What is already known on this topic

Many authors have commented on the difficulties experienced by researchers in obtaining ethics approval for multicentre studies. Much of this work has been anecdotal

Since the introduction of the new system of multicentre research ethics committees a systematic audit has not been undertaken to evaluate its performance

What this study adds

Although review by multicentre research ethics committees could substantially reduce previous difficulties described, changes are still needed to allow the system to function as intended

culties rather than the substance of ethical review itself.[6] The multicentre research ethics committee system was set up to deal with such procedural difficulties. Improvements in the system have occurred. However, local research ethics committees have been reluctant to abandon their autonomy sufficiently to allow efficient functioning of this system, and this has been identified as a potential reason for continuing concerns about the new system.[7] Whereas administrators of local research ethics committees face significant problems in trying to achieve turnaround targets that may be unrealistic without important new resource input, substantial frustrations remain for researchers working within a system that at times presents an unethical barrier to potentially beneficial research.

Contributors: JT collected the data and prepared the manuscript for publication. NN provided background data and contributed to the preparation of the manuscript. RB provided statistical advice. RV and RB made major contributions to preparing the manuscript for publication; RV will act as guarantor for the paper.

Funding: JT and NN were funded by the Meningitis Research Foundation and RB was funded by the Wellcome Trust.

Competing interests: None declared.

1 Busby A, Dolk H. Local research ethics committees' approval in a national population study. *J R Coll Physicians Lond* 1998;32:142-5.
2 Harries UJ, Fentem PH, Tuxworth W, Hoinville GW. Local reseach ethics committees' widely differing responses to a national survey protocol. *J R Coll Physicians Lond* 1994;28:150-4.
3 While AE. Ethics committees: impediments to research or guardians of ethical standards? *BMJ* 1995;311:661.
4 Stacey TE. How should an LREC handle an MREC approved application: interim guidance circular letter. 1-3. 28 Sep, 1998.
5 Foster C, Holley S. Ethical review of multi-centre research: a survey of multi-centre researchers in the South Thames region. *J R Coll Physicians Lond* 1998;32:242-5.
6 Holley S, Foster C. Ethical review of multi-centre research: a survey of local research ethics committees in the South Thames region. *J R Coll Physicians Lond* 1998;32:238-41.
7 Stacey TE. Ethical review of research in the NHS: the need for change. *J R Coll Physicians Lond* 1998;32:190-2.

(Accepted 2 December)

Responses of local research ethics committees to a study with approval from a multicentre research ethics committee

Andrew L Lux, Stuart W Edwards, John P Osborne

Editorial by Alberti, pp 1179, 1217

Children's Centre, Royal United Hospital, Combe Park, Bath BA1 3NG

Andrew L Lux
clinical research fellow

Stuart W Edwards
research coordinator

John P Osborne
professor of paediatrics and child health

Correspondence to:
A L Lux
andrew.lux@ruh-bath.swest.nhs.uk

BMJ 2000;320:1182–3

Studies approved by multicentre research ethics committees in the United Kingdom are submitted to a local research ethics committee in each health district. Guidelines on handling such submissions were issued in September 1998.[1] The United Kingdom infantile spasm study was approved that same month: as members of the steering committee we attempted to assess the impact of the guidelines on the practice of local research ethics committees.

Participants, methods, and results

We made 113 submissions on behalf of local investigators to 99 local research ethics committees between September 1998 and September 1999. We analysed the committees' responses to the first submission. A committee was classified as "fast track" if the administrator stated that the submission would be reviewed by an executive subcommittee, as recommended by the guidelines. Our main outcome measure was response time, defined as the number of days between arrival of the submission and the date on which written confirmation of the committee's decision was typed. We considered a response time of 21 days or less to be satisfactory since this was the upper limit suggested by the guidelines.[1] In a survey of 26 committees, submissions arrived a median of three days (range 1-7) after they were sent. For the other committees, we took the date of receipt to be seven days after the documents were sent. We defined earlier submissions as those received before April 1999.

Submissions were classified as approved if complete or conditional approval was granted, even if requests for clarification were made to the multicentre research ethics committee, the trial steering committee, or the local investigator. Requests for opinions from third parties, failure to grant at least conditional approval, and requests for amendments to study documents were classified as non-approval. Requests for minor amendments to study documents (such as changes to letter headings) were classified as approval, except in two cases when the local committee asked to review such changes before granting full approval.

Fewer than half of the committees used a fast track system (table), with 21 (44%) of earlier submissions

Response times, numbers of copies of documents required, and decisions of 99 local research ethics committees for submissions made between September 1998 and September 1999

	Median (5th, 95th centiles) response time (days)	No (%) of committees responding within 21 days	Median (5th, 95th centiles) No of document copies required	No (%) of submissions approved after first review
Time of submission*:				
Earlier (n=48)	26 (6, 57)	15 (31)	4 (1, 15)	39 (81)
Later (n=51)	28 (3, 98)	18 (35)	4 (1, 15)	43 (84)
Type of committee†:				
Fast track (n=44)	30 (4, 85)	14 (32)	3 (2, 13)	35 (80)
Standard (n=55)	25 (7, 64)	19 (35)	11 (1, 15)	47 (85)
Total (n=99)	28 (4, 73)	33 (33)	4 (1, 15)	82 (83)

*Earlier submissions were those received before April 1999.
†Fast track committees stated an intention to use executive subcommittees for quick response.

and 23 (45%) of later submissions being reviewed by an executive subcommittee. A third of the committees reached a decision within 21 days. There were no significant differences in median response times between standard and fast track committees, or between earlier and later submissions. Seventeen committees did not approve the study after the first review. One committee had not had a quorum for over six months and, when it did meet, requested an opinion from a third party. Another committee recommended several amendments which the multicentre research ethics committee did not consider important enough to merit global amendments to the study protocol. The resulting impasse was unresolved six months later. The required number of complete copies of protocols and documents from the multicentre research ethics committee was significantly lower for local committees that used a fast track system (Mann-Whitney rank-sum test: $z=3.11$, $P<0.002$). However, four fast track committees requested 12 or more copies.

Comment

The two tier system of ethical approval of multicentre research was intended to combine rigorous local review with expedient timing.[2] We found that only a third of committees responded to submission of a study that had been approved by a multicentre research ethics committee within the recommended period of 21 days. A sixth of committees did not approve the study after the first review. There was no evidence of more efficient review or wider adoption of the NHS Executive's guidelines six months after these guidelines had been issued. Fewer copies of documents were required by committees using an executive subcommittee for fast track decisions, but these committees did not make faster decisions. Our findings echo the comments of other researchers, that the two tier system of ethical review retains the inefficiencies of the former system.[3]

We thank the members of the United Kingdom infantile spasm study (UKISS) steering committee and local investigators for their support.

Contributors: ALL, SWE, and JPO designed the study and wrote the paper. ALL and SWE collected the data, and ALL analysed the data. ALL is guarantor for the study.

Funding: Bath Unit for Research in Paediatrics (BURP) and Cow and Gate.

Competing interests: The authors are involved in a charitably funded, national study that would benefit financially from faster ethical approval.

1 NHS Executive. *Interim guidance: how should an LREC handle an MREC approved application?* London: Department of Health, 1998.
2 Alberti KGMM. Local research ethics committees: time to grab several bulls by the horns. *BMJ* 1995;311:639-40.
3 Larcombe I, Mott M. Multicentre research ethics committees: have they helped? *J R Soc Med* 1999;92:500-1.

(Accepted 11 February 2000)

The cost of getting approval

Multicentre research ethics committees are intended to simplify the process of gaining ethical approval for large scale studies. However, for a nationwide study of sudden deaths in psychiatric inpatients we obtained ethical approval from the local multicentre committee and then had to face the "formality" of seeking approval from all 176 local research ethics committees in England and Wales. In total this involved photocopying over 60 000 sheets of paper, taking 50 hours of photocopying time, not including the period of time when the machine was out of action due to exhaustion. This also excludes the cost of other people's frustration because they could not access the photocopier. Postage and packaging cost £900. One committee asked for a £10 fee for considering the proposal.

Sandra Flynn *research secretary*, Clare Dixon *project manager*, Tim Amos *clinical research fellow*, Louis Appleby *professor, School of Psychiatry and Behavioural Sciences, University of Manchester*

We welcome articles of up to 600 words on topics such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk. Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for "Endpieces," consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.