Ethical review of multi-centre research: a survey of local research ethics committees in the South Thames region

ABSTRACT – **Objective:** To generate baseline data about the standards of practice of local research ethics committees (LRECs) in order to describe accurately the situation of ethical review procedures prior to the establishment of multi-centre research ethics committees (MRECs).

**Design:** The LRECs in the South Thames NHS Region were asked to describe their current practices, and to send us a copy of their application forms and guidance notes for researchers.

**Results:** All of the 27 LRECs approached for the survey responded. The results indicate that there are generally high standards of practice, and that most LRECs work in accordance with published guidelines.

**Conclusion:** The problems that researchers face in seeking to obtain ethical approval for multi-centre research (pages 242–5) do not seem to have been caused by substandard LRECs. Hence the new system needs to sustain the high standards of practice whilst confronting the difficulties.

In April 1997 the NHS Executive issued a guidance note on the ethics of multi-centre research. It established new multi-centre research ethics committees (MRECs) responsible for reviewing the ethics of research proposals involving human subjects that are to take place within the geographical boundaries of five or more local research ethics committees (LRECs). LRECs will check local details, but will not have the power to change the main research protocol. For the effort expended in its establishment and maintenance to be worthwhile, the new system must offer a more timely and efficient service to multi-centre researchers than previously existed. South Thames Research and Development Directorate, the body responsible for instituting the new system, funded the Centre of Medical Law and Ethics at King’s College to generate some baseline data describing the pre-MREC situation, against which the new system can be evaluated. This article describes a survey of the standards of practice of LRECs. It is the latest in a line of surveys conducted between 1986 and 1992, that show a steady improvement over time. In order to interpret the results of this survey and, indeed, to appreciate why the proposals for MRECs have taken the form they have, it helps to know something of the background of LRECs.

In response to growing concern about the ethics of research on human subjects during the 1960s, the Royal College of Physicians issued a report calling for the establishment of independent committees to review proposals for such projects. Little initial guidance was given on the committees’ remit, accountability or procedures. More guidance was offered during the 1970s and 1980s but this was not (regarded as) mandatory. By the time more formal advice was offered, giving responsibility to LRECs to health authorities, many LRECs were virtually independent and working in isolation. They had established their policies, and felt the need to remain free to continue to respond to changing medical and ethical environments. In many cases, health authorities showed a lack of interest in the work of their LRECs and provided little support.

Hence a combination of factors – lack of initial guidance, lack of structural support, and the essential fluidity of ethical decision-making – has meant that LRECs remain relatively isolated and largely independent. A variety of attempts, mainly by regional research and development directors, have been made to bring LRECs together for training and cross-referencing. This has met with some success, but the tradition of independence remains strong. We should, therefore, be encouraged by the similarities amongst LRECs identified in this survey, given that they are there less by virtue of external suggestion than by isolated efforts leading to the same goal.

**Method**

The study population encompassed the 27 LRECs in the South Thames Region. The sample is representative of LRECs in the UK, as the region not only includes both teaching and non-teaching hospitals and urban and rural districts, but the different workloads of its LRECs reflect those of LRECs elsewhere. Contact between the LRECs themselves and between LRECs and the Regional Office was comparable with that in other regions – namely, South, West and Northern regions.

Questionnaires were sent to all 27 LRECs in the sample, and were divided into six sections covering:

1. their views on their remit
2. their constitution and membership
3. their working procedures
4. the level of their administrative support
5. their attitudes to the idea of standardised paperwork
6. their experience of, and policies regarding, multi-centre research.

In this article we omit results about attitudes to standardised paperwork for LRECs, since this aspect is not relevant to the new system.

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Results

The content of ethical review

All LRECs who answered this question (26 of 27) agreed with each of the categories of ethical concern listed in Table 1. These covered: the scientific validity of each research project and its ability to answer the scientific question it posed; the welfare of the research subjects, including procedures they would have to undergo and availability of compensation; and the consent and confidentiality of the research subjects.

Constitution and membership

Out of the 27 LRECs surveyed, 25 had a written constitution or were in the process of introducing one at the time of the survey. Four LRECs’ constitutions had not been ratified by their parent health authority. Twenty-one LRECs had between eight and twelve members, the number recommended by the Department of Health\(^1\). Of the six exceptions, all had more than twelve members, and three were LRECs serving teaching hospitals where representation from the respective medical schools was required. All committees had a broad range of membership. Eight did not have a pharmacist or pharmacologist member, although clinical pharmacologists may have figured amongst their hospital consultants, whose specialties were not always identified in the responses. All but two had either a lay chairman or vice-chairman. Terms of membership were, in all but two cases, limited to a maximum of ten years, the exceptions having terms of office that were open-ended.

Working procedures

Twenty-six LRECs had a written application form. Of these, seven used the same form as each other; three shared another one. Seventeen LRECs had their forms available on disk and fifteen had computerised systems for filing applications.

Thirteen LRECs met every two months, nine every month, two every six weeks and two quarterly (one LREC did not answer this question). While some LRECs did use a shared application form (eg the LRECs in Kent), most did not. This, and the infrequency of meeting dates for some LRECs, has posed a serious burden for the multi-centre researcher.

Thirteen LRECs routinely interviewed researchers, ten sometimes did and three did not interview. Most committees co-opted expertise when necessary. All but one offered informal advice to researchers before the meetings, usually via the chairman or secretary. Most committees came to their decisions by consensus; one voted, accepting a two-thirds majority. All LRECs wrote to applicant researchers to advise them of the decision of the committee, and all but two gave reasons for their decisions to researchers (one LREC did not answer this question and the other wrote ‘generally’).

Policy issues

LRECs were asked to submit their application forms and guidance for researchers. This paperwork was analysed under 25 different headings related to the initial six areas of ethical concern and to guidance from the Department of Health\(^2\)\(^3\)\(^4\) and elsewhere\(^5\) (Table 2).

One LREC did not use an application form and so it was impossible to deduce whether the issues listed in Table 2

Table 1. LRECs’ views on the content of ethical review.

| Twenty-six LRECs agreed that the following questions should be covered by the ethical review process: |
| --- |
| • Is the research project asking a reasonable/important question? |
| • Will the research project, as designed, answer the question being asked? |
| • Are the procedures which research subjects will have to undergo acceptable? |
| • Will compensation be made available to research subjects? |
| • Is adequate care being taken over the research subject’s confidentiality? |
| • What procedures will be followed to seek consent of the research subjects? |

Table 2. Analysis of LREC application forms and guidance to researchers.

| Issues raised in LRECs’ paperwork | No. of LRECs that mention this issue (n=26) |
| --- | --- |
| • Competence of researcher | 26 |
| • Suitability of site | 25 |
| • Adequacy of supervision where applicable | 22 |
| • Scientific acceptability of proposal | 26 |
| • Safety and necessity of procedures undertaken | 26 |
| • Status of drugs to be used | 26 |
| • ARSAC approval of radioactive isotopes if used | 23 |
| • Compliance with EC Directives when medical devices used | 6 |
| • Compliance with the requirements of the Data Protection Act | 20 |
| • Confidentiality of patient records | 17 |
| • Levels of discomfort of procedures used | 26 |
| • Health status of research subjects | 26 |
| • Number of subjects | 26 |
| • Patients or volunteers | 26 |
| • How recruited | 26 |
| • Suitability of conditions when consent sought | 26 |
| • Use of a standard consent form | 12 |
| • Suitability of patient information sheet | 26 |
| • Relationship between researcher and subject | 20 |
| • Advice to subjects’ GPs | 26 |
| • Protection of vulnerable groups | 26 |
| • Adequacy of indemnity and compensation arrangements | 24 |
| • Payment to researchers | 24 |
| • Statistical advice | 15 |
were considered by that committee. Moreover, the absence of some issues from an LREC's paperwork did not necessarily mean that the issues were not addressed, only that they were not explicitly raised in writing.

A significant number of LRECs did not address: the use of the European Commission Directives on medical devices\(^\text{16,17}\); the confidentiality of patient records; the use of a standard consent form; and the seeking of statistical advice. The lack of mention of the use of a standard consent form is probably unimportant: what it indicates is that 14 out of 26 committees do not ask researchers to use the committees' own standard consent form; it does not imply that these LRECs do not ask about consent forms at all. However, the absence of questions about the confidentiality of patient records is more puzzling, particularly in view of the unanimous response from LRECs that confidentiality was an issue that fell under their remit (Table 1). Similarly, given the (again) unanimous view that the design of research projects is an ethical issue (Table 1), it is both surprising and worrying that statistical advice is not mentioned by 11 of the 26 LRECs with paperwork.

However, most LRECs asked a comprehensive set of questions that were broadly similar. Hence, LRECs do present a united view of what they are concerned about, even if the way they approach their task, and the conclusions they come to, are different.

**Attitudes toward multi-centre research**

LRECs were asked about their policies for dealing with multi-centre research proposals that had gone, or were going, to other LRECs. Of the 27 LRECs surveyed, 18 had no policy, 3 usually dealt with multi-centre research proposals by chairman's action, and 2 took account of the decisions of other LRECs\(^*\). Committees were also asked what type of research the majority of multi-centre proposals related to; the response was, unsurprisingly, pharmaceutical company-sponsored research. The number of multi-centre trials (not all involving five or more LRECs) reviewed varied from \(5-10\) to \('150\) per year (the median being 30).

Finally, committees were asked their views on the creation of a new multi-centre research ethics committee in their region. Twelve LRECs were happy to support the idea of a new committee for multi-centre research, provided that the local issues were protected, four were opposed, three commented largely on safeguarding the LRECs, and one had yet to decide.

**Discussion**

The results of this survey show that LRECs do comply with Department of Health guidelines and standards. LRECs are working to high standards of practice when measured against published guidance. It must be observed that standards of practice are not the same as standards of ethical review, and some LRECs, whilst observing all the administrative rules, nevertheless fail in the rigour and relevance of their ethical review. The absence of references to statistical analysis and to confidentiality in some application forms may indicate lower standards of ethical review by those LRECs. To our knowledge, no studies have been undertaken that show the link between process and review.

We would argue that standards of ethical review are more likely to be high if the LREC is careful about its procedures, on the grounds that good ethical decision-making requires care and attention to detail. Our belief that (with some exceptions) the standard of ethical review is generally high, is supported by a cautious interpretation of the results of this survey, anecdotal evidence and our experience of the committees themselves. However, no firm conclusion can be reached on the basis of these results alone.

The survey of researchers in the article that follows (pages 242–5) shows a high level of dissatisfaction with the administrative procedures for ethical review. The new multi-centre review system is intended to deal with these procedural difficulties without losing the strengths of the old system. Indeed, the system reinforces the independence and autonomy of LRECs. There are some questions, relevant to the ethical acceptability of the research proposals, with which only LRECs can deal, namely: the qualifications and capabilities of local researchers; the local facilities; the population from which the local researcher will draw his or her subjects; and local arrangements for finance, safety, use of radioactive materials, storage of trial medicines, and confidentiality records. These questions appear on a local form, supplementary to the MREC application form, and LRECs retain the right to veto a proposal in their own location for local reasons. The Department of Health guidance gives LRECs the opportunity to raise issues of general concern with the MREC that gave approval to a project, but not the right to change the overall proposal.

MREC approval will be advantageous only where LRECs accept the competence of each of the MRECs to conduct a proper ethical review of all but the local issues. LRECs that recognise this might begin to conduct the local review by chairman's action or a sub-group of the LREC, thus speeding up the process for the researchers. There is nothing, however, in the formal MREC process to ensure that this facilitative approach is used. It is entirely dependent upon confidence and goodwill developing between LRECs and MRECs.

The fact that the MRECs will be working to an established high standard of practice is an excellent start, but for the system to operate effectively this must be supplemented by lines of communication additional to those laid down in the Department of Health guidance. A national system that evolves in a uniform way is the essential condition for the MREC system to work. To achieve this, the MREC chairmen and administrators must meet regularly and work as a group. The other basic requirement for the success of the process is the need for MRECs to gain the confidence and goodwill of LRECs. This will require MREC chairmen and administrators to meet LRECs within their regions regularly and feed the views of LRECs into the national forum. In this
way a framework will emerge within which MRECs and LRECs will be able to exchange views and concerns. From these beginnings, it is hoped, a structure will develop to guide the way in which the ethical review process is conducted and evolves.

"The survey questionnaire and a fuller table of results showing LRECs' attitudes to multi-centre research are available from the authors.

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