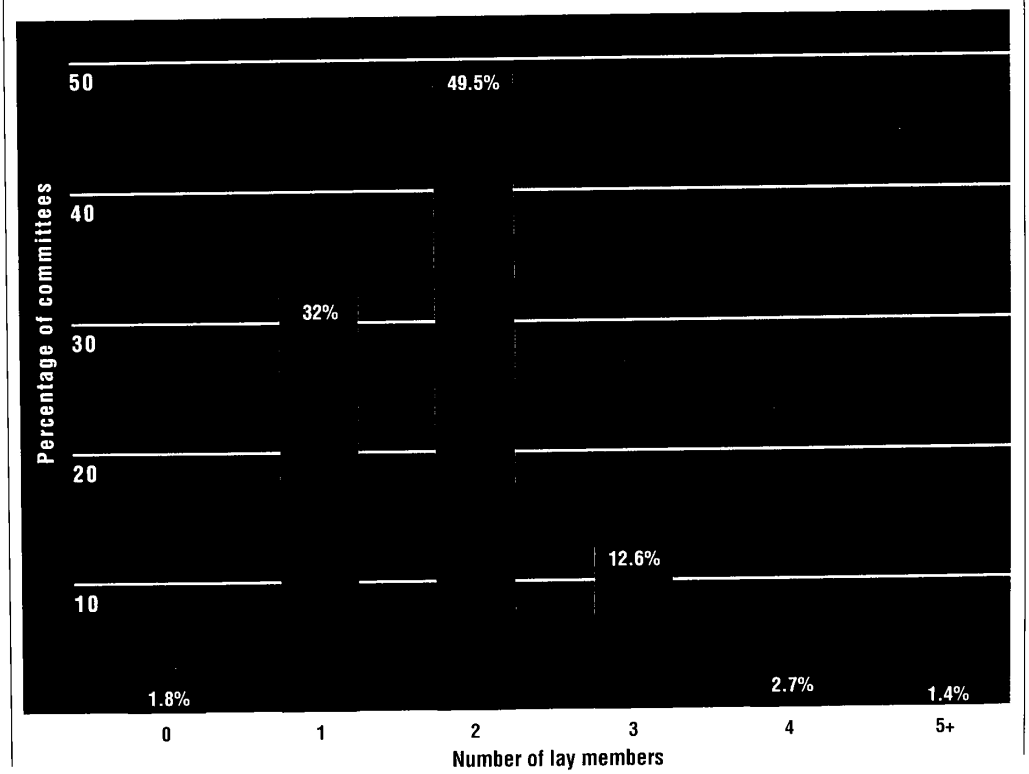
This justification for nurse members seems to argue in favour of hands-on rather than senior nurses. When this was raised with senior nurse members, they argued that junior nurses would be hesitant in expressing their views in such a forum. My own observations suggest that nurse members do play a valuable role in drawing other non-doctors into the discussion. On one of the committees I attended, the nurse members were clearly discouraged from participating, but in most of the committees this was not the case. The three junior nurses I saw were not in fact inhibited from playing a part. Indeed, several nurses clearly felt able to make scientific points in the debate. In a television programme, whilst one committee was being filmed, the commentator remarked with surprise as he watched a senior nurse raise an issue of scientific validity of data. This was not unusual in my observations.

Lay members

The DoH guidelines stipulate that RECs should contain at least two lay members, and at least one lay member should be unconnected professionally with health care. There are a number of reasons for wanting a reasonable number of lay members on an REC. First, it is important that the REC is independent, and is seen to be independent, of the DHA it is advising. This can most easily be achieved by having a substantial proportion of members who are not employed by the DHA. Second, the range of issues confronting the REC goes beyond the narrowly medical and scientific. Lawyers, clergy and moral philosophers, among others, have a useful professional contribution to make to the debate. Third, the issues being debated should not be the exclusive preserve of professional experts: if the REC is to command public support, it must be able to draw on the sound judgement and common sense of members with no particular professional training.

On the basis of the questionnaire returns, the number of lay members of RECs is set out in Figure 5, which shows that one third of the committees had fewer than the minimum two lay members and only one committee in six had more than two lay members. In half the committees, lay members

Figure 5 Composition of RECs



constituted less than 20 per cent of the total membership. In view of the importance of the role played by lay members, their representation seems small.

But there are further concerns. In-depth interviewing of 28 committees revealed that the questionnaire returns may actually overstate the number of members who were truly independent of the DHA and were not medically qualified. Of the 61 members on the committees visited who were classified as lay, seven were members of the DHA and a further three were retired nurses. While not doubting that they have a valuable contribution to make, they cannot provide the same independent role that a true outsider can play.

One obvious source for lay members is the Community Health Councils (CHCs), and their Scottish and Northern Irish equivalents, which are established to represent patients' interests in the NHS. The DoH guidelines state that lay members should be selected in consultation with the local CHC. However, only half the RECs have lay members who are also on the CHC. A number of chairmen when interviewed were dubious about the quality of their local CHC and preferred to invite people they knew to become members. In one case the local CHC had been approached but had not been able to nominate anyone.

Non-healthcare professionals

Among the lay members of the RECs are those who by virtue of their training can provide a different professional input from that available within the medical profession. Figure 6 shows the proportion of the total membership of RECs who are either lawyers or members of the clergy. Around a quarter of the committees in the sample had a clergyperson, and about the same number had a lawyer. Some committees felt that it was important to have clergy on the committee. In interviews members said: 'It sends out good signals to the public'; 'The committee likes to feel they have a moral specialist on board'; and 'It would not be possible to have a research ethics committee in this authority without a clergyperson'. Yet, with two exceptions (both of these being in Scotland) the clergy were not trained moral philosophers.

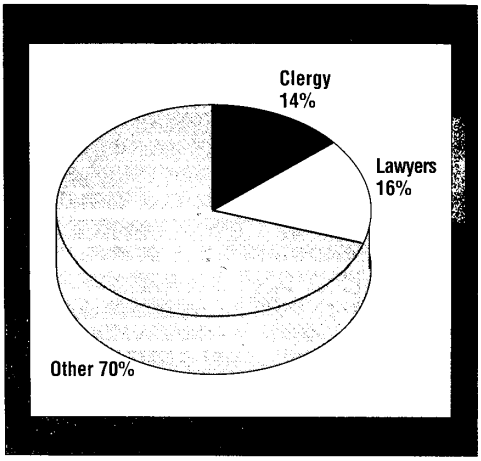
There was little feeling among committee chairmen that they needed a trained philosopher on board. Three thought it would not be helpful, while four others conceded that one who was 'not too airy-fairy' could be a valuable addition. One chairman was however searching for a suitable academic philosopher to join his committee, and has since succeeded.

The attitude to the role of trained philosophers was best summed up by one of the two philosopher members interviewed who said that 'these committees are not necessarily sure that they should be making moral judgements, or indeed that they need to be explicit at all about how they make their judgements'. Four of the clergy, not philosophers, echoed that by saying that they thought a lot of the work of their committee was done on a basis of 'That's all right then; we have no objections...' rather than with clear criteria about what kind of research was acceptable and what not. The general view appeared to be that sensible lay people, not moral specialists, were what was needed, rather along the lines of the VLA's guidelines for ethics committees:

> *It is not necessary that those who become members of the committee are experts in moral philosophy or in particular disciplines; they need to be reflective people of goodwill, with a high regard for the human personality, for truthfulness and for the continued advance of reproductive medicine and medical science.* (VLA, 1989, p.38)

Yet it was apparent from observing the committees in action that a person who was trained to think clearly and analytically about moral questions would have been a valuable addition to the committees. Their very lack of clarity – both about their purpose and in analysing protocols – in itself made the case for a philosopher member.

Figure 6 Lay members of RECs



Breadth of membership

The DoH guidelines call for a sufficiently broad range of experience and expertise so that the scientific and medical aspects of a research proposal can be reconciled with the welfare of research subjects and broader ethical implications. Given the nature of the decisions being taken, it is essential that the RECs be sensitive to the diverse values of NHS patients. It is questionable how far the current membership actually reflects this imperative. Eight committees (4 per cent) had no

women members, and in half of the committees women constituted one quarter or less of the membership. Ethnic minorities were grossly under-represented. Of the 337 members of the committees I visited, all but two were white. While not arguing that the REC membership should mirror the composition of the population exactly, it is difficult to believe that the concerns of a diverse population can be adequately understood by such a restricted membership.

Committee chairmen

At the time of writing, nine of the twenty-eight committees visited had lay chairmen, a change from eight at the beginning of the study. It would greatly strengthen the position of lay members, and the independence of the committee itself in the eyes of the public, if the chairman were generally a lay appointment. The main argument against this lies in the technical nature of the research protocols, but that could readily be dealt with by having a professionally qualified vice-chairman. The DoH guidelines ask for a lay chairman or vice-chairman. That change was taking place slowly in the course of the study; lay vice-chairmen were gradually being appointed where the chairman was medically qualified, and the duties of chairing meetings were being shared between the chairman and vice-chairman to a considerable extent.

Methods of appointment

In most cases, appointments to the REC are made either by the DHA or the Health Board. The chairman is usually appointed by the chairman of the DHA. Normally, that is an entirely separate appointment from any other NHS or clinical appointment. But in one case, the membership of the ethics committee and the District Medical Committee (DMC) were identical, which led to the lay member of the research ethics committee being party to all the debates of the DMC. One chairman was extremely concerned that none of the members of his committee should regard themselves as a representative, since each person had been appointed in their own right. This is a point emphasised in the DoH guidelines. Others, three in particular, were keen to display their lists of membership with notes by the sides of names: 'CHC representative' or 'Representative from the division of surgery.'

The DoH guidelines make it clear that the committee is appointed in full by the DHA. In most cases this is what happens. If it is a joint committee, the members are appointed by a combination of the DHA (or Health Board in Scotland) and the university. However, in two of the committees, the medical members are elected, not appointed. One committee (West Lambeth) has elections for the medical members, except for the chairman and vice-chairman (who is currently a lay person). The elected medical members have a three year period of office, non-renewable, whilst the appointed medical and non-medical members have a renewable three year term. West Lambeth emphasise that they like to have a rough balance between medical and non-medical on the committee, and it certainly has that feel. The chairman is an appointee of the DHA.

The West Lambeth committee is very different – because the chairman and lay members are appointed – from the other 'elected' committee visited in the sample, West Somerset. There the committee is chaired by a consultant elected for a period of three years by the Senior Hospital Medical Staff Committee by a simple majority. The fact that there are contested elections for a position on the REC suggests that the committee has considerable status. It is noteworthy that both committees which have some kind of election to membership also operate by interviewing most of the lead researchers who make applications. Several others do the same, though still a minority. Both West Lambeth and West Somerset also allow some chairman's action, a matter to be discussed below (see p. 25).

In all but four cases in England and Wales, the chairman was appointed by the DHA. These four had chairmen appointed or elected by the District Medical Committee. In two cases of DHA appointees, the chairman was vice-chairman of the health authority, showing that the committee was highly regarded by the DHA itself. In one case, the chairman was the chairman of the DHA as well, a deliberate move to heighten the status of the committee. One other lay chairman was a member of the DHA.

The fact that the DHA could appoint members without the chairman's agreement was a source of concern to some chairmen. At the time of one visit, the committee was debating its membership. There had been a dispute between the chairman and the DHA administrators and others. The dispute centred on two new members who had been drafted on to the committee without full consultation with the chairman and the members. There was considerable ill-feeling, leading to the chairman's resignation.

Although such events were far from common, a measurable change occurred over membership issues during the fifteen months of visiting. The RCP guidelines had suggested that an established committee might propose some of its own names to the appointing authority. In fact, that is what happens in most cases, though the DHAs and Health Boards are taking a keener interest and may have strong views about precisely who should be on. It is not uncommon to find the District General Manager (DGM) (on two of my visits), or the deputy DGM, serving on the committee.

The RCP also suggests that the appointment of lay members may need wider consultation than the appointment of professional members. In one case, in Scotland, the Health Board wrote to all sorts of possible interested groups, including the Health Councils, the churches, university departments and the like, inviting suggestions for members, a course of action which was regarded as having been very successful. Otherwise, apart from the CHCs – which sent a representative in one case and whose nominee is on in fifteen cases – there appeared to be no clear route for the appointment of lay people except in the joint DHA/university committees where the university provided a selection of academics in subjects unrelated to medicine.

4

EXTRACTS FROM THE CONSTITUTION, MEMBERSHIP, FUNCTION, PROCEDURES AND GUIDELINES OF THE WEST LAMBETH HEALTH AUTHORITY ETHICS COMMITTEE, JANUARY 1990

CONSTITUTION

The Committee has appointed and elected members of both sexes comprising Chairman, Deputy Chairman, Elected Medical Members including one from the Institute of Dermatology, the Chairman of the Lewisham and North Southwark Ethics Committee, a General Practitioner, Nursing Members, a Legal Member, Lay Members and an Administrator. The Constitution aims to provide an approximately equal balance of medical and non-medical representation. Appointed members are invited to join the Committee on a personal basis; they do not represent any official organisations of which they may be members.

Appointment to the Committee is for 3 years and is renewable. Election to the Committee is for 3 years and is not renewable.

FUNCTION AND PROCEDURES

2 All research involving clinical trials and/or other investigations on patients, healthy volunteers or medical records must receive approval by the Committee. Where studies are done both for the benefit of patients and for research purposes, the investigator should attempt to assess which is the primary purpose. The Committee expects to receive applications only where the primary purpose is research, as it would be improper for the Committee to interfere with investigations or treatment aimed principally at helping individual patients. In case of doubt investigators are invited to consult the Chairman.

4 The Committee hold that to be ethical research must be scientifically valid. On this basis, minor procedures such as the taking of a single blood sample or administration of a simple questionnaire are unethical if the scientific basis is invalid. By the same token, research involving major invasive procedures such as a biopsy or cardiac catheterisation can be ethical provided always that there is adequate scientific justification.

5 The Committee believes that in all such research every effort should be made to preserve the autonomy of the patient or healthy volunteer. To this end, it requires that all participants receive a written and appropriately worded description of the research, have adequate opportunity to ask questions of the investigator and give their written consent to participation. It is normally expected that the investigator shall use the standard Consent Form, on which space is provided for a written explanation. Copies are available from Acute Unit Administration.

Particular care is needed in the conduct of research on subjects whose ability to give informed consent is diminished. The investigator is responsible for ensuring that such research is both ethical and legal.

7 Applications for ethical consideration are received by the Committee and dealt with in one of two ways:

(a) By Chairman's action, alone or after consultation with another Committee member. Proposals involving minor, medically trivial, procedures are approved in this way, as are extensions to previously approved projects. Such approvals are presented individually at the next available meeting of the Committee and subject thereby to its scrutiny.

(b) In Committee. Applications are circulated to members in advance. At the meeting applicants appear in person, present their proposals and answer questions. Discussion and decisions, where appropriate guided by co-opted experts in the field, take place in the absence of the applicant. The outcome is communicated to the applicant immediately.

All decisions of the Committee are notified in writing.

12 The Committee may at its discretion identify particular research projects for selective monitoring, perhaps because they are highly invasive, because they are in particularly sensitive areas or because they involve patients whose ability to give fully informed consent is diminished. The principal investigator involved is required to report progress to the Chairman at intervals to be decided, thus providing the Committee with opportunity to review research over which it has special concern.

5

PROPOSED CONSTITUTION OF THE WEST SOMERSET ETHICAL COMMITTEE

Membership

The Committee shall consist of:

1 A Chairman, who will be elected by the West Somerset Senior Hospital Medical Staff Committee by a simple majority, for a period of three years.

2 A secretary, who will be appointed by the West Somerset Ethical Committee from amongst its own members.

3 Four consultant members from the West Somerset Senior Hospital Medical Staff, each of whom is considered by the Committee to have sufficient clinical and research experience to assess the scientific and ethical merits of applications made to the Committee.

4 A General Practitioner.

5 A Nurse who is an active practice with patients.

6 A lay representative, not trained in or practising any medical or paramedical discipline.

7 A non-medical representative from the Somerset Health Authority.

8 The present and past Chairmen of the West Somerset Senior Medical Staff Committee.

Function and Structure of the West Somerset Ethical Committee

1 Meetings will be held in the MEC Office at Musgrove Park Hospital, on the second Tuesday of each month quarterly (January, April, July, October).

2 Agenda and Minutes will be kept and distributed to customary practice.

3 A quorum shall be deemed to exist at any meeting at which five members are present.

APPROVED BY WEST SOMERSET SENIOR HOSPITAL MEDICAL STAFF COMMITTEE ON 15 MARCH 1989

Written constitutions

Of the 28 committees visited one-quarter had no written constitution; one other had a constitution but could not find it. Constitutions tend to be quite narrow in their scope, covering the numbers of members, length and method of appointment of members, frequency of meetings and some very basic procedural points, such as quorum and voting procedures. They do not generally lay out the purpose of the committee, nor do they indicate how applications are to be made or how the committee will operate.

There are some exceptions. One REC, West Lambeth, has a very detailed booklet on its constitution, membership, function, procedures and guidelines. Extracts from that booklet can be seen in Box 4. But other committees which also appear to operate well have a much more limited document. A clear example of that can be seen in West Somerset's REC constitution, in Box 5.

There is also considerable variation in the terms of appointments. Most committees lay down a maximum of two or three 3 or 4 year terms (the DOH guidelines suggest no more than two 3-5 year terms). But in some committees there is no maximum period of appointment, and one chairman had been in post for 16 years. In general, lay members tend to be appointed for a longer period than medical members because they take longer getting used to the material.

Training for members

There was widespread concern among both chairmen and members at the lack of training of committee members, and their sense of isolation. All the chairmen interviewed, bar one, said unprompted that they would welcome more contact with other chairmen, and more training. They felt that they themselves, and their colleagues and the secretariat, were putting a lot of time into something without being certain that they were quite getting it right, pushing at the right issues, or, indeed, acting as others did. They felt far too little was done to bring them together. All of them felt that more could be done in this regard.

A conference was held for the Scottish committees in April 1991, in the wake of considerable concern at the situation in Scotland. It was chaired by the then Chief Medical Officer for Scotland, ensuring that it would be taken seriously, and it raised many of the issues and allowed considerable discussion. It was felt to be important that some note was being taken by the Home and Health Department of the Scottish Office. The committees in England and Wales fare less well, as do the two lone committees in Northern Ireland.

Few of the members of the committees, professional or lay, have had any specific training. At the various conferences which took place for chairmen and members in the course of this research, the people attending were anxious for more information and more help. Apart from a conference for chairmen only, none of these was overbooked, and all but one were for one day only. In some cases, members of RECs had difficulty getting the DHA to pay for their attendance, and in other cases it was impossible for lay members of other professions to make themselves free during the week in order to attend. There was also the

feeling that these conferences needed to be held regularly if they were to provide a continuing source of information on what other RECs were doing, and to filter through changes in thinking that were taking place all over the country.

Two Regional Health Authorities laid on some training for members of RECs as well, and one district which had sub-committees laid on a kind of discussion or seminar roughly once a year, principally, but not wholly, for the sub- committee chairmen.

But the demand is far greater than this. There has been some attempt to train professional and lay members separately. The College of Health and the Riverside Health Authority in London ran a seminar for lay members only, for instance, and the Association of Community Health Councils in England and Wales has published a guidebook for lay members of RECs. Nevertheless, most of those interviewed preferred training with a mixture of disciplines, precisely because the role of an REC is to look at the material from a cross-disciplinary point of view.

The parallel with magistrates is worth making. They have a training day at least once a year as a matter of course, with considerable pressure to attend. Some do far more, particularly at the beginning. They sit in on court sessions, and there is no reason why future members of RECs should not do the equivalent. It would not be impossible to ask for a day's training a year, to be set up, perhaps, by the RHAs in England and Wales in consortia, and by the respective Departments in Scotland and Northern Ireland. These one-day sessions could cover the way that clinical trials are organised, deal with the vexed issues of informed consent, discuss changes in the law, look at risk and benefit analysis, and suggest different methods of analysing the protocols with which the RECs are confronted.

There would be value in bringing members from different areas together, helping them think through the implications of the decisions they are taking and increasing consistency throughout the UK.

Members are poorly briefed by their committees on general developments relevant to research ethics. Only three committees circulated the *Bulletin of Medical Ethics* on a regular basis, and only two circulated the *Journal of Medical Ethics.* Only one circulated the contents page of the *Hastings Centre Report* from the USA, one of the journals with the clearest exposition of difficult matters, even if written very much from a US perspective. The new RCP guidelines were not circulated automatically to members, and very little interesting material from the *BMJ* or the *Lancet,* or the *Nursing Times* and *Nursing Standard,* was photocopied and passed on. While some members keep themselves well informed, it is apparent that many soldier on in ignorance of the debates which are taking place nationally or internationally between doctors and patient groups, between doctors and philosophers, between medical professionals and lawyers.

A related source of concern is the poor briefing of new members. Two committee chairmen said that new members did receive a briefing pack, but this was contested by people recently appointed. Six committees provided lay members with a basic medical dictionary, but only one issued a full pack as a basic minimum; it consisted of the RCP guidelines (both volumes), the WHO/CIOMS guidelines 'for biomedical research involving human subjects', the British Paediatric Association's working party report on 'Ethics of Research in Children', the Department of Health guidelines or the equivalents in Scotland and Northern Ireland, and the Human Fertilisation and Embryology Act plus its accompanying Code of Practice for those involved in human embryo research. To these ought to be added the ABPI guidelines for medical experiments in nonpatient volunteers, their guidelines on compensation for medicine-induced injury and their guidelines on good clinical research practice. This is by no means a complete list, but would be a basic minimum for reference even if not read from cover to cover.

One useful measure would be some kind of briefing or newsletter for members of RECs. Many of them are keen to have such a journal. It could be a simple operation, such as a four page news-sheet produced every couple of months by some people already involved. It would need funding from the DHAs and Boards, or from the DoH, but its value in terms of helping to standardise the way committees approach specific issues and in informing members would be immense.

A further measure that would be helpful would be to encourage more informal contact among committee members both around meetings (by offering something to eat and drink) or by having a regular lunch or dinner for the committee. This gives an opportunity for more general concerns about the committee's work to be discussed and it encourages a more fluid and open debate within the committee. Providing refreshments at meetings is important for two other reasons. It is unreasonable to expect members to operate efficiently at the end of the day if they are not given something to eat and drink. It is also discourteous to members who are giving their time freely. Few committees provide adequate refreshments at present, and only one of the committees observed has a regular annual dinner for its members. It is significant that members of that particular committee were on friendly terms with each other across professional boundaries, and that there was no sense of some members pulling rank on others as contributions were made.

How do they operate?

Meetings are held between three and twelve times a year. At the beginning of the period of research two committees did the bulk of their business by post, but both have now moved to formal meetings. Two committees with a relatively light workload met jointly with the District Medical Committee; in all other cases, the REC meetings were separate.

Three committees interviewed all main applicants (one interviewed all applicants) on a regular basis, and allowed anything between 10 and 20 minutes for the interviews. Ten others interviewed on some occasions. One chairman felt that applicants should only be interviewed in exceptional cases. He argued that the committee might be over-influenced by the personality of the applicant at the expense of the soundness of the research. He admitted that reviewing paper applications was duller for all members, and made it more difficult for lay members to play an active role, but thought it a much fairer process.

Fairness is a real issue. Often the members of the committee and the applicant will know each other personally, and it is probably easier to avoid bias when written applications are reviewed. On the other hand, dullness is not a matter to be ignored. Most of the meetings take place in the early evenings. Members are not always totally alert. During the course of my visits, fourteen members fell asleep at meetings, but only in one case was the committee interviewing a candidate. As already noted, this could be rectified to some extent by ensuring adequate refreshments at meetings, but a committee reviewing paper applications is always likely to be less lively than one interviewing.

There are clearly arguments both ways. One argument which is frequently cited, that interviewing takes too much time, is not valid. One committee which has switched to an interview system has found that it takes about the same time. This is because there are not the constant references back and forth between the committee and the applicants with queries and amendments.

How public are they about their workings?

Only four of the 28 committees in the sample publish a report which is in the public domain. Others keep a register of research in progress, which is available for consultation, though never consulted. In one case, the register is a year out of date so that commercial confidentiality can be assured. Six committees were considering producing an annual report the first time, anticipating the requirements of the DoH guidelines, which require RECs to produce an annual report. Practice on publicity varies widely: one committee was going to launch its annual report with a press conference, while others still refuse even to name their members.

All but four committees produce for the DHA a list of projects considered over the past year. This does not necessarily go into the public domain as such. Only one chairman said that he would not be able to track down what they had approved over the course of any one year, although another suggested he was finding it very difficult!

Chairman's action

Almost all the committees permitted limited chairman's action. In four cases, chairman's action was disapproved of by the rest of the committee and they strongly discouraged it, making it unusual in practice. In three more, it was taken for only the most minor research protocols. In the case of committees with a lay chairman, there was a vice-chairman who could take decisions on behalf of the committee if necessary. But the very fact of his not being chairman discouraged decisions being taken in this way. At the other end of the spectrum, some committees gave their chairman a wide degree of discretion.

The issue of chairman's action is vexed. Committee members (both medical and non-medical) are becoming increasingly reluctant to permit it. The reluctance is fuelled less by a concern that the chairman will become too powerful than by a feeling that it is dangerous for him to be so exposed. This is felt particularly strongly given the fear that committee members have of being subject to litigation. Yet some committees meet only quarterly, and this could well lead to a substantial delay in carrying out research. Eight chairmen argued that researchers know when the meetings are held and should organise themselves accordingly.

Yet there are two serious considerations here. First, RECs have no powers to force researchers to clear proposals with them. The power rests with the DHA to which they are advisory. It is a matter for the DHA as to whether carrying out research which has not been vetted by a REC is a disciplinary offence. If, however, the REC makes it unduly difficult to get research vetted, some researchers will simply go ahead without approval. Two such instances were cited during the course of this research.

Second, with the financial pressures on health authorities and departments in medical schools, contract research plays an important role in providing incremental funds. But the authorities and departments are in intense competition with the contract research houses, particularly for research on healthy volunteers. If there is undue delay, they will lose the contract and be worse off

as a result. In any case, the wider point needs to be made that research in general ought to be supported and regarded as beneficial. If that is the case, RECs should not hinder it with undue delays. If research is poor, it should not be done anyway, and a speedy response from a REC to that effect is valuable in preventing researchers from wasting their time, and proposing poor research in the future.

It is therefore unreasonable, particularly when meetings are three months apart, to refuse to allow chairman's action at all. One solution, used by four committees, is to insist that the chairman consults at least two (in one case three) other members of the committee, including a lay person. But there would not be general support for much wider chairman's action, as recommended in the RCP Guidelines.

> *An ethics committee should provide for the chairman or deputy, alone or sometimes consulting another member, to receive a proposal by title plus a summary, and expeditiously issue approval on its behalf, always reporting these approvals to the next meeting of the Committee...*
>
> *Rarely, chairman's approval may be given in circumstances of urgency.* (RCP, 1990a, 4.4,5)

Vetting multi-centre trials

There is also considerable resistance to the idea of chairman's action for multi-centre trials and epidemiological studies. The RCP has reserved its position on this to some extent, but makes it clear that medical epidemiological studies do need to be taken to ethical review.

Multi-centre trials pose particular problems when the same protocol comes to RECs all over the country. It can require the approval of upwards of fifty separate RECs, and researchers conducting trials find the difficulties of getting approval so considerable that they would like to see the creation of a national committee to consider multi-centre trials. This has been discussed in detail by several of the committees visited and is the subject of debate in the medical press from time to time. The RCP is also considering it, as is the ABPI and the MRC. It is discussed as a policy issue below (p.29).

Administrative support

Research ethics committees are usually serviced by an administrator of the DHA. That is by no means universal, and several visited had all the administration conducted by the chairman or secretary. RECs produce large amounts of paper, from copies of research applications to minutes with detailed records of approvals of protocols. The administrative load is considerable, often far beyond the time allocated by the DHA for the administrator concerned, and several of the administrators put in vast amounts of unpaid time into making sure the paperwork was in order.

Only 10 of the RECs observed have so standardised their forms as to make the reading tolerable. Most standard forms for researchers were between four and eight pages in length. The shorter ones meant that would-be researchers tended to continue on another sheet of paper. In the larger committees, would-be researchers could not submit the standard protocol as given to them by the pharmaceutical company. They were required to make the material understandable for non-scientists and to enter the application on a standard form in a particular way, ensuring that basic questions to which the committee needed to know the answers, such as insurance arrangements or payments, were included. Also they almost always had to submit the information sheet for research subjects and the consent form. They frequently had to submit sufficient copies for each member of the REC to have one, leading to vast bulky packs of paper.

In many of the smaller RECs, however, it was customary to receive the full protocol from the pharmaceutical company. These were usually beautifully produced, with clear instructions about consent. Many of them were more protective of the patients' interests than were the other applications. This was partly because some of the pharmaceutical companies were keen to promote the ABPI's Good Clinical Practice, including proper consent procedures and strict control over the acquiring of data. It was also because some of the companies wanted the protocol to satisfy the requirements of the very strict American Food and Drug Administration. But they often did not satisfy the requirements the larger committees would have made in the way of information sheets and details about payments to researchers or to healthy volunteers.

Standard protocol forms are obviously a great help to the administrators of these committees. Only seven committees still do not have them. Both lay members and administrators find a standard form easier to deal with. When administrators want to follow up a research application some months later, although not all RECs require a follow-up, it is easier to do so if questions about dates for commencement of the project have already been entered in a standard form.

Most committees kept detailed records of their discussions and a copy of every protocol examined. But few RECs had their records computerised. One harassed chairman said that they could not tell whether they had passed or refused an application similar to the one before them over the previous couple of years. He was clearly desperate for more administrative help and for a computer. He was having trouble acquiring a

computer from his health authority and university jointly. The desire was to devise a system which he could install on a laptop computer that could then be taken to and from meetings. One member of that committee was so concerned about the dearth of recordkeeping that she was quite prepared to resign. She felt that the patients, and the researchers, were inadequately protected by the administration as it was being conducted.

Nor was she alone. Three members of RECs complained about inadequate storage of information. Only one committee had a computerised system which listed all research and flagged it up at the six month and one year stages after initial approval for a progress report.

The variation was immense. Two committees, for instance, have a standard cross-checking system. Three committees do not appear to have any problems and can fish out an old protocol at the drop of a hat. One REC's records had been thrown away except for the preceding two years! However, with four exceptions, the storage of records, almost entirely manual, was more or less adequate most of the time. But the nature of the recordkeeping each REC required varied immensely, as did the extent to which there was any follow-up to check whether the research had begun, whether any difficulties had emerged, and whether a copy of the publication at the end of the period had been requested.

As well as these variations, ten of the committees observed insist on the subject's GP being informed when the patient is entered into a trial. Yet there is virtually no monitoring of this (with one, very cursory, exception). Nor is there an automatic stamping or pinning system of the notes of patients to indicate that they are in a trial. This does not occur in any of the DHAs concerned, even though all the committees insist that consent is obtained and entered into the notes.

It is for this reason that four of the administrators interviewed are so keen to see a mandatory system of marking of notes and patient records. They cannot see how it can be safe to run trials without it being clear who is involved, and whether they have been involved in a trial before. They also wish to see mandatory informing of GPs. There are those who wish to see the whole system computerised, including hospital records and GP notes, with patients given a single number and with easy access into the system for healthcare professionals.

Generally there was insufficient administrative backup to do even the very basics of checking and ensuring adequate papers, leading to a huge load being put on willing administrators doing the work in their own time, and on chairmen of RECs who find the task very time-consuming.

In general the committees visited attached considerable importance to the work they were set up to do and carried it out conscientiously and with good sense. There are a number of areas in which practice could be improved, many of which are already reflected in the DoH guidelines.

3 | Policy issues

In the course of my investigation of RECs, a number of issues were raised about the functions and responsibilities of the committees. These are discussed in this chapter. The issues are summarised in the form of questions in Box 6.

Vetting the research

The DoH guidelines say that the REC will need to know whether the scientific merit of a proposal has been properly assessed. It is not clear whether this should extend to the REC satisfying itself that the research is well designed. Several of the RECs visited regarded it as part of their function to examine the protocol design, claiming that 'bad research is unethical research'. They have to assess whether the expected benefits from the research are likely to justify the demands made on the human subjects. It is debatable whether they can do this without making some assessment of the research itself. The issue becomes particularly acute when the applicant may be motivated by other concerns than the advancement of medical knowledge, for example where he is receiving substantial funds for carrying out the research, or is carrying it out as part of his training.

Against this it can be argued that the RECs do not have the skills or expertise to make such an assessment. They may also reflect their own personal biases; a case in point is nursing research. Much nursing research concerns patients' attitudes and views rather than the objective evaluation of different treatments. Some RECs view such research very positively, while others feel it is non-scientific, as well as unduly intrusive for patients, and should not be permitted.

Scientific assessment of research

There was no objective definition of 'scientific 'and 'non-scientific' research. The tendency was for any research involving the use of questionnaires, and submitted by whatever discipline, to be regarded as 'non-scientific'. Those RECs which were largely medically dominated thus tended to class as 'non-scientific' a great deal of research that was submitted by nurses, psychologists, medical students and psychiatrists. Discussion often focused on the delivery of 'soft data' and on the poor design of questionnaires. It was clear that those who took that view thought the research methods used by other disciplines were inadequate and that the data were not to be trusted. It was therefore remarkable to see other RECs welcome non-medical research, and, in two cases, discuss ways of encouraging more qualitative research on the effects of certain treatments on patients.

One possible solution to the unsatisfactory nature of debate about the quality of the research is to ensure a wider spread of interest on the committee, as the DoH and RCP guidelines both suggest. For the technically complex scientific and medical research there is also an argument for a separate research methods committee, as exists in many US institutions and is under active discussion at a few UK institutions as well, to ensure that the research is vetted properly for its scientific validity before the REC sees it. Alternatively, members could be co-opted to the REC as necessity arose to discuss the complex issues, though lengthy technical discussion of very specialist issues might be difficult for lay and other non-specialist members. The solution followed by each REC and DHA might depend on the quantity of such complex and technical research that takes place in the institution. It is, however, clear that a

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POLICY QUESTIONS FOR RECs

1 **Should the REC satisfy itself that the research proposal is well designed to achieve its stated objectives?**

2 **How should multi-centre trials be handled?**

3 **How should student research proposals, whose primary objective is an educational one for the students themselves, be treated?**

4 **Is the financing of the research a proper area for the REC to concern itself with?**

5 **Should the REC concern itself with compensation mechanisms available to someone harmed as a result of participating in a trial?**

6 **What sanctions should there be in the case of research undertaken without prior clearance from the REC?**

7 **How far should RECs be responsible for the enforcement of their decisions?**

8 **Should RECs approve all research carried on by GPs in their area?**

9 **How should research on 'me-too preparations' (which duplicate the function of existing preparations) be treated?**

confusion of roles exists, so that the RECs often act as both research and research ethics committees, often beyond their capabilities.

Multi-centre trials

Because of the problems explained earlier (page 26), there have been various proposals for a national committee for multi-centre trials. A considerable amount of correspondence about it has appeared over the years in the *British Medical Journal* and the *Lancet*. It focuses on the impossibility, particularly for epidemiological research, of getting consent to a trial from many different research ethics committees. They cause delays, have different patterns of working, and some of them demand personal attendance at the committee. (See Berry *et al, BMJ*, 1990;301:1274)

There is, however, gradual acceptance amongst chairmen and members of the idea of the formation of a national committee for multi-centre trials of particular kinds. These would include those involving over twenty centres and large-scale epidemiological studies. Local RECs guard their independence jealously, and stress their knowledge of local attitudes, so the prospect of such a national committee would mean an important change in their perceived independence. To gain acceptance of such a proposal, a national committee would need to approve studies conditionally, leaving the final decision to the local REC. It would be the local committee which would have the right to approve or reject the study for its locality. It could not amend the study in any way, a habit which has so frustrated those researchers designing large- scale studies. Local RECs might also wish to amend the information sheets and consent forms in accordance with their standard pattern.

Twenty chairmen interviewed accepted this as a sensible way forward. It seemed broadly speaking to have the sympathetic consideration or approval of the President of the Royal College of Physicians, the Medical Research Council, the ABPI and several of the medical directors of the pharmaceutical companies. It would not go as far as some researchers engaged in large studies would wish, and it might be much resented by some RECs who would feel their independence was being removed. Nevertheless, it would certainly limit some of the delays, as well as leaving local RECs and their appointing DHAs with the final authority.

Student research applications

RECs serving authorities where there is a teaching hospital, or a nursing studies unit at a polytechnic, tend to be faced with large numbers of student research proposals. Some deal with these by chairman's action. Others set up sub- committees to look at student research. A few actually examine the projects, and in one case there was a separate sub- committee for that purpose.

Student research, which is primarily for the purpose of educating future nurses and doctors rather than for the public good per se, poses particular ethical problems, similar to those raised by the training of student doctors and nurses in carrying out invasive procedures. Since research on human subjects poses problems of its own, as well as those associated with the training of students, it is obvious that these student research proposals need careful vetting, however harmless they may seem. It was clear that several RECs facing large quantities of student research were concerned that patients were being subjected to useless and often unduly intrusive questionnaires. They saw their role as being two- fold. First, to protect patients from what was pointless and/or unduly intrusive. Second, to encourage students to learn to carry out research projects well. A separate committee which had a fair proportion of regular members of the REC, including lay members, was considered a sensible way forward, but chairman's action on student protocols was viewed askance in all but two RECs.

Financing of research

Issues about payment in the area of research on human subjects tend to be emotive. Should human guinea pigs be used for others' financial gain? Are they being exploited when they are already vulnerable as patients, or as medical students who wish to please their teachers? Should researchers be paid personally for their research, or should the money go to the NHS department or to the university?

Guidelines

The DoH guidelines make it clear that it is the duty of RECs to consider the financial aspects of research proposals. As a minimum, they are to know:

> *What monetary or other inducements are being offered to the NHS body, doctors, researchers, subjects or anyone else involved.* (DoH, 1991, 3.2,vi),

The guidelines continue by insisting that:

> *The REC should examine any financial aspect of a research proposal which may influence the patient's judgment in consenting, or the researcher's judgment in his/her treatment of subjects, in such a way as to call the ethics of the research into question. Clearly, any payments to a subject or researcher must be considered, but it is also possible that benefits to an institution or department may raise similar ethical questions. Undue variations in payments between different sites in a multi-centre project may*

also raise questions. In general, however, the resource implications of a research project for the NHS body concerned are for consideration by the NHS management, not by the REC.

Payment in cash or kind to volunteers should only be for expense, time and inconvenience reasonably incurred. It should not be at a level of inducement which would encourage people to take part in studies against their better judgment, or which would encourage them to take part in multiple studies. (DoH, 1991, 3.15-16)

In many ways, the RCP guidelines are even stronger on this subject, as can be seen from Box 7.

Current practice

Current practice does not accord with these guidelines. Most RECs asked at some point in their application form or in interview about the financing of the research project. There were, however, six which did not raise the issue at all. In three of these, the chairman stated: 'We do not regard it as our business to find out what the researcher is paid...'. Of those that do, all make it a rule that money from the pharmaceutical industry must not go into the researcher's own pocket. Nevertheless, there is disquiet about the amounts of money paid and what happens to it.

Amounts vary considerably. They seem to vary over the same multi-centre trial, depending on where the research is being carried out. In one case the same trial was being paid for at the rate of four times as much per patient at a famous London teaching hospital as was being paid in a rural district general hospital (DGH). This is, perhaps, not surprising. But the Royal College of Physicians has made it clear that even if researchers are paid, the payment should not in any case be on a per capita basis (RCP, 1990a, para. 7.86. Given such a strong statement, it is surprising to find the high incidence of the continuation of the practice of per capita payments which benefit either the researcher directly or his/her department. Quite considerable sums are often paid on a per capita basis. There was no discussion of this issue in any of the research ethics committees visited. All committees observed approved projects where subjects were being recruited on a per capita basis.

One objection to per capita payments has always been that it will tempt a researcher to try to include more people in a trial than otherwise would be regarded as suitable. It might be a temptation to extend the age range of suitable patients for a trial. There were several requests to research ethics committees to change a protocol to allow older patients into a trial, which could be related to this issue. But it also seems to be the case that most pharmaceutical companies give researchers a limit on how many patients they wish to be recruited into a trial. Problems only arise if the researchers cannot get enough recruits within the population for which the protocol has been designed.

In one case, it was felt that it was the concern of the committee and the DHA what individuals were paid. It was also to their benefit. A 5 per cent levy was taken by the DHA (with bills being sent out by the District Administrator who was responsible to the authority for running the REC). This was ostensibly to pay for the administration of the REC. It goes against the DoH guideline which

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RCP GUIDELINES ON FINANCIAL ASPECTS OF RESEARCH

It may be improper for a doctor to accept per capita or other payments from a pharmaceutical firm in relation to a research project such as a clinical trial of a new drug, unless the payments have been specified in the protocol for the project which has been approved by the relevant national or local ethical committee.

(Quoting the General Medical Council RCP, 1990b, 17.8 and RCP, 1990a, 7.86)

In this statement, payments, (whether or not on a per capita basis) are regarded as proper provided they have been declared beforehand and approved by a research ethics committee. We take a different view and consider that payments made on a per capita basis are unethical and should not be made whether or not they have been declared and approved by a research ethics committee. We recommend that Research Ethics Committees should not approve projects which are funded on this basis.

(RCP, 1990a, 7.86)

Even when payments in the form of fees are made to an institution or department, payment on a per capita basis may lead to undue pressure on the investigator to recruit additional patient volunteers. In some studies, it is uncertain how many patients will be recruited (eg in a multi-centre study) and it may be appropriate for the sponsor of the research to meet the cost of studying patients in proportion to their numbers. In such circumstances, we make the following recommendations:

i The payments should never be such as to induce the recruitment of patients who would not otherwise be considered appropriate.

ii Payment for recruitment should not exceed a reasonable estimate of the cost of studying the patient together with any legitimate expenses. There should be no element of profit to the institution or department related to the number of patients recruited.

iii All payment should be declared to the Research Ethics Committee.

(RCP, 1990a, 7.87)

suggests that the cost to the DHA of the research and, presumably, although not stated specifically, the costs of the REC which vets that research, are not the concern of the REC.

None of the RECs when being observed discussed the issue of their right to know the details of financial arrangements. But the chairmen and some of the members of committees discussed it later in interview, on several occasions raising it themselves. Several were concerned that the money was not going to the department or the institution. They felt that the research funds of the departments concerned were not properly audited.

Costs of research to DHAs and health boards

Twenty RECs ask researchers what the net cost of the research will be to the DHA or Health Board, despite the DoH view that this is not properly their concern. It is clearly increasingly their view that the pharmaceutical companies which sponsor the research ought to pay for the real costs. As they are examining the projects in some detail, they are well- placed to look at the costs to the DHA or university concerned.

Why RECs should know about the financing of research

The arguments for RECs gaining full information about the financial arrangements in individual research proposals are strong. First, if human subjects who are NHS patients have been entered into the trial, there is a strong public interest argument for ensuring that monies earned are returned to the NHS or university department, rather than kept for personal gain. Second, it is clear that a check on the motivation for conducting research is useful. If research is purely for financial gain from a pharmaceutical company then the REC ought to know, and be able to inform patients or healthy volunteers accordingly. Third, per capita payments do make it attractive for researchers to seek out additional subjects, leading to the possibility of abuse. It is therefore sensible for RECs to keep a check on this. Fourth, it is clearly wrong that a human subject in one part of the country is recompensed at a wholly different rate from a similar subject in another part. The costs of conducting the investigation on the particular human subject in different parts of the country cannot vary by a factor of four. There is a strong argument for RECs knowing what is being paid to researchers in the same multi-centre trial in other parts of the country. Fifth, if there is a strong financial motivation on the part of researchers to gain funds with which to conduct other research, or purchase equipment for a department, then DHAs ought to be made aware of this as, arguably, should the wider public. If it is the case that many researchers conduct research precisely to fund other work and equipment, then there are questions to be raised about shortfalls in funding for specific departments.

It therefore seems essential that full financial disclosure is made to the REC. The REC should know amounts, destination of payments, details of payment to healthy volunteers, to researchers, and, in the case of multi-centre trials, amounts of payment elsewhere. It is only with this information that it can adequately assess the motivations behind the research, its potential benefits to the individual subjects, the DHA or university, and whether undue pressure is likely to be applied to individuals to take part.

Legal liability

There is a great deal of concern about legal liability and indemnification issues within RECs. Some insist on seeing the extent to which cover is provided for patients and healthy volunteers. Others merely look to see whether compensation is likely to be offered under the ABPI guidelines. The Royal College of Physicians holds the view that it is not the duty of research ethics committees to examine all the issues involved, such as whether the pharmaceutical company sponsoring the research offers any indemnity to the DHA concerned. Nevertheless, the RCP guidelines insist that:

> *The Ethics Committee can point out the position regarding responsibility for injury to research subjects to its appointing authority and to grant-giving bodies supporting research that is before it, and ask for a reply either in general terms or in respect of an individual project, and take their reply into consideration in its review* (RCP, 1990b, 16.21).

The DoH guidelines are more specific, and raise genuine concerns about how ethical it is to ask patients and others to volunteer to take part in a study when their indemnification is not clear.

> *NHS bodies are not empowered to offer advance indemnity to participants in research projects. A person suffering injury as a result of having taken part in research would be able to pursue a claim for negligence through litigation. Each case would of course have to be considered on its merits* (DoH, 1991, 3.18).

> *Volunteers must therefore be told in advance of all known risks and be made aware that there could also be unforeseen risks and of the possible difficulties in obtaining compensation* (DoH, 1991, 3.20).

Current practice

Several RECs would regard these guidelines as worryingly insufficient. One REC was concerned that many patients (not healthy volunteers, for whom a separate policy is usually taken out) would still be left unprotected because not all research is sponsored by the pharmaceutical industry. Those

projects which were the bright ideas of individual researchers or departments would have to be indemnified by the university or DHA or Board, yet according to the DoH guidelines a NHS body cannot undertake to do this.

The argument ran as follows. If the committee was there as a public watchdog, and if they were there to protect the interests of patients, then however low the risk of injury, the research could not go ahead unless it was covered by an insurance policy. The certainty, rather than the likelihood, of an *ex gratia* payment (which was made without any admission of liability), would also be acceptable.

To some extent at least, the RCP accepts that this is the proper concern of RECs. It advises that the details of the availability or otherwise of compensation ought to be put into the patient information sheet. This was very rare in practice, except in the case of healthy volunteers. One committee, wrestling with these issues at the time, argued that to advise research subjects of the non-availability of compensation was not good enough. Research subjects should not, unless in very specific circumstances, be put in the position of taking on that kind of risk without the assurance of compensation should something go wrong. The RCP acknowledges that principle to a limited extent:

> *Research subjects who are accepting risk are entitled to the information that is material to their decision to participate...* (RCP, 1990b, 16.22)

One committee stopped all uninsured research while a decision was reached about whether it was possible to get a general insurance policy to cover all research. Two others, on hearsay evidence, did the same. When a general policy could not be achieved for a variety of reasons, including cost, it was decided ultimately to set up a 'Three Wise Men' procedure to look at the likely risk in certain trials. They would be allowed if there was minimum risk, such as with venepuncture. More stringent precautions would be taken if there was some risk. Cases of considerable risk would require either disclosure to the participants in a very open way, or specific insurance cover for the trial, or both.

This problem was exacerbated by what was described on three occasions as the dislike on the part of universities as a whole for their own medical schools. Medical schools seem very expensive compared with other academic schools and departments. Universities seem unwilling, in many cases, to pick up the costs of indemnifying researchers, and a joint indemnification by the university along with the DHA or Health Board seems impossible to achieve.

The issue is a complicated one. Some of the injuries in a trial can come about through no fault of the investigator. They need not be due to negligence. Injury could come about as a result of the research design, for instance, where there were too many endoscopies (as cited in RCP, 1990b 16.17), and the patient could not take the strain, although they were conducted perfectly properly. In other words, there could be a mishap in the course of research which would not be attributable to a product, nor to the negligence of a researcher. In these cases, neither the industry nor, in many cases, the DHA, would be willing to pick up the tab. The RCP argues that 'the companies can reasonably be expected to accept responsibility for these as well as for the medicine itself (though the ABPI guidelines do not apply)' (RCP, 1990b, 16.17). But it does not appear that this would be generally accepted. The patient (or volunteer) would then have to rely on the uncertain generosity of an ex gratia payment. Two REC chairmen felt that the arrangements were wholly inadequate to cover these sorts of eventualities, and that research subjects should be made aware of their lack of protection.

Two Regional Health Authorities have issued guidelines for indemnification to their DHAs. They led to a letter being sent by the district general manager to the pharmaceutical company concerned, insisting that it adhered to the ABPI guidelines, and that it would agree to 'indemnify the authority against liability in law and expenses arising out of claims by or on behalf of patients or volunteers taking part in the trial caused directly or indirectly by the administration of the medicinal product'. These demands are clearly increasing, and other regions are expressing an interest. An example of such a letter and accompanying guarantee is to be found in Box 8.

But neither does this meet all the worries. The situation is uncertain as to compensation at present. One of the obvious answers is some form of no-fault compensation scheme, so that those who are injured in research for whatever reason do not have to go through the courts. Yet only four of the RECs observed did more than agonise over this issue. This is despite the fact that taking legal action is difficult in the extreme for those injured in research, a position the RCP obviously views as unfair upon those who have entered trials in good faith (RCP, 1990b, 16, passim). Companies or research departments could claim a 'state of the art' defence, or even a 'material risk' one. Therefore the only claim that could be brought would be for negligence, notoriously hard to prove. It would in any case often be wholly inappropriate, because there was no negligence, and the injury happened as the result of unforeseen circumstances.

Recommendations

Because it cannot be ethical to allow patients to enter a trial without being certain that they would be compensated for injury, the DoH must either rethink its statement in its guidelines, which suggests that the citizen is inadequately protected

8

CLINICAL TRIALS – LEGAL INDEMNITY

Dear Sirs,

I am writing further to your proposal that this Health Authority should agree to participate in a sponsored clinical trial involving your medicinal product.

I am writing to confirm that the Authority is prepared to participate, subject to ethical approval (and resolution of any issues in respect of revenue consequences for the Authority if appropriate) if this has not already been obtained, provided that your Company agrees to indemnify this Authority and its employees or agents against all liability in law and expenses arising from claims by or on behalf of patients or volunteers taking part in the trial or arising from the death of such patients of volunteers caused directly or indirectly by the administration of the medicinal product.

It is agreed that the indemnity referred to will not cover liabilities insofar as they arise as a result of negligence or wrongful acts or omissions on the part of the Authority, its employees or agents. The said indemnity shall not operate if the Authority or such of its agents or employees as are participating in the clinical trial do not comply with the approved trial protocol drawn up by your Company and approved by the local Ethics Committee, a copy of which is annexed hereto.

It is also a condition of the Authority's participation in the trial that your Company will accept and operate by reference to the guidelines laid down by The Association of the British Pharmaceutical Industry and entitled "Clinical Trials: Compensation for Medicine Induced Injury".

It is agreed by this Authority that it will promptly notify your Company of any claim or potential claim as soon as it becomes aware thereof. In the event of a claim being made, and your Company agreeing to provide a full indemnity hereunder, it is agreed that your Company may deal with the claim on behalf of the Authority and shall also, at its own expense, have conduct of any subsequent legal proceedings brought against the Authority. The Authority will give such help to your Company as may reasonably be required in the conduct and handling of the claim.

If the Authority decides to forego its right to an indemnity hereunder, it will nevertheless keep your Company informed of any settlement negotiations being conducted/concluded with the claimant.

This agreement shall be governed and construed in accordance with English Law.

If these provisions are acceptable, would you please sign and return the accompanying duplicate of this letter.

Yours sincerely,

DISTRICT GENERAL MANAGER

THIS DEED OF GUARANTEE is made the __ day of _____ 198__ BETWEEN _____LIMITED, whose Registered Office is situated at _____ (hereinafter called the "Guarantor") of the one part and HEALTH AUTHORITY of _____ (hereinafter called "The Authority") of the other part.

WHEREAS

1 _____ Limited, whose Registered Office is situated at (hereinafter called "The Company") has entered into arrangements with the Authority for the carrying out of a clinical trial.

2 The Company has provided an indemnity in relation thereto, the terms of which are set out in a letter dated the day of _____ 198__ a copy of which annexed hereto.

NOW THEREFORE BY THIS DEED the Guarantor agrees with the Authority as follows:

1 If the Company shall in any respect fail to comply with the obligations as set out in the said letter, or shall commit any breach of the Company's obligations thereunder the Guarantor will upon demand indemnify the Authority against all losses damages costs and expenses which may be incurred by the Authority by reason of any default on the part of the Company in performing and observing the provisions of the said letter.

2 The Guarantor shall not be discharged or released from this guarantee by any arrangement made between the Company and the Authority without the assent of the Guarantor or by any alteration in the obligation undertaken by the Company or by any forbearance whether as to payment time performance or otherwise.

IN WITNESS WHEREOF the Common
Seal of _____ limited was hereunto
affixed in the presence of:

Dated _____ 198__
_____LIMITED
to
_____HEALTH AUTHORITY

DEED OF GUARANTEE

A Gibbons, Legal Adviser, Mersey Regional Health Authority, Hamilton House, 24 Pall Mall, Liverpool L3 6AL

Source: Mersey Regional Health Authority

at present, or some form of no-fault compensation scheme for those injured in the course of research needs to be set up. This could cover universities and NHS research, or it could include all research which takes place on NHS premises.

In the meantime, RECs need to make absolutely certain that information sheets are clear about the compensation arrangements in the event of injury. University departments need to ensure coverage for their researchers and their research subjects. The present position, where the majority of research subjects – outside studies sponsored by the pharmaceutical industry – simply have no idea that they may be without any insurance protection, is plainly unacceptable.

Fear of litigation

Members of RECs have been concerned at the prospect of litigation against them, unsurprising given the indemnification concerns above. They have requested DHA or Health Board indemnification against litigation for several years. The new DoH guidelines provide for that. They state:

> *Legal advice available to the DoH is that there is little prospect of a successful claim against an REC member for a mishap involving research approved as ethical by the REC. Any such claim would lie principally with the researcher concerned and against the NHS body under the auspices of which the research took place. The principal defendants should seek to have any claim against an REC member struck out. Those members of an REC who are employees of an NHS body are already covered by NHS indemnity arrangements. The DHA should also bear all costs in the case of other REC members unless the member concerned is guilty of misconduct or gross lack of care in the performance of his or her duties and provided that, if any claim is threatened or made, the member notifies the DHA and assists it in all reasonable ways. If necessary, the DHA may give the following undertaking to this effect to REC members who are not employees of an NHS body:*
>
> *We confirm that the DHA will take full responsibility for your actions in the course of the performance of your duties as a member of the REC other than those involving bad faith, wilful default, or gross negligence; you should, however, notify the DHA if any action or claim is threatened or made, and in such an event be ready to assist the authority as required* (DoH, 1991, 2.11).

The RCP had already pointed out that a disgruntled subject of research, who did not feel that the full risks and discomforts had been spelled out to him, might take action against members of a research ethics committee corporately or severally. That is a view strongly echoed by Professor Ian Kennedy in a speech at the conference for members of RECs held at King's College, London, in November 1990. It is partly for these reasons that the DoH has provided reassurance on this matter in the guidelines.

Enforcement and sanctions

RECs do not have adequate sanctions against those who ignore their advice. In some DHAs, it would be a disciplinary offence to conduct research on human subjects without getting ethical approval first. But that would by no means be the majority. Several clinicians cited the difficulty of getting work published in reputable journals if an approval letter from a research ethics committee could not be shown, but once again this is not universal. Several clinicians thought there might be no proper insurance cover for doctors involved in research who had not got approval from an REC. But it is not clear that this would be universally true. Some university departments would not provide insurance cover for researchers who had not sought the approval of an REC. Again it is by no means clear that this is universal.

The DoH guidelines state that:

> *If it comes to the attention of a committee that research is being carried out which it has not been asked to consider or which it has considered but its recommendations have been ignored, then the REC should bring the matter to the attention of its appointing authority, the relevant NHS body and to the appropriate professional body* (DoH, 1991, 3.22)

It is not, therefore, a matter for RECs to take action themselves against those who do not bring their research for consideration, or ignore their advice. But they need to know what is going on. It is the DHA administrators, more than anyone else, who look at the function and constitution of the research ethics committees and ask questions about the degree to which there is, and should be, monitoring and enforcement.

There is a growing view amongst the members of RECs that some kind of monitoring role is to be expected of them, though very few carry it out. The DoH guidelines merely require a follow-up by virtue of researchers being required to notify the committee of changes, or of difficulty in recruiting subjects. But many RECs do not see themselves in a monitoring role at all. At the Royal College of Physicians' meeting for chairmen of RECs in February 1990, many chairmen argued that it was beyond their resources to monitor the research they had approved.

But there is a deeper concern than that, frequently expressed during this research. If the committee has no teeth, however hard it works, however carefully it comes to its decisions, it cannot fulfil its alleged task of protecting the public. It can perform a variety of valuable tasks. It can educate the medical and nursing and other healthcare staff

about how to submit a research protocol. It can teach people how to consider the issues which might raise ethical doubts. It can chew over various issues beyond strict research, but have no locus in the decision-making. It can discuss the issues relating to IVF and to surrogacy. It can question the value of various trials and procedures. But it cannot enforce its decisions. The DHAs and Boards have an important role in increasing the status of RECs. It also became clear that the newly established RECs, set up in the last few years, already have a higher status than many of the long-established ones. This seems to have come about purely as a result of being set up with determination by the DHAs and Boards rather than having grown up somewhat randomly from a small committee of doctors in the 1960s or early 1970s.

Current practice

All the chairmen said that they rely heavily on the goodwill and honesty of colleagues or doctors. Some clearly felt that the role of the REC is more to educate than to police, and others felt that the two roles are distinct and should both be carried out. Two chairmen were adamant in their view that it would be wrong for the REC to carry out any kind of policing role at all, since the committees were advisory rather than enforcement orientated. Nevertheless, the majority view was that there was a role for some kinds of enforcement. Policing is undoubtedly difficult, but all the REC administrators interviewed regarded policing of a sort as essential. That would clearly be the responsibility of the parent DHA concerned, but the REC would have a strong interest in any evidence that its advice was being ignored. Lay members also tended to take this view, as did two chairmen.

Only one REC had a computerised system which showed projects that were at the six-month and one year stages and reminded researchers that the REC required a report. Only one REC had conducted spot-checks, solely because the administrator felt they were essential. Most required notification of changes in the protocol, or of difficulty gaining subjects, but had no method of knowing whether they were being given the information. Yet adverse events do appear to be reported to RECs. On three occasions during this research, an adverse event was reported. It was felt most sensitively in committees where a death had taken place at any time, or where fraud had been recorded. All RECs observed have as part of their guidelines or as an ever-present assumption the requirement that such events will be reported.

Policy options

It is clear that the sanctions RECs or their appointing authorities can impose and the degree to which RECs need to monitor research they have approved needs clarification. Although only advisory bodies, they are well placed to find out what is happening in an individual DHA and should be charged with some monitoring function. They should also be empowered to make spot-checks on the research in progress, to ensure it is being carried out in accord with their advice. This could range from checks on the consent arrangements to checks on the recruitment policy. Unless they do this, they cannot fulfil their public watchdog role adequately.

GP studies

Despite DoH guidelines suggesting that any research conducted under NHS auspices should come to an REC, it is clear that Family Health Service Authorities (FHSAs) do not insist that GPs under their authority apply to the REC for approval. Nor is there any monitoring of research which takes place in GP practices, dental practices, in NHS trust hospitals and in nursing homes under NHS auspices. REC chairmen are concerned that the committee simply does not see all the research within the DHA.

There is particular concern about some GP studies. This is because GPs are often paid to conduct post-marketing surveillance of drugs, where studies at an earlier stage have already been vetted by the REC. In some cases, the study is not a proper Phase IV study at all, but a thinly disguised marketing exercise. Several REC members felt this was a major cause for concern, as did the medical directors of two pharmaceutical companies (who argued that such fake Phase IV studies did indeed go on, but were not sponsored by their own companies).

It is clearly the case that serious Phase IV work needs to be done. Genuine post-marketing surveillance is essential to discover the nature of side-effects. Pharmaceutical company medical directors argued that it was particularly important in a country where notification of adverse effects of drugs is in any case a rather haphazard process, relying on the energy of GPs to fill in the adverse reaction cards. But they felt that it was extremely difficult to get such studies done properly. One medical director raised the issue of fraud, saying how he personally had reported GPs to the GMC for falsifying the data, rendering the study entirely pointless (Shaw, 1991).

But it is GP and nursing research which come to a REC least frequently. In the case of GP research, it is because the REC is seen as totally hospital based. It is perceived as a DHA committee, whereas GPs are governed by the FHSA. Only once did a chairman argue that the relationship with the FHSA was so strong that the FHSA's insistence was taken seriously, namely that trials to be conducted by GPs be vetted by the district's REC. At the same time, one London

FHSA was discussing setting up its own ethics committee because it felt it would be more likely to encounter the studies GPs wished to carry out and be able to monitor what they were being paid. The issue of what patients ought to know about the financing of studies would be high on the new committee's agenda, precisely because of the worry that appears to exist in relation to GP trials.

A wider issue which emerges from this is whether it is appropriate for the individual pharmaceutical companies to conduct this Phase IV work at all, however conscientiously. Only two members of RECs seriously addressed the question of whether Phase IV studies should not be taken over by, say, the Medicines Control Agency, funded corporately by the pharmaceutical industry. This would, of course, have two effects. First, it would prevent the danger of the Phase IV studies being marketing exercises and not proper studies at all. Second, and even more significantly, it would allow the comparison between different drugs, produced by different companies, to take place.

It is clear that persuading GPs to submit their research proposals to an REC will be an uphill task. FHSAs will have to insist that they do, and RECs will have to use their GP members to encourage this to take place. The pharmaceutical industry could help by requiring that the proposal submitted be to an REC before they sanction payment.

The ethical debate

4

Although all aspects of the work of RECs are to do with the ethics of research on human subjects, there are some subjects which REC members particularly refer to as 'ethical' matters. This chapter therefore looks at the nature of the issues discussed which REC members would describe as the 'ethical' content of their meetings. Opinion is divided amongst REC members. Some feel RECs should be setting ethical standards themselves- such as clear requirements on valid consent, limits on how invasive any research might be or what research is acceptable on people who are mentally ill, in intensive care, or otherwise unable to give valid consent. Others think the job of a REC is purely to make sure, as a jury, that there is no undue invasive procedure being proposed, and that the people responsible for the research are well qualified to do it.

This chapter examines issues of consent, discussed at all REC meetings. It looks at the problems of explaining the nature of randomised controlled trials, of ensuring that consent is valid, and of designing information sheets which are comprehensible and sufficiently informative. It also considers some of the difficult cases, such as research on children, the mentally ill and mentally handicapped, and on the very frail or very sick. It discusses the problems of recruiting healthy volunteers and women of child-bearing years, and touches on the debates held at RECs which were unrelated to research issues.

Consent

It has been generally accepted that valid consent is a requirement for adults participating in research. 'Informed' consent has no particular and precise meaning in the UK as it has in the USA. Valid consent, which implies an autonomous deliberate judgement on the basis of sufficient and comprehensible information, is an appropriate term. Nevertheless, the use of the term 'informed consent' is almost universal in the debates at RECs. It is rarely defined.

The fact that consent ranks high on the RECs' agenda is unsurprising given that this research was conducted in the wake of revelations about a cervical cancer trial in New Zealand, where the British REC system had been used. Patients had died as a result of the trial (Paul, 1988). Although New Zealand is very different in some ways, major concern was expressed by REC members that the same sort of thing could happen in the UK. There was also concern about recent breast cancer trials, where patients had been randomised into treatment groups without their knowledge or consent, leading to discussion in the national press. Gaining valid consent is extremely difficult. RECs are worried by a number of factors.

Randomisation.
Randomised controlled trials – the majority of studies vetted by RECs – present a number of factors that worry committee members. First, it is very difficult for many patients to understand the principle of randomisation. Individual patients often tend to say, 'Oh, doctor, you decide what's best for me...', precisely the decision a doctor cannot make under the randomisation procedure. Second, even with improved patient information sheets and improved medical communication skills, studies of comprehension amongst patients have shown that many patients do not understand what is said to them. Third, even if the information is understood, it is hard to be certain that the element of risk, however slight, has really been absorbed.

Randomised controlled trials are not easy to design, particularly when the subjects to be studied form part of a vocal group or a particularly vulnerable one. This has been the case with AIDS patients (See Box 9), and to some extent with breast cancer patients as well, because they have strong views on trial design and patient choice. Subjects are usually randomised into groups. The randomisation in a drugs trial might then be between the old 'normal' treatment for the condition, the 'new' drug, and a placebo-controlled group who are being given no drug at all. It might merely be a two arm trial with placebo and new drug, or it might have more than three options. In any case, the significant factor here is that the patient stands to benefit if randomised into the 'best' treatment option in a therapeutic study.

Most randomised controlled trials are also double-blind studies. Neither the patient nor the doctor in charge of the patient knows what the patient is being given (although there is always an emergency code which can be broken if essential). This is done because of

> *the tendency of investigators to perceive improvement in patients who are known to have received active treatment (and of their enthusiasm to be readily conveyed to the patients who then report improvement.) This is accompanied by an understandable tendency to perceive no change in patients who are known to have received the placebo...* (RCP, 1990a, 7.97).

9

PROBLEMS OF RANDOMISATION: A CASE STUDY

This example is of a study of a new drug for patients with AIDS who were intolerant of AZT, the now standard treatment. As a multi-centre trial, it came up repeatedly at RECs, and was debated differently each time. The following paragraphs record one such debate

The trial design was two-fold. One was to test a high dose of the new drug against a low dose and placebo. But some of the patients were known to have adopted the American pattern of re-randomising themselves by sharing out the drugs outside the clinic, due to desperation at their plight. They were convinced that the drug in some dose was better than no drug. Because of patient unwillingness to be put into a no-dose placebo group, the other trial design was high-dose versus low-dose only. This was referred to as a "dirty trial."

The proposal was put by the consultant concerned to run the trial with all three arms. She was not optimistic that the patients would accept it. A lay member then queried it. She argued that if they were going to do it with all three arms at this hospital, when others had given up the attempt and were doing high versus low dose only, the patients would surely simply move to other hospitals. That would benefit nobody.

The consultant agreed that was a possibility but said she would like to try the three-arm version first. At this point she made it clear how unscientific she thought the two-arm version was. She felt that the researchers would simply not discover what they needed to know from carrying out research that was not placebo controlled. The patients would all want, by the very nature of the disease, to show an improvement. One of the lay members and the chairman said simultaneously that this made it clear that some research conducted on human beings was not pure science. Human frailty prevented it from always being so. Perhaps one ought to accept that, and not try to fight it. Perhaps the trial ought to be conducted in such a way that the patients felt they were getting every possible help.

The decision was made unanimously that the consultant should begin by consulting the patients, and try to persuade them to go into the three-arm trial. If she failed, then the two-arm trial was perfectly acceptable. It was emphasised at the end of the discussion with the consultant that some of this research was unlikely ever to be done properly. The consultant countered by arguing that it is unethical to ask people to take part in poorly designed or executed research, since the results will be less valid. But the counter-argument was put that it was precisely the patients who wanted a less scientifically sound piece of research to be done because of their predicament. The patients' choice, and feelings, had to take precedence over scientific accuracy. The trial proceeded, with a requirement that the consultant reported back two months later.

Investigators find it difficult to convey the principle of randomisation. Nor is it easy to explain bias on the part of investigators and research subjects. Various models are proposed within RECs which might make it easier. One suggestion is that patients should be pre-randomised and then asked to consent to one arm of the trial only. The objection is that they will not fully understand that they are participating in a trial, a state of affairs which almost everyone rejects as unethical. The Royal College of Physicians is clear that this is, on the whole, an unsatisfactory arrangement. Others have suggested that the subjects should be pre-randomised and not told. This is viewed as unethical unless there are exceptional circumstances, though it is difficult to imagine what these exceptional circumstances might be. One committee spent a considerable amount of time addressing a patient information sheet which suggested that taking part in the trial was likely to be of benefit to patients, it being thought dishonest to argue in this way because the whole point of the trial was that no one knew, patient or doctor, whether they were in a placebo or high or low dose group.

Consent forms

The RCP guidelines contain a good and serviceable standard consent form, to be found in Box 10, which is, as yet, only in use in one REC in the sample seen. Nicholson points out that it is

> *a very useful document which has the advantages of being short and written in user-friendly English with the requirement that the seven answers should be indicated simply as being either 'Yes/No'. Whilst there have fortunately been few legal cases in which it has been alleged that consent to treatment (and even more rarely consent to involvement in research) has not been obtained, there has been considerable discussion of this topic in recent years in Guidelines...Investigators might be forgiven for feeling overwhelmed by the expansion in the number of points which these various documents recommend that they should bear in mind in obtaining consent in practice. For this reason it was thought that it might be helpful for a Consent Checklist for Investigators to be drawn up which summarises the current considerations. This checklist has recently been adopted by Harrow Health Authority Ethics Committee...The committee thought it might be a useful aide-memoire for investigators and is thinking of printing it on the back of the Patient Consent Form. It is not, however, required that the checklist should be completed in every (or any) case, although investigators might wish to do so, particularly in difficult or unusual situations, in which it would form part of the documentation to be kept with the medical notes* (Nicholson, 1991).

This checklist, not yet in general use, can be seen in Box 11.

10

RESEARCH CONSENT FORM

TITLE OF PROJECT

(The patient should complete the whole of this sheet himself/herself)	**Please cross out as necessary**
Have you read the Patient Information Sheet?	**YES/NO**
Have you had an opportunity to ask questions and discuss this study?	**YES/NO**
Have you received satisfactory answers to all of your questions?	**YES/NO**
Have you received enough information about the study?	**YES/NO**
Who have you spoken to? Dr/Mr/Mrs	
Do you understand that you are free to withdraw from the study:	
▮ at any time	
▮ without having to give a reason for withdrawing	
▮ and without affecting your future medical care?	**YES/NO**
Do you agree to take part in this study?	**YES/NO**

Signed **Date**

(NAME IN BLOCK LETTERS):

Source: **RCP, 1990a, 7.20**

The Royal College of Physicians makes the excellent point that the written consent form 'can be used as a tool to assist patient and researcher to consider the essential components of the consent, point by point.' (RCP, 1990a 7.19) Yet few RECs suggested to researchers that that is what they should do.

Of the committees observed all were concerned with the issue of consent and all examined the method of obtaining consent in some detail. Under 50 per cent (12) had a standardised consent form, but 70 per cent had a standard application form for the submission of protocols in which the details of seeking consent were elicited from the applicant.

But discussion was more about the legal status of consent forms than about their use as an explanatory aid. Some RECs operate a system whereby the information sheet and the consent form are on the same piece of paper. Although most committees automatically keep the consent forms and the patient information sheets separate, very few try to insist that the information sheet is given on a different day, or at least at a different time, from the seeking of consent. Yet this was much discussed. The RCP guidelines (RCP, 1990a 7.11.ii) are less insistent and prescriptive on this issue than on many others: 'Time to reflect may be arranged to allow the patient to consider the question of enrolment'. Many members of RECs felt it should have been put more strongly, and that a time for reflection should be the norm. In the view of some REC members, not to provide time for consideration would in itself be unethical, unless it is a question of research on those in intensive care or accident and emergency, whose consent can only be assumed and where RECs have to be particularly careful.

Information sheets

Many patient information sheets leave much to be desired. RECs regard them as the most important part of their work after consent forms. They return an average of 35 per cent of information sheets for reworking, and ask for slight alterations in a further 20 per cent. But they fail to enforce a high quality, and some REC chairmen feel that the speed at which they are educating research applicants to provide adequate information sheets is woefully slow: 'We try to persuade researchers to use the information sheets to inform patients properly, but it is an uphill struggle, and as it is we send back 50 per cent of them for amendment'. They have to deal with resistance from researchers: 'Patients in some groups are already by the nature of their disease, such as hyperlipidaemia, very well informed and it does not have to be done by way of the consent form'. 'Patients are already extremely worried about their condition, and it seems unfair to give them additional information to what they really need...'

11

CONSENT CHECKLIST FOR INVESTIGATORS

1 Have you given the Information Sheet to the subject?

2 Have you given an oral explanation to the subject, including:

this is a research project?

participation is voluntary?

the aims of the project?

the likely duration of the subject's involvement?

the expected benefits to the subject and/or others?

the expected nature of the drug or device being tested?

that the subject may instead receive a reference treatment or placebo?

what risks, inconvenience, discomfort or distress may reasonably be anticipated for this patient?

that a refusal to participate may be given without reasons and will not affect the care which will be given to the subject?

that the subject may withdraw at any time without giving reasons and without affecting the care which will be given to the subject?

that personal information may be scrutinised during audit by competent authorities and properly authorised people, but all personal information will treated as strictly confidential and will not be made publicly available?

what compensation arrangements are available?

whom to contact in an emergency and how?

3 Have you asked the subject:

for authorisation to approach his/her GP and for permission for the GP to disclose medical information?

to tell you if he/she is or has been involved in any other research studies?

to tell you if he/she is or has recently been taking any other medicines or preparations?

4 If you have answered "No" or not answered any of the above questions in section 2 or 3, record why:

5 Have you allowed the subject sufficient time to consider the matter on his/her own, discuss with others if wished, or ask you questions?

6 In your opinion, has the subject understood and consented to take part in this research?

7 Has the patient signed and dated the consent form? (This is essential for non-therapeutic research)

8 If not, has the consent form been signed and dated by some other independent person (usually a senior nurse) recording that the subject has understood and given consent?

9 Or, for a procedure of less than minimal risk, in therapeutic research (e.g. taking blood) has consent been documented?

10 If the subject is not capable of giving consent:

has the relevant Ethics Committee agreed to this research in principle?

are you of the opinion that this patient's participation will promote the welfare and interest of the patient?

has signed, dated consent been obtained from any legal representative of the patient?

11 If neither the patient's signed consent nor witnessed oral consent has been obtained, explain why.

(checklist written by Christopher Hodges of McKenna & Co)

All good information sheets deal straightforwardly with the patients. They make it clear that the optimum treatment is not known (because, if it were, the research would be unjustifiable). They make it clear the patient can withdraw, and that there is gratitude for their participation. They also make it clear that there is some risk, if minimal, in being involved in the study, something continually pressed by REC members. They should say something about the finances, a vexed issue at RECs. Some REC members take the view that research subjects, other than healthy volunteers, should not know that there is financial benefit to the reseachers or the department. They feel this because undue pressure to help the department might be applied if patients knew that by entering a trial the department would be better off by £500. Others feel that patients should know – and should be able to question researchers on – the extent of the true scientific interest, and the extent to which the study is a money-maker.

Gaining Consent

Many RECs advocate that another person should be present when the doctor is seeking consent from a patient to take part in a trial. This is in order to avoid undue pressure on the subject, and so that the other person can go through the details afterwards with the patient. But several REC members, particularly nurses, are privately concerned that if that other person is a nurse, she will be under pressure to help the doctor gain the patient's agreement.

Furthermore, unless the committees take on a 'policing' role beyond their remit and something with which many of them are uncomfortable, it is difficult for them to make sure that consent has genuinely been sought and given. Yet the DoH guidelines are explicit in requiring that 'for

therapeutic research consent should be recorded in the patient's medical records' (DoH, 1991 3.8.)

Unless a copy of the consent form is filed in the notes, it cannot be assumed that consent was properly sought and given. Even then, it is hard to know whether the patient understood. This is an issue which concerns many REC members.

To add to that, there are specific problems with the reading abilities of the general public. They may not understand a written information sheet as well as they would understand a video. Good videos about the principles of randomised double-blind studies are not freely available for patients to borrow. Fruitful and useful work could be done to improve patient understanding. One London teaching hospital's information service provides an excellent if simple book about clinical trials. Even there the difficulty of explaining the principle of randomisation is considerable. To help patients deal with their concerns, the organisation Consumers for Ethics in Research have produced a leaflet with the title 'Medical research and You'. The suggested list of questions for the public to address if they are asked to take part in a research project is reproduced in Box 12.

12

MEDICAL RESEARCH AND YOU

QUESTIONS FOR RESEARCH SUBJECTS TO ASK

- **what will happen to me?**
- **do I have to say Yes?**
- **what will happen if I say No?**
- **do I have to decide at once?**
- **what is the research for?**
- **how will the research help me?**
- **can research be done on my child?**
- **what is a randomised trial?**
- **what is a blind trial?**
- **what is a placebo?**
- **can I change my mind?**

(CERES, *Bulletin of Medical Ethics* Bulletin, 67, p.4 April 1991)

Therapeutic Trial Benefits

If the subject is fortunate enough to be randomised into a group where the drug is beneficial, there is an additional problem. The study is likely to be for a limited term. By the time the drug seems helpful to the individual, the trial is often ending. In most cases, there is unlikely to be any special generous arrangement by which extra supplies could be provided. In exceptional cases, supplies are provided for patients after a trial is finished. This can either be done on a named patient basis, recorded occasionally in the observations, with particular new cancer drugs, or it can be done by virtue of a Doctor's or Dentist's Exemption Certificate from the Medicines Control Agency, where a group of patients is to be given a drug. This becomes what is effectively an uncontrolled trial. It can go on indefinitely. The named patient basis is usually used for giving drugs to small groups on compassionate grounds.

RECs debate this at length. They regard it as difficult to justify testing a drug on a patient which begins to be helpful and is then stopped. They find this particularly disturbing with some of the anti-depressants and other drugs where efficacy cannot even begin to be judged in less than two or three weeks. In some cases, they regard beginning the study in the knowledge that disturbed patients would have to come off the drug again very quickly to be unethical.

Children

There are particular problems with studies to be conducted on children. A child is not thought able to give informed consent. The prevailing view is that research on children is unethical unless the child him or herself stands to benefit from it.

The RCP has produced guidelines on the issue which suggest that research on children which is non-therapeutic but which benefits other children, and can only be done on children, is in fact justified (RCP, 1990a, 7.25). They base this view largely on the guidelines of the British Paediatric Association (1980). This concerns members of RECs considerably. Several voiced a doubt over the way research was conducted, particularly on neonates.

The Department of Health and Social Security's (DHSS) view of 1975 had been that consent by a parent or guardian to non-therapeutic research was not enough to bring it within the law. The DoH guidelines of 1991 echo this, arguing that the consent of a parent or guardian for therapeutic research is essential, and that for non-therapeutic research the child must be subject to no more than minimal risk as the result of his/her participation.

> *Those acting for the child can only legally give their consent provided that the intervention is for the benefit of the child. If they are responsible for allowing the child to be subjected to any risk (other than one so insignificant as to be negligible) which is not for the benefit of that child, it could be said that they were acting illegally.* (DoH, 1991 4.4)

Yet the definition of minimal risk poses problems for RECs, since opinions vary considerably, as can be seen in the debate recorded in Box 13. Questions

13

RESEARCH ON CHILDREN:
AN ILLUSTRATIVE DEBATE

The protocol was for a preparation for allergic rhinitis. The preparation was to be given over a two-month period. Parents were to keep a diary of symptoms. Half the children recruited were to get the new preparation, as a nasal spray. Half were to get placebo. This was a pharmaceutical company sponsored study, and was being carried out on a multi-centre basis. Children were to be aged five to twelve. The debate ran along the lines that it was not a sufficiently serious condition to warrant trying out a new preparation on children when there were adequate treatments on the market for those who were really troubled.

The GP member said that he did not think there were adequate preparations for all cases. He thought there was a tendency to prescribe things when children should learn to live with some conditions. The pharmacist argued that he would not let his children take it. He was shocked that the preparation was being tested on children before the data were fully available for adults. A trial on adults was in progress at the time. He did not feel they should pass it. One of the medical members argued that they should allow it. But the information sheet (provided by the company) should state that if the symptoms persisted for two weeks or more, the child should come back. A change of prescription would be made. In other words, they did not want children to be penalised by the placebo, if that was where they fell in the randomisation.

One doctor asked whether the older children could not assent to the trial. The lay member said she thought that the ten-year olds and up should be asked to assent. The pharmacist said he thought younger children should get a full explanation, and that they too could probably assent. The chairman said that parents should give consent.

It was pointed out by three people that parental consent was of no legal significance. He argued it was of strong moral significance. (Consent by a parent does have legal significance if the research is therapeutic, and is essential in trials conducted on children under sixteen, according to the new DoH guidelines.)

The pharmacist asked them to undertake a risk-benefit analysis. Was the gain likely to be sufficient to make the risk worth taking in a preparation with data on adult reactions not yet known? The committee agreed, and decided it was not worth taking. They agreed to ask the researcher to come back when adult data, adverse reactions and benefits, were known, when they would reconsider. The debate about whether the research should be conducted on children at all never took place.

as to whether a pure risk-benefit approach of a utilitarian nature is the best one for this vexed issue are raised at RECs. Some regard it as unthinkable that children should be research subjects in any circumstances other than for their own potential benefit. Others view research as a public good, and to be encouraged, and see no reason why children of parents who are sympathetic to scientific advance should not participate in research projects. Of all the issues raised at RECs, this one seems the most likely to continue, and to be the one which requires wider debate between RECs and others.

The mentally disordered

The DoH guidelines state that:

> *research on mentally disordered people requires particular care and sensitivity bearing in mind that they are vulnerable and some may not be able to give consent. There is a need to weigh the rights of an individual to consent or refuse to take part in research, and the particular status of those unable to consent, against the need for research to advance the knowledge and treatment of mental disorders.* (DoH, 1991 4.7)

There are legal and moral questions about whether consent sought from a relative of a mentally ill or mentally handicapped person is in itself adequate. The DoH argues that there is no provision in law for this to take place, but 25 per cent of the RECs observed allowed such proxy consent.

The level of debate on research on the mentally disordered was much lower than that on the subject of children. Despite the legal complexities, there was little concern about consent except in two committees. It is clear that this is an area where RECs are uncertain, and have tended to ignore the difficulties. Yet there was a considerable number of pharmaceutical trials of anti-depressant and other drugs for the mentally ill.

Recruitment issues

Healthy volunteers

The recruitment of healthy volunteers poses major problems for some RECs. Some NHS institutions operate like the contract research houses, with a regular bank of healthy volunteers who are paid for their time and trouble. But the majority do not have this system. RECs are faced with healthy volunteers who turn out to be the students of the lead researcher, despite the Royal College of Physicians being convinced that this can lead to difficulties. In those institutions where researchers no longer ask for medical student volunteers, their places have often been taken by nurses; here some of the same concerns may apply, though less acutely.

RECs often query both the amount of the payment and the nature of the recruitment of

healthy volunteers, and tend, except in a few institutions, to discourage the use of medical students. This is an area where RECs need stronger national guidelines.

Women

Some researchers argue that the population to be studied, with the required exclusions, may not provide adequate and unbiased evidence. This issue is now receiving considerable attention in the United States as a result of the exclusion of women of child-bearing age from many studies. Consequently little knowledge is obtained about how women of a relatively young age-group are affected by the drugs being tested. The possibility of litigation has led to the exclusion of women of child-bearing age from much research. These women are, in the words of three researchers who also served on RECs, apparently 'not always to be trusted to say whether they are pregnant or not'.

However, the costs of compensation if a child is born handicapped as a result of a trial could be enormous. The fear of another thalidomide case is very much in the minds of many pharmaceutical company executives when talking about this issue. There is now a US Senate committee looking at this, and the National Institutes of Health have established a permanent Office of Research on Women's Health. Nevertheless, the General Accounting Office of the United States reported in June 1990 that progress on dealing with the issues raised in 1985 by the US Public Health Service Task Force on Women's Health had been unacceptably slow. It was only in July 1990 that Dr. William Raub, then acting director of the National Institutes of Health, agreed 'that the matter warrants sustained, high priority attention' (White, 1990). This is essential if women are to be included in research at all, since the fear of the pharmaceutical industry, post- thalidomide, is of devastating effects on unborn children and consequent massive pay-outs.

Nevertheless, the exclusion may raise several questions. First, should women be asked to sign statements that they are not pregnant? Second, should women who are using contraception regularly not be included in research studies? Third, how is it possible to acquire detailed information about drug effects on younger women? REC members frequently challenge the exclusions, but end up accepting the status quo.

Local Factors

Population type

One of the justifications frequently made for having local RECs is that they can be representative of local populations. In fact, this is barely the case in debate. RECs in districts with a high Muslim population originating in the Indian subcontinent, for instance, were not concerned about modesty requirements of female patients or the adequacy of translated information sheets and consent forms. RECs, with one exception, in districts with very mixed populations in race and language did not query the exclusion of non-English speakers from a variety of questionnaire – based psychological studies. RECs with a high Catholic population did not question local sensitivity to embryo research.

Where local factors did come into play was in the discussion of recruitment. It was felt that many groups within the population did not understand the nature of the research proposals at all. These RECs debated whether they had a duty to carry out some outreach work within their own communities, to explain about research, and to encourage participation.

Non-research issues

Only two committees regularly reconstituted themselves at the end of their full meeting addressing protocols to look at any other ethical matters which people within the DHA or institution concerned wanted to bring to their attention. In one case, this was unofficial. In the other, it had been standard practice for so long it was regarded as the norm. The sorts of issues which arose were varied, but displayed a need for a forum in which concerns of these kinds could be debated. Amongst the issues were questions about life-sustaining treatment against patients' wishes, about different views of patients' wishes between doctors and nurses, and about disagreement between clinicians and their students over appropriate treatment, when the students had been shown to be more up-to-date with their information. There was also one example of a research-related issue, concerning the breaking of the randomisation code in a randomised controlled trial, where the subject wanted to know which arm of the trial he had been assigned to.

The main concerns REC members referred to as 'ethical' were largely relating to consent. It was in this area that they most concerned themselves with human subjects' rights, and in this area that they felt they had most to contribute. The debates were held with great seriousness and devotion to duty. Although they were frequently somewhat chaotic in debate, many RECs achieved a considerable degree of consensus, as well as shared misconceptions.

5 | Conclusions

Research on human subjects is a vital part of furthering human knowledge. It ranges from research carried out broadly within the NHS to research carried out in academic psychology and anthropology departments all over the UK. It can be as invasive as requiring additional gastroscopies, and other procedures, to apparently unintrusive questionnaires about eating habits. In the medical area, it involves a considerable amount of testing of new drugs, as well as detailed questioning about the nature of disease. All research involving human beings carries with it the risk that the subjects will be unaware of the full significance of what they are being asked to do, and that they will sometimes be asked to enter research studies which are poorly designed, carry some material risk, or could in some way cause emotional or physical distress.

It is for these reasons that RECs were set up in the first place, and it is these concerns they bear in mind. Yet RECs observed in the course of this research have limited objectives, to the extent that few vet research other than that which is conducted on NHS patients, leaving academic departments to set up their own RECs, such as those at Liverpool, Hatfield and Sunderland Polytechnics (George, 1989). Nor do RECs have the power to insist that all research within a DHA is presented to them. That rests with the DHA itself, or the FHSA, leaving the REC to proceed as an advisory body, examining only the material with which it is confronted.

It is clear from observing RECs in operation that they take their task very seriously. Both chairmen and members devote a considerable amount of time to the work, and all were concerned to carry out their task as efficiently as possible, protecting human subjects, protecting would-be researchers and encouraging good research. The fundamental flaw in their operation was their own lack of clarity as to what their task should be. They had taken on board Stephen Lock's *BMJ* editorial of January 1990 that it was time the profession put its house in order, but they were unclear how this could be achieved. Most were concerned that they should be, and be seen to be, public watchdogs, but were dubious that they were fulfilling that role adequately at present.

The overall impression is one of RECs doing the best they can in difficult circumstances. Some were exceptionally devoted, and were at the forefront of discussions about how these issues should be dealt with. But problems have been caused by delays in publication of the DoH guidelines, finally issued in August 1991 after the original draft appeared in October 1989. Difficulties have also arisen from proposed European legislation, making REC members concerned that they will have to change practice yet again. They have also arisen from a confusion between the role of a research committee vetting proposed research for its scientific quality, rather than for its problems as far as research subjects are concerned. There is ambivalence arising from the sense that REC members should be supporting and facilitating research rather than criticising it, and from the knowledge that RECs have inadequate powers, and often insufficient status, within their DHAs.

Thus, although the new DoH guidelines for RECs were published as part of the Citizens' Charter in August 1991, the power of RECs is limited and the extent to which they have a relationship with the public, whose rights they are supposed to protect, is inadequate. Although most RECs take their public watchdog role seriously, they are not the final arbiters of whether research can go ahead; that rests with the appointing authority. They have no powers to insist that all research proposed is submitted to them; that also rests with the appointing authority. Whilst they can, and do, raise questions about research carried out for income generation purposes, it is not, in the end, up to them to decide whether that is to be encouraged, discouraged, or irrelevant to the final decision.

For these reasons, the confusion about their role is a genuine one. They often fall between what could properly be called research committees and what ethics committees should be, at the same time as having few powers and an advisory role which is taken more or less seriously according to the appointing authority concerned.

It is remarkable, therefore, that on the whole they perform much of their task with such energy and enthusiasm. But it is unsurprising that they do not perceive themselves as general policy makers, nor as the imposers of standards of what is acceptable and what is not.

Nevertheless, there are major tasks they should be performing in which many of them fall short. Amongst these is their role in the public arena. Rather than maintaining their present secrecy, as many do, they should make sure the public knows of their existence by virtue of an annual report, lodged with the CHC, by holding

open discussions on general principles, and possibly by being open to hearing complaints from research subjects who regard themselves as dissatisfied. Rather than operating on a case-by-case basis in all circumstances, they should publish, for distribution within their local area, guidelines about what kind of research involving human subjects is regarded as acceptable. Rather than waiting for protocols to be submitted to them by would-be researchers, they should encourage researchers to submit proposals, and perform an educational role, thus improving the quality of information given to research subjects.

All these are proactive roles RECs could take on. It would give them higher public standing and greater standing within their own institutions. It would make it clear that their role is both to act as public watchdog and to encourage good quality research. But in order to achieve that, many basic questions need to be addressed.

- There must be a serious attempt to standardise the major variations in their membership and practice, including their appointments system. This will require networking between RECs and a far greater degree of cooperation between them and shared training for their members.
- Vexed moral questions must be taken on board in a more systematic way, such as issues relating to research on children, or the mentally disordered, or payment to healthy volunteers.
- They must have a clear channel of communication with the public as well as with their appointing authority.
- They must resolve issues where research is uninsured, or where risk is considerable.
- They must be clear about how their advice is to be enforced.
- They must be involved in some monitoring role of research they have approved.
- They must be clear that all research – GP, dental, hospital, and academic – within an area, is to be considered by them.
- They must be clear about valid consent, and apply uniform standards in consent forms and information sheets for research subjects.
- They must be responsive to the particular concerns and needs of their local population.

These considerations lead to detailed proposals below, which would much enhance the work of RECs. But they leave some major concerns unresolved, notably issues about research policy, which RECs do not address but are well placed to discuss because of the research they examine, and questions about the funding of research, and whether it is appropriate for research to be conducted purely for income generation. But most important is the issue of whether RECs need to have their hand strengthened by statute. The extent to which RECs followed previous guidelines from the DoH or the RCP was limited. There is a strong argument in favour of legislation in this area, both to ensure proper public protection and to give RECs the degree of power and influence they need if they are to be able carry out their tasks properly. With legislation:

- it is likely that funding would be found for proper monitoring, some form of policing, and for adequate staffing.
- it would become the norm for committee members to be trained on a regular basis.
- RECs would be perceived as an essential part of the research machine, rather than, as in some cases, an irritating barrier which has to be overcome.
- the public could rest assured that all research conducted on human subjects would have been vetted by a properly constituted committee of people from different backgrounds, well-informed and properly trained to carry out their task.

Thus, although recommendations follow which would improve and standardise practice, the major recommendation of this report is that there should be legislation to strengthen RECs' role, and to empower them to carry out their genuine tasks properly, with the support and training they require.

DETAILED RECOMMENDATIONS

The constitution and workings of the RECs

1 Membership should be kept to between eight and 12 members.

2 At least one third of the membership should be non- medical and independent of the DHA.

3 Among the members should be hospital doctors, at least one nurse (preferably one with regular patient contact), and a GP. It would also be desirable to include a pharmacologist, pharmacist or pathologist.

4 Greater efforts should be made to recruit high calibre lay members from more diverse backgrounds. CHCs should always be asked to put suitable candidates forward, though final decisions would continue to rest with the DHA.

5 Committees should consider having hospital doctor members elected in order to give the REC higher status.

6 No member should serve consecutively for more than 10 years. It would be acceptable for lay members to serve longer than medical members because of the time it takes for them to become used to the material.

7 RECs should publish their constitutions, and also an annual report.

8 Greater efforts should be made to set up training sessions for members of RECs. These should be cross-disciplinary and bring together members from different RECs. A newsletter and an association of RECs would also help to avoid a sense of isolation and lead to more standard practice.

9 New members of RECs should be given a basic reference package consisting of DoH, RCP, and ABPI guidelines, as well as the WHO CIOMS guidelines, the British Paediatric Association's working party report on the ethics of research in children, and the HFEA Code of Practice. In addition, members should be regularly circulated with the Bulletin of Medical Ethics, the contents page at least of the Journal of Medical Ethics, and suitable and useful articles from the medical and nursing press.

10 More should be done to encourage informal interaction between members by provision of refreshments at meetings and by having an occasional lunch or dinner.

11 Chairman's action should be permitted under carefully defined conditions, at least for those committees which do not meet monthly.

12 It is essential that committees keep proper records to enable them to report to their appointing authority, check on previous decisions, carry out some follow-up on applications already made and refer back to decisions in case of any problem. They could also reduce the burden on themselves by having standard application forms. RECs are understaffed.

Consent and other ethical issues

1 A standard consent form would make it easier for research subjects and researchers to understand what is required of them. It should not be on the same sheet as the information sheet.

2 A consent checklist for investigators, agreed with local RECs, would also be helpful.

3 Information sheets should be given to potential research subjects in advance where possible.

4 Information sheets should be clear, concise, and honest. They should inform the research subject about the study, about financial benefits to the researchers, the subjects, and the institutions. They should also be explicit about risk, and about insurance cover in case of injury.

5 Where possible, someone other than the researcher should be present when consent is being sought.

6 Consent form copies should be kept on the patient's file.

7 More public education is needed for people to understand randomised trials.

8 Research subjects should not be told it is to their benefit to be entered into a trial.

9 The issue of research on children needs to be fully debated again. Practice does not accord with guidelines, and REC members are concerned.

10 Similarly, issues about research on mentally disordered people need to be more widely aired than in the professional press. RECs are not sufficiently concerned about this, but practice is variable.

11 Healthy volunteers should not be recruited from amongst the researcher's own medical students because of fears of undue pressure. Strong national guidelines need to be drawn up on this issue and adhered to.

12 Allegations of gender bias in research design should be investigated. Exclusion of women of child-bearing years from pharmaceutical trials may not always be justifiable. RECs need to consider these issues more carefully, rather than accept the pharmaceutical company's exclusion criteria.

13 Concerns of the local population should be born in mind by RECs.

14 DHAs and institutions should think about a place for debate of non-research ethical issues. In many institutions and DHAs the REC is not ideal, but it serves the purpose unofficially.

Policy Issues

Research Design

1 In DHAs and other places where there is a large amount of technical and complex scientific and medical research, there should be a separate research methods committee which can vet the research design for scientific validity.

2 In all other situations, RECs should be encouraged to co-opt specialists for individual meetings where appropriate, to comment on the methodology of particular projects.

3 A national committee for multi-centre trials should be instituted, with clear limitations to its role, so that it vets purpose and method but allows RECs to opt in or out.

4 Student research should be considered very seriously and not left to chairman's action. The public should be protected from invasion of their privacy, but students should be encouraged to learn research methods, including submitting a protocol to the REC. If student protocols are a great burden on an REC, it should set up a sub-committee, with both medical and lay members, which would advise the REC on them.

Financial issues

1 Financial arrangements should always be declared to an REC. This should include details of payments to researchers, subjects, research funds and departments, monies to be used for equipment for a department, and the per capita payment to be made, plus the numbers to be recruited into the study.

2 RECs should consider carefully whether the payments constitute an improper inducement to researcher or research subject.

3 Because per capita payments are likely to persist, despite the RCP view that they are unethical, it is essential that RECs know what is being paid on a per capita basis in other DHAs.

Legal liability

1 RECs should ensure that they understand the precise nature of any indemnification offered to research subjects. They should consider whether it is ethical to allow research subjects, particularly those who might be vulnerable, to enter a trial when there are inadequate safeguards in case of mishap.

2 RECs which see a great deal of university sponsored and purely academic research should consider setting up a 'Three Wise Men' system to look at all uninsured research, and to recommend to the REC as to whether they think it carries more than minimal risk.

3 The DoH should be asked to reconsider its position on compensation for mishap, and RECs should join with researchers and others in pressing for a no-fault compensation scheme for the victims of mishap in research.

4 RECs should ensure that information sheets for research subjects always explain in full what the position is on compensation. They should not be satisfied with a statement which merely records that the research in question is not indemnified, but require explanation of that statement.

5 REC members who are not NHS employees should be reassured by their appointing authority that they will be indemnified in any case brought against them as members of the REC.

Enforcement and sanctions

1 RECs and their appointing authorities need to have a clear view about how REC advice is to be enforced. DHAs should make it a disciplinary offence to conduct research without the approval of the REC.

2 Some monitoring is essential if there are to be any teeth to the public watchdog role. This could be done by the DHA or the REC. The REC is well placed to take a view on what it has approved and amended. It should therefore be responsible for the monitoring, but a paid official of the DHA would need to be responsible for carrying it out.

3 Monitoring should include reports back from researchers on a regular basis, and specific reports of difficulties, changes in research design, difficulties in recruiting subjects, or mishaps. There would need to be the possibility of spot-checks on consent, research information, and methods of recruitment.

GP studies

1 The DoH guidelines should be followed closely. All research carried out in an NHS setting should go to an REC. RECs should encourage GPs to submit research, and FHSAs should insist that they do so.

2 Emphasis should be placed on the important role pharmaceutical companies could play in refusing to pay GPs for Phase IV studies if they have not sought the approval of an REC.

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Other r *g* ***include:***

Financing Family Health Service Authorities: the allocation of their administrative resources, Occasional paper No 3, Michaela Benzeval and Ken Judge, 1991, £5.00 + £1.00p p&p.

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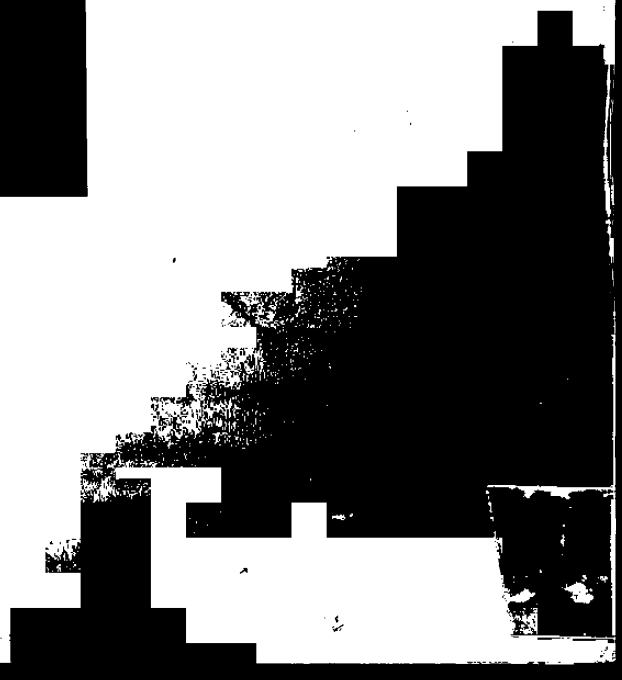

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