match the research design, and advised on qualitative data analysis (which the researchers were unfamiliar with) and resubmission to the ethics committee.

To minimise disruption, funding was continued to allow the research team to develop the protocol and patient information sheets before resubmission. If the researchers had expressed concern that this represented misuse of resources, the funding could have been re-profiled. Trust approval was given two months later for the pilot research project to restart, after a favourable opinion from the research ethics committee. Subsequently, we worked with the researchers to provide funding to extend their data collection and analysis.

Introduction of a qualitative component represents an important change to a study, originally peer reviewed and funded as a quantitative study. Research participants have a right to be presented with accurate and complete information when being asked for informed consent. However, further public debate is needed on research governance measures implemented in the NHS—for example, on linking research project management more closely with risk assessment. Such public debate will help ensure that NHS research is conducted according to research governance and ethical standards.

Competing interests: TS chairs the national NHS Research and Development Forum's research governance working group.

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Bureaucracy of ethics applications

David S Wald

One research group decided to determine exactly how much effort is required to get ethical approval by recording the submission of its first application under the new UK system

Editorial by Warlow

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March 2004 heralded the introduction of the new Central Office for Research Ethics Committees (COREC) application form and a bad time for anyone aiming to conduct clinical research in the United Kingdom. Here I recount the experience of a clinical research group submitting the first application at their university hospital. We logged the time and activity required for the application process.

We designed a double blind randomised, placebo controlled, factorial study in 50 volunteers to determine whether the blood pressure lowering effects of a low dose β blocker and low dose angiotensin converting enzyme inhibitor are independent. We sought no external funding for the study and expected no ethical obstacles.

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Application process

The application procedure began with a phone call to the local research ethics committee to find out the dates of the forthcoming committee meetings and submission deadlines. We received a list of dates and were advised that the local 10 page application form was no longer in use and that we should download the new four part, 68 page form from the COREC website (www.corec.org.uk). Two files could be completed online; the first, COREC 2, was a 57 page form divided into three parts (A, B, and C) and was required by the local research ethics committee for a decision on whether the proposed research was ethical. The second "COREC application," comprised part D and was an 11 page finance form for the research and development department.

COREC 2

Part A

Part A contained 68 questions on 26 pages. Most of these related to the scientific justification for the study and the proposed methods. Six questions related to issues of funding and conflicts of interest and two to data monitoring and audit. One question required five reference numbers: a research and development number, a sponsor's number, a funder's number, an international standard randomised control trial number (ISRCTN), and a European clinical trials database (EudraCT) number. No guidance was given on how to obtain these reference numbers.

We resorted to phoning the local research and development department whenever faced with uncertainties about the COREC form, but they could

provide advice on only the first three numbers. Research and development departments do not issue a reference number until the application has been submitted, and neither a sponsor's nor a funder's reference number applied to our project. For further assistance we were referred to the COREC inquiry line (box). However, we got an answerphone message stating that opening hours were between 9 30 am and 12 30 pm. When we called back the next day, the staff were unable to help and referred us back to the COREC website, which provided no information on the ISRCTN or the EudraCT numbers.

We then turned to Google, and discovered that ISRCTN is a numerical system for the unique identification of clinical trials worldwide. A number is required for "all randomised clinical trials relevant to health care," and it has its own online application procedure. The EudraCT number is a European Commission led directive to provide European regulatory authorities with an overview of clinical trials being conducted in the community. The directive was initiated in 2000 but ran out of funds in 2002, so had yet to be implemented. This number was therefore not required. The scheme did, however, start on 1 May 2004.

Completion of part A required four drafts, two reviews by colleagues, six phone calls to research and development, four phone calls to the local research committee, two to COREC, 1.5 hours of online internet inquiry, 340 pages of printed material, and a total of 23 hours of staff time. One question, A68, asked, "What do you consider to be the main ethical issues or problems which may arise with the proposed study?" This was the only specific question on ethics in the form.

Part B

Part B consisted of 59 fields to complete on 20 pages, requiring detailed information on the use of medicinal products and medical devices. If the research involved human biological materials, radiation, existing stored samples, or research on prisoners, signatures of authorisation were required from the radiation specialist, the tissue bank manager, and the prison governor after they had read and agreed with the trial protocol. This did not apply to our application, but as our research involved a placebo, details of its chemical composition were required, which we sought from the firm supplying the drugs.

Part B also asked whether a clinical trials authorisation form had been applied for from the Medicines and Healthcare Products Regulatory Agency. This form is required by the European Union clinical trials directive to authorise clinical trials in healthy volunteers. It would become a requirement for all clinical trials on 1 May 2004. Until then, non-sponsored trials (for example a university trial like ours) could apply for exemption by applying for a doctors and dentists exemption (DDX) certificate, which after 1 May 2004 would automatically be converted into a clinical trials authorisation.

When we contacted the agency there was some confusion about whether we required any form of authorisation or exemption certificate for a clinical trial that was using licensed drugs for their licensed uses. Given the uncertainty and the expectation of "worse to come" after May 2004 we were encouraged to apply for a doctors and dentists exemption. This required signatures from the firm supplying the drugs and our hospital's clinical director. Although the application was hurried through the agency's administrative system, it took four weeks to be issued. Part B required two drafts, eight phone calls, two faxes, half an hour of internet inquiry, and four hours of staff time. There were no questions on ethics in this part.

Part C

The final part of the form was the site specific assessment. It consisted of 11 pages and 22 questions, four of which were automatically completed (by the computer) with information that had been provided earlier. This part was swiftly completed, requiring only half an hour of staff time and no phone calls. There were no questions on ethics in this part.

COREC application

Part D consisted of 11 pages, 25 questions, and a jolt back to reality after being lulled into a false sense of security at having breezed through part C. This section was required by the research and development department to determine whether the trial was adequately funded, whether the project would divert NHS resources away from patient care, and, if so, how to cost these.

Questions 5 and 6 required information on what measures had been taken to provide indemnity against negligent and non-negligent claims arising from the proposed research. For this we had to complete a further project registration form and obtain a signed letter from the finance director of research and development. Questions 18 and 19 related to patient data protection. We had to complete a separate local application form registering our use of personal data for research purposes, to submit it to the local Data Protection Service, and to have it signed by the head of information security. Part D also required authorising signatures from the clinical directors of departments from which patients would be recruited and from the drug administrator. All signatories should have read and agreed with the study protocol. Part D required two drafts, nine phone calls, four faxes, 20 minutes of online internet activity, and 7.5 hours of staff time. There were no questions on ethics.

Other requirements

Other documents required for a complete application included copies of the research protocol, patient information leaflet, patient questionnaire, investigator

Contact information

Central Office for Research Ethics Committees
www.corec.org.uk
Telephone inquiries: 0207 725 2755

Controlled Clinical Trials (ISRCTN number)
www.controlled-trials.com

European Clinical Trials Database (EudraCT number)
http://eudract.emea.eu.int

brochure for medicinal products, letters to general practitioners, and consent form. These were produced within the time needed to complete and submit the forms. We sent one set of application documents by cycle courier to the research and development department so that they could be approved by the finance director before the submission deadline for consideration at the next meeting of the local research ethics committee.

Completion of the application material took two weeks and required 44.5 hours of activity. Taking into account staff time, travel, phoning and faxing, online internet activity, and consumables, we estimated the total cost to be about £850. The local ethics committee considers 36 applications each month. The annual cost is therefore likely to be about £370 000 for the application process alone.

Summary points

Medical research with human subjects requires independent ethical review

In Britain ethical application forms have been standardised by the Central Office for Research Ethics Committees

The form is 68 pages long, has 174 fields to fill in, requires up to eight signatures of authorisation, and takes over 40 hours to complete

The complexity of ethical committee application forms has increased, is increasing, and ought to be diminished

Discussion

Our randomised trial is likely to generate a paper considerably shorter than the application form required for its ethical approval. The £850 could have been better spent on blood pressure monitors, bought to avoid using NHS resources. This was the cost from the perspective of the research group and does not consider the subsequent costs to the local research ethics committee.

Medical research that involves human participation requires independent ethical review—this is not at issue. The problem is the complexity of the process that has evolved to meet this need. Researchers should be required to provide only sufficient information to satisfy the ethics committee in three essential areas:

- The proposed research has scientific and medical value
- The risk to individuals participating in the research is minimal or non-existent or otherwise compensated for by possible benefits
- The participants are adequately informed and give appropriate consent.

A process is needed that ensures that this information is collected for independent review. To the extent that the COREC application procedure accomplishes this, it has a public benefit. The problem with the form is that it is subsumed with non-ethical concerns:

(i) *COREC application* (part D) is largely a financial accounting questionnaire designed to collect costs for the use of NHS facilities—effectively, a stealth tax for researchers, which may itself be unethical when the marginal costs of additional resources are minimal

(ii) The requirement to register for European (EudraCT) and worldwide (ISRCTN) reference numbers for clinical trials is an issue of collective rather than individual responsibility, does not contribute to the ethical review process, and is duplicative

(iii) The provision of legal indemnity in the event of negligent or non-negligent harm to research participants is a prerequisite for clinical research in which there is a reasonable chance that such harm may arise but not a requirement for ethical approval

(iv) Although it is essential for researchers to declare conflicts of interest at the time research is reported, it is not for an ethics committee to adjudicate on whether research should proceed based on such a declaration

(v) The provision of data protection is a duty of all healthcare professionals and need not be a separate requirement of ethical review.

These considerations need to be separated from the COREC application process. Part D should be removed altogether, referred to more transparently as a financial audit form (or FAF for short), and dealt with locally. This would make the application process simpler and more relevant to ethics and allow members of local research ethics committees to focus on what is essential.

COREC and the European directive claim to support research, but their ethics forms serve more to obstruct research than protect patients. The current COREC requirements add to a level of regulation that is making it increasingly difficult for practising clinicians to conduct small scale clinical research. Action is urgently needed to reduce a research bureaucracy that has largely lost sight of the patient, advancing medical knowledge, and improving medical care. What is needed is appreciable deregulation.

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Contributors and sources: DSW is a specialist registrar in cardiology currently engaged in clinical research.

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