Better research ethics committees: comments on guidance from the Department of Health and the European Community

The disparate procedures and uneven standards operated by local research ethics committees (LRECs) are a cause for concern. The Royal College of Physicians (RCP) has published guidelines on practice [1], and has continued to give advice, but the College carries no authority to demand that its advice be implemented to meet the criticisms levelled at LRECs. It is necessary to offer formal authoritative guidance on how LRECs should proceed, to whom they are responsible, and to define the role of health authorities.

The Department of Health (DoH) has now issued formal guidance on LRECs [2]. This requires every health district to have an LREC, and gives detailed directions. At much the same time the European Community (EC) issued important amendments to its directive to govern the conduct of clinical trials in the development of medicines (that is, in applications for product licences) [3]. Governments in EC countries are under an obligation to incorporate its provisions in national law. This directive too requires the research with which it is concerned to be referred to an ethics committee. There is also EC guidance on good clinical practice for trials of medicinal products in the EC [3]. This latter document is directed primarily towards the pharmaceutical industry, but also to all who are involved in the generation of clinical data for inclusion in regulatory submissions for medicinal products. It is theoretically possible that LRECs may find themselves applying rules for industrially sponsored drug studies that differ in some respects from those for research in general. But the EC document adds that its principles can be applied more widely by those who undertake experimental investigation in human subjects, and research subjects may reasonably expect that the standards applied will never fall below those of the EC document.

In this paper we offer a commentary on selected aspects of the DoH document, Local research ethics committees, that may be useful to LRECs and to NHS management (numbers in brackets refer to paragraphs in the document), and relate it, where appropriate, to the EC standards.

Scope of DoH guidance

NHS research

The DoH document applies to research 'which will take place broadly within the NHS' or 'under the auspices of an NHS body' (1.1) or where there is 'use of, or potential access to, NHS premises or facilities' (1.3). The NHS bodies referred to are district and special health authorities, family health services authorities, and NHS trusts (1.2). Other classes of research are listed and include the recently dead 'in NHS premises' (1.3).

Relations with NHS management and management responsibility

LRECs 'are not in any sense management arms of the district health authority' (DHA) (1.1), and members are not 'in any way representative of, nor beholden to, any of the NHS bodies which collaborate in its establishment' (2.2).

Joint NHS/university LRECs are not mentioned and are, we assume, acceptable, but some of the university work will be non-NHS research (see below).

'The NHS has a key role in enabling' research (1.1) and 'the approval of research projects is an important management responsibility, involving availability of resources, financial implications, and ethical issues' (1.1). Resources and finance 'are generally best left to the local management team' (1.1).

After listing the classes of activity that require independent ethical review (1.3), the document states that 'no NHS body should agree to such a research proposal without the approval of the relevant LREC. No such proposal should proceed without permission of the responsible NHS body' (1.4). This clear statement of dual assessment would seem to prohibit delegation by management to the LREC of its responsibility to issue...
the final approval. Thus LREC approval alone is not, as hitherto, sufficient to allow research to proceed.

Our understanding is that while consideration of resources and finance will be the principal concerns of management, it has authority to override, on ethical grounds, a favourable LREC recommendation, but not to reverse an unfavourable ethical recommendation.

A possible interpretation is that, after, or in tandem with, LREC review, management would assess a statement, provided by the investigator, on resource and financial implications. When the outcomes of both ethical and resource reviews are satisfactory, then, we suggest, a person designated by the DHA, eg the director of public health (of the DHA), would act to issue the final approval on its behalf. The process should not require a new committee. Reasonable nationwide conformity of the decision-taking process seems desirable, and it would seem sensible for NHS managers to get together and recommend procedures for management approval of research projects.

It does not seem wise, or indeed acceptable, to seek to streamline the procedure by appointing manager(s) to LRECs (as members or observers); nor is this envisaged in the document; indeed, ‘LREC members are not in any way representatives’ of the groups from which they are drawn (2.6).

Management is responsible for providing ‘adequate administrative support’ for the LRECs (HSG (91) 5) [2]. Our information is that many LRECs currently lack adequate administrative support.

**Non-NHS research**

Research that does not involve ‘NHS patients, records, or premises’, eg some research conducted by ‘private sector companies, the Medical Research Council, or universities’ (1.6), may be submitted to LRECs for advice ‘by agreement’ (1.6), and this ‘should be encouraged’ (2.17), subject to the body concerned paying the cost of the LREC assessment and providing ‘full indemnity . . . against the possibility of future legal action’ (2.17). The ‘cost of the LREC assessment’ will have to be calculated and notified to the health authority management by the LREC secretariat. It is no doubt envisaged that the cost will comprise travel expenses and secretarial time; it is not clear whether the professional time of members should be charged for.

Since NHS management is concerned only with, and has responsibility only for, NHS research, its approval for non-NHS research is not required. In consequence, the DHA indemnity to LREC members (see below) is considered not to apply, and it is up to LRECs to ensure that they are covered for the assessment of non-NHS research, including possible legal action against individual members (see below). Whether the fact that management has billed the research sponsor for LREC costs permits it to dissociate itself in this way could give rise to argument.

**Membership of LRECs**

The DHA should consult ‘local professional advisory committees and relevant health professional associations’ in addition to NHS bodies (2.7) regarding appointment of health professionals. It is not clear what bodies are meant. Lay members should be appointed after consultation with the Community Health Council.

**Legal liability of members of LRECs (2.11)**

**NHS research**

‘DHAs will wish to advise appointees on these matters’. Members who are NHS employees are covered (against a charge of negligence) ‘by NHS indemnity arrangements’. General practitioners are covered (against a charge of negligence) by membership of one of the medical protection organisations. (Medical members who serve after retirement should look to their position.) But lay members do not fit these medical categories and are offered indemnity for any costs, including those of defending a writ, and damages, provided they are not guilty of ‘bad faith, wilful default, or gross (our emphasis) negligence’. We do not think it useful to seek to establish grades of negligence, nor do we know how they might be assessed. NHS indemnity does not stratify negligence. Of course no individuals deserve to be protected against their own gross misconduct, but refusal by the NHS body to take responsibility for such a member (having small resources, as is likely) could, in some circumstances, have serious consequences for research subjects seeking compensation for injury. Health authorities themselves have a duty of care to appoint only appropriate members.

We think that all members of LRECs should be offered the same comprehensive indemnity—they are all volunteers performing a public service, after all—and that, if the NHS body has to pay costs and compensation (damages) on behalf of a LREC, it should reserve the right to seek reimbursement from any member(s) who can be shown to have been guilty of bad faith, ‘gross’ negligence, etc., rather than to disown defaulting or negligent members so that an injured subject might be left without redress. In this paragraph (2.11) it seems to us that, in its desire to protect itself (and the NHS), the DoH is in danger of losing sight of the principal objective, ie to protect research subjects.

**Non-NHS research (see above)**

To obtain an effective indemnity there will be a need for legal input, whether supplied by a legally qualified member of the LREC, by the legal adviser to the DHA, or by an outside solicitor (whose fees would, no doubt, be included in the cost charged to the research sponsor). We doubt that a simple form appropriate to all
situations can be laid down: in our experience, research sponsors will often have their own ideas on the matter and will wish to negotiate.

Although ‘there is little prospect of a successful claim against a LREC member’ (2.11), the temper of modern society is such that writs issued against all and sundry are likely to become more common. Writs have to be answered even where it is probable that they will eventually be withdrawn or defeated. Answering a writ is costly in terms of both money and anxiety. Members of LRECs, especially those not members of a defence organisation, will reasonably wish to have adequate protection.

Working procedures

Standing orders should be drawn up by the DHA, and ‘situations in which chairman’s action can be taken should be clearly described’ (2.12). No guidance is offered; model standing orders for local use or adaptation would have been useful, and should be produced, perhaps by the Royal College of Physicians. Reasons for rejecting an application should be given and recorded for ‘the LREC should always be able to demonstrate that it has acted reasonably’.

‘Conducting business by post or telephone should be discouraged’ (2.12). We think it reasonable to use these modes to expedite minor business arising out of a meeting and forming part of the review process, eg approving variations in a patient information sheet sought by the LREC.

The LREC should submit an annual report to the DHA which should be open to public inspection; it should include a list of proposals (presumably the titles) that ‘were approved, approved after amendment, rejected or withdrawn’ (2.16). But applications are amended, withdrawn, and rejected for a variety of reasons, many quite innocent, and we think it would be undesirable that all such listed applications should be suspected of being attempts to engage in unethical behaviour. The title of a project will often allow identification of the department and even of the individual applicant. We appreciate the intention behind this advice and we do not wish to protect people who should not be protected. But we are uneasy about the proposal. The RCP advises [1] that the titles only of projects approved should be listed in the annual report, and we think this should satisfy legitimate public interest.

Multicentre research (2.18)
The DoH advises voluntary arrangements of collaboration between LRECs. This would only be practicable if adequate administrative resources are supplied. Proposals for central assessment of large and national studies are under discussion, but there is no suggestion that LRECs will be bypassed or overridden.

Scientific merit

‘The LREC will need to know: has the scientific merit of the proposal been properly assessed?’ (3.2). We interpret this as meaning that the committee has a responsibility to satisfy itself. It may, according to circumstances, have to rely on the known reputation of the investigators and their department, or ‘on its own initiative to seek the advice of specialist referees, or co-opt members to the committee, so as to cover any aspect, professional, scientific, or ethical, of a research proposal which lies beyond the expertise of the existing members’ (2.10).

Since LRECs should be comprised of four classes of members (not exceeding 12 members in all) (2.4,5), matters beyond their scientific expertise may be fairly common; and local experts may be involved in the proposal. Some committees, apprehensive of the possible legal consequence of not fulfilling this official guidance to the letter, may feel tempted to embark on what could amount to a research council type of independent scientific review. We do not think this is practicable other than in exceptional circumstances, and we doubt whether routine use of such expensive (in time and resources) procedures by the hundreds of LRECs in the country can be what is intended. We note that the Medical Research Council will only conduct scientific review of grant applications after an LREC has given its approval.

Personal medical records

LREC review

‘An LREC must be consulted about any research proposal involving access to the records of past or present NHS patients’ (1.3). However, an exception is made for ‘certain enquiries and surveys involving only (our emphasis) access to patient records’ (3.14). ‘Examples’ of these are given (3.14 and Appendix A), some of which can also involve patient contact. But we are given to understand that the list in Appendix A is definitive, and to be enlarged only by the DoH. This matter is of particular importance to epidemiologists who have found that some research that is undoubtedly in the public interest has been seriously impaired by the impracticalities and delays imposed by consultation with large numbers of LRECs. We wonder whether it should really be necessary to seek prior ethical approval in such cases from the LRECs in every district where personal medical records alone are to be consulted.

Patient consent

Both the DoH [2] and the RCP [1] recognise that patients ‘should in principle be asked if they consent to their own records being released to research work-
ers’. (3.12). However, in epidemiology, for example, individual consent may be ‘difficult or impossible to obtain’. An LREC may approve such research if it is ‘satisfied that the value of such a project outweighs, in the public interest, the principle that individual consent should be obtained’ (3.12). This guidance recognises that patient privacy is not an absolute right.

The World Medical Association Declaration of Helsinki on biomedical research involving human subjects (Hong Kong amendment 1989) is reprinted by the DoH (Appendix C). It is worth noting that under the 1991 EC Directive [3] the ethical principles laid down in the Declaration will have legal effect in clinical trials. The Declaration of Helsinki twice states that the interests of the individual must always prevail over the interests of science and of society. We have heard it said that epidemiology, where it is confined to research on personal medical records, does not ‘involve human subjects’ in terms of the Helsinki Declaration, but we note that the Declaration specifically states the ‘every precaution should be taken to respect the privacy of the subject’. Nevertheless, notwithstanding the terms of the Declaration of Helsinki, we conclude that overriding a patient’s privacy in the interests of society (above) is not considered by the DoH to be a breach of the Declaration (provided proper precautions to maintain confidentiality are taken and there is no significant possibility of detriment to the patient). This matter is of particular importance to epidemiologists. It also illustrates that ethical statements are relative, not absolute.

Confidentiality (3.11–14)

Confidentiality is emphasised in the document. ‘All data from which an individual is identifiable should be destroyed when no longer required for the purposes of the original research’ (3.11) unless the NHS body, the LREC, and the research subject are told the reasons for retaining it and the subject’s consent is recorded. It is doubtful that the cumbersome multiple procedure proposed adds any protection to present or future subjects, the sole justification for imposing such an administrative burden.

In any event, ‘for the purposes of the original research’ must no doubt be widely interpreted: in drug studies prolonged retention of records is increasingly thought to be in the subject’s interests. Thus the EC directive [3] imposes formidable requirements for the retention of data: ‘The investigator shall arrange for the retention of the patient identification codes for at least 15 years . . .’, and ‘Patient files and other source data shall be kept for the maximum period of time permitted by the hospital, institution, or private practice’. ‘The sponsor or other owner of the data shall retain all other documentation pertaining to the trial for as long as the product is authorised’. There is no guidance from the DoH as to whether or not LRECs have any responsibility in this regard.

Compensation for injury to research subjects whether or not there is fault (3.17–20)

Although injury caused by participation in research is rare, ethics committees have long seen it as an important role to ensure that if something does go wrong, research subjects are adequately compensated.

There are four aspects to compensation. The first relates to the circumstances in which compensation becomes payable, and in particular whether payment depends on proof of negligence under the ordinary law or will be made even if no one is at fault. The second relates to the machinery for compensation: litigation in the courts, with its attendant expense and delay, or a speedy, more informal process. The third aspect is the provision of full information on these issues to research subjects so that they may take it into account in deciding whether to participate. The fourth deals with the mundane but important question: if compensation is payable, on whatever basis, will the money actually be available?

The DoH document concentrates on the third and fourth issues. It has little to say, and that ambiguous, on the first issue, except that whatever the position it must be revealed to the subject at the outset (3.17). No doubt LRECs will continue to insist that pharmaceutical companies, whether or not members of the Association of the British Pharmaceutical Industry (ABPI), must adhere to the APBI guidelines which provide for a separate written contract with each healthy volunteer, with full compensation irrespective of fault [6], and in the case of patient volunteers commit the company to favourable consideration of claims, again irrespective of fault [7]. Both sets of ABPI guidelines contemplate a smooth procedure without the need to resort to litigation.

Unfortunately this favourable situation does not extend to research involving patients wholly arranged within the NHS. According to the DoH, NHS bodies are ‘not empowered to offer advance indemnity to participants in research projects. A person suffering injury . . . would be able to pursue a claim for negligence through litigation’, provided of course that there is evidence of fault. On injury where there is no negligence, the more likely event, the document is silent, and, curiously, makes no mention of the known position that NHS bodies have in the past made ex gratia payments, with the necessary DoH and Treasury approval. However, we doubt that having to rely on these two government departments for sympathetic and prompt consideration will wholly ease the minds of potential volunteer subjects, healthy or patient, who may be deterred from participating.

This refusal of the NHS to offer advance indemnity contrasts with the approach to ‘private sector companies’, which are expected to offer advance indemnity for injury to research subjects. LRECs ‘should seek confirmation’ that a ‘company conducting or sponsoring a patient or healthy volunteer study accepts...
responsibility for compensation and provides details of the basis on which it will be provided. . . ’ (3.19). This does not, in terms, make it mandatory for private sector companies to accept responsibility in the absence of fault, but LRECs will no doubt continue to expect such a commitment.

On the third aspect of compensation, the DoH document is unequivocal (and the EC guidance on good clinical practice [3] is in broad agreement): in studies ‘that may involve some risk’, research subjects should be ‘told at the outset what arrangements [for compensation] will apply in their case’ (3.17), and also ‘of the possible difficulties in obtaining compensation’ (3.20). No doubt a paragraph or two will now be a universal feature of information sheets. Unfortunately, given the fact that ‘arrangements for compensation in the event of a research subject being harmed, whether by negligence or not, will vary according to what type of body is sponsoring the research proposal’ (3.17), no standard form of words can be devised to suit all cases, and we fear that investigators, often lacking special knowledge of liability issues, and perhaps LRECs which do not have a member who is a lawyer, may have difficulty in implementing these requirements so that research subjects can understand the position. The ABPI-recommended contract for healthy volunteers [6] will no doubt adequately provide clear information, but for patients what will be needed is a passage briefly summarising the ABPI guidelines [7] as they apply to the patient’s particular circumstances. A copy of the guidelines themselves would contain much that is irrelevant to the individual patient or to the research in progress, and no standard paragraph could suit all cases while remaining comprehensible.

The fourth aspect of compensation arrangements rests on the financial stability of the person, company, or institution which will be liable to pay. LRECs are told by the DoH that they should satisfy themselves on this point (3.17, 3.19). Two matters spring to mind: no doubt some LRECs will ask for a sight of company balance sheets and accounts; others may seek evidence of satisfactory insurance coverage. Where the commitment goes beyond ordinary legal liability for negligence, a trained eye will be needed to ensure that the approved arrangements are actually covered by the insurance policy: such important matters cannot be taken on trust. For NHS research our understanding is that management approval provides NHS indemnity (in respect of negligence liability) for doctors and all other NHS staff. Non-NHS research, eg on healthy volunteers, will at the least lead LRECs to seek assurance that medical staff belong to an appropriate defence organisation.

Risks

The DoH states that ‘volunteers’, presumably both patient and healthy, must ‘be told in advance of all known risks and be made aware that there could be unforeseen risks’ (3.20). The telling of ‘all known risks’, though at first sight an obviously sensible requirement, appropriately mandatory, can be unrealistic to the point of impracticability, or result in such detail as to distort rather than to assist choice. This is an area in which LREC discretion is particularly important.

Safety requirements

The LREC, in the case of drugs/medicines, should require ‘details of any relevant clinical trial exemption certificate’, or, in its absence, a ‘certified statement’ (3.21) that pre-clinical studies have been carried out to a standard no less than that required by the DoH under the clinical trial exemption scheme [8]. A certified statement involves a company adviser or consultant formally committing himself to the accuracy of the information, and that it is reasonable for the trial to take place.

Where LREC advice is not sought or is ignored

The LREC should report failure to seek its approval or non-compliance with its advice (both serious matters) to ‘its appointing authority, the relevant NHS body and (our emphasis) to the appropriate professional body’ (3.22). We suppose this must mean a body that has disciplinary powers. Some professions engaged in research involving human subjects may not have a professional disciplinary body.

In conclusion

We congratulate the DoH on producing a document on this subject. It is good that the DoH insists that ‘every health district should have a local research ethics committee’, and that all NHS research must secure LREC approval [2]. But the document has aspects that need clarification or revision if LRECs are to develop consistent procedures and to fulfil their essential objective—the protection of research subjects.

References

1 Royal College of Physicians. Guidelines on the practice of ethics committees in medical research involving human subjects. London: RCP, 1990.
2 Department of Health. Local Research Ethics Committees. London, undated, but accompanied by Health Service Guidelines HSG(91)5: 19 Aug 1991.
3 (a) EC Commission Directive 91/507/EEC of 19 July 1991 (OJ L 270/32, 26 September 1991), amending Council Directive 75/318/EEC of 20 May 1975. (b) Commission of the European Communities: CPMP (Committee on Proprietary Medicinal Products) Working Party on Efficacy of Medicinal Products. Notes for guidance on Good clinical practice for trials on medicinal products in the European Community. Brussels, 1990 (operational 1991).
Medical Ethics Publications

| Ethical Issues in clinical genetics | Price |
|-----------------------------------|-------|
| Fraud and misconduct in medical research: cause, prevention and investigation | £6.00 (UK) |
| Medicine and the Law (based on a conference organised by the Royal College of Physicians) | £7.00 or US $16.00 (overseas) |
| *Guidelines on the practice of ethics committees in medical research involving human subjects (2nd edition) | £5.00 (UK) |
| *Research involving patients | £6.00 (UK) |
| Research on healthy volunteers | £7.00 or US $13.00 (overseas) |
| Relationship between physicians and the pharmaceutical industry | £6.00 (UK) |
| Guidance on ethics for occupational physicians | £7.00 or US $15.00 (overseas) |
| *Special rates for UK customers. Research involving patients and Guidelines on the practice of Ethics Committees may be purchased together, price £14.00. Orders of 10 copies or more may be purchased at a special rate of £6.00 per copy. Remittance with order to: The Royal College of Physicians, 11 St Andrew's Place, Regent's Park, London NW1 4LE. | £8.00 (UK) |
| | £10.00 or US$20.00 (overseas) |
| | £3.00 (UK) |
| | £4.00 or US$9.00 (overseas) |
| | £5.00 |

Address for correspondence: Dr D R Laurence, 37 Denning Road, London NW3 1ST.

Other College Publications are listed elsewhere.