New governance arrangements for research ethics committees: is facilitating research achieved at the cost of participants' interest

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Abstract

This paper examines the UK's response to a recent European Clinical Trials Directive, namely the Department of Health, Central Office for Research Ethics Committee guidance, Governance Arrangements for NHS Research Ethics Committees. The revisions have been long awaited by researchers and research ethics committee members alike. They substantially reform the ethical review system in the UK. We examine the new arrangements and argue that though they go a long way toward addressing the uncertainty surrounding ethics committee function, the system favours the facilitation of research over the protection of the dignity and welfare of research participants.

INTRODUCTION

The recent clinical trials directive1 aims to standardise aspects of medical research across Europe. It endeavours to allow drugs that have been tested and licensed in one country to be adopted in another without further delay and research. It lays down requirements for research ethics committees, which will prompt revision of guidelines in a number of member states. Whilst the directive provides a framework, member states will have some latitude when revising their ethical review systems. In the UK, research ethics committees review not only clinical trials but also a wide range of other research protocols, ranging from epidemiological to qualitative research. The directive will necessitate legislation giving ethics committees statutory authority with regard to clinical trials and potentially the statute will be extended to cover their whole remit. Though reducing flexibility, this would ultimately give ethics committees the "teeth" they currently lack. The response to date, however, has not been encapsulated in statute but in guidance from the Department of Health, Central Office for Research Ethics Committees, namely the *Governance Arrangements for NHS Research Ethics Committees.*2

The guidance seeks to interpret elements of good clinical practice ensconced in the directive, but applies not only to clinical trials, but to all areas of National Health Service (NHS) research. The governance arrangements are to be read in

conjunction with the Department of Health *Research Governance Framework for Health and Social Care*.3

We argue that the new arrangements go a long way toward addressing the uncertainty surrounding ethics committee function. The clinical trials directive was, however, industry-led and its interpolation into UK guidance has led to a subtle change of emphasis from the protection of research participants to the facilitation of research.

BRIEF HISTORY OF UK RESEARCH ETHICS COMMITTEES

In the UK a centralised system of research ethics committees was introduced as late as 1991.4 At least one independent "local research ethics committee" was set up in each district in order to advise NHS bodies which research should go ahead.

Local research ethics committees are funded by local health authorities, but remain independent. Until recently, each committee had up to 12 members, and included individuals from a range of medical and lay positions. Working procedures were largely left to each committee and funding was sporadic. In 1991 there was little to impel consistency between committees, though they were asked to "cooperate" in multicentre research applications. It soon emerged that the system was at best inconsistent and at worst prohibitive of research, particularly in the case of multicentre trials.

The result was a spate of empirical research outlining disgruntled researchers' complaints about the system.5 They detailed the different procedures demanded by each committee, the time delays and the inconsistencies. This weight of opinion coincided with a desire to put in place a system whereby the UK could give one definitive ethical review of a protocol that would take place across a number of European countries, prompted by the pending introduction of the clinical trials directive. The result was that in 1997 the introduction of "multicentre research ethics committees"6 temporarily reduced the onslaught of complaints by multicentre researchers.

Where health care research involved five or more local research ethics committee geographical sites, the application would instead be put to one multicentre research ethics committee. Unfortunately this method failed to address the inadequate financing, training, and guidance available to local research ethics committees. Part of the remit of the local research ethics committee is, as their name suggests, to consider local issues. They may, for example, feel that a research population has been involved in research excessively and refuse to approve the protocol. Therefore a multicentre protocol would go to the multicentre research ethics committee which would rule on whether it was ethical. It would then go on to each local research ethics committee for consideration of local issues. "Pertinent local issues" were, however, poorly defined. In some instances the local research ethics committee did

not even pretend that their concern was with local issues. When they recognised a matter of ethical concern they wrote to the multicentre research ethics committee, which was often too busy to respond. As a result some local research ethics committees withheld approval.7 A renewed spate of empirical research emphasised researchers' continuing complaints about the research ethics committee system.

Consequently the chief medical officer issued interim guidance better defining the contentious term "pertinent local issues" and attempting to reduce time delays by allowing expedited review outside the normal committee cycle.8 Though the guidance clarified the situation it did notend the problems associated with multicentre review.9 Further, little had been done to aid consistency in local research ethics committee review. When applying to four different local research ethics committees it was quite possible to have to fill in four different forms, present a verbal explanation to some committees, and receive a mixture of favourable and unfavourable responses over a long period of time.10 Researchers viewed the research ethics committee system as an unduly overbearing one. They felt that ethical review often delayed or even prevented research that could benefit the population.11 In the light of this, the European clinical trials directive, and a number of research scandals, it became clear that a comprehensive review of the system was necessary. Consequently in 2001 the governance arrangements replaced the health service guidelines of 1991 and 1997.

WHAT NEEDED TO BE DONE?

The Declaration of Helsinki states at article 5: "In medical research on human subjects, considerations related to the wellbeing of the human subject should take precedence over the interests of science and society".12 It is perhaps this that the ethics committee reveres above all other principles. Delays, bureaucracy, and expense are undesirable but acceptable if they are necessary to achieve this goal. Prior to the new governance arrangements ethics committee members suffered inadequate guidance, poor funding, lack of facilitated communication between committees, and poor access to training. Members come largely from busy professions where time is at a premium. Yet neither they, nor their employer were paid for the time they spent preparing for and attending meetings. It seems that to fulfil article 5 of the Declaration of Helsinki, the independent ethics committee must continue to place the wellbeing of the participant above the interests of science and society. Yet the system must be better resourced and guided so as to reduce bureaucracy and thereby facilitate ethical research.

The new arrangements undoubtedly address the vital issues of resourcing ethics committees and reducing bureaucracy. They go beyond this, however, and it is questionable whether this is in the interests of the furtherance of article 5 of the Declaration of Helsinki. On a close examination of the literature detailing complaints from the research community, issues of delay and bureaucracy feature strongly. There is also an underlying notion, however, that the ethics committees' insistence

on participant wellbeing is disproportionately balanced with the value of medical science. Some commentators argue that the ethics committees' remit should be reduced—for example, to prevent them reviewing legal or scientific aspects of the protocol,13 or to keep local research ethics committees out of multicentre research review.14 The confidence of researchers in the ethical review system has diminished amid complaints that local research ethics committees frequently ignore the guidance relating to operational procedures,15 lack accountability, and do not adequately justify their decisions.16 Ethics committees were perceived as getting in the way of valuable research. It created a danger that the UK would not be seen as a viable site for lucrative international research. What resulted was pressure, particularly from industry, to refine the remit and freedom of research ethics committees in the interests of facilitating research.

In May 2001 a European directive was enacted which, in part, sought to standardise the function of ethics committees. Coming into force in 2004, the directive seeks to make binding elements of the good clinical practice guidelines produced by the International Conference on Harmonisation.17 The aim of "good clinical practice" undoubtedly constitutes an element of good *ethical* clinical practice, and the directive is based in part on the Declaration of Helsinki. Article 9 of the directive provides that: "No clinical trial can commence until an appropriate ethics committee approves the protocol". The directive is, however, equally concerned with procedural conformity. Thus, "good clinical practice" is as much a question of facilitating research as it is of ensuring that research is ethical. The aim is to ensure that Europe is an attractive location for lucrative research. It applies to clinical trials, many of which will be multicentred and commercially sponsored. It requires each member state to make one single opinion with regard to multicentre research, even if that research is limited to one member state.18

The research ethics committee governance arrangements build upon these foundations. Taken together, the new guidance will produce a number of favourable outcomes with regard to ethics committee procedure and consistency. The clinical trials directive was, however, industry-led and this is reflected in the governance arrangements. In terms of clinical research, the interests of industry will come to the fore. In terms of other types of research, the facilitation of research is given increasing significance over the protection of research participants. Paragraph 1.1 outlines the essential nature of research and the research ethics committee's duty to enable relevant research of good quality. The fact that this principle is stated first and foremost surely stands testament to its prominence. This principle potentially stands in opposition to article 5 of the Declaration of Helsinki which demands that "the well-being of the human subject should take precedence over the interests of science and society". Paragraph 1.3 of the governance arrangements states that the dignity, rights, safety, and wellbeing of participants must be the primary consideration in a research study. Later, in paragraph 2.3, more concession is made to article 5 of the Helsinki Declaration. It states that the goals of research are

secondary to the interests of participants. However, the fact that paragraph 1.3 does not state that participants' interests are the primary consideration of the *ethics committee* and that the arrangements do not put primary consideration on the principle by placing it numerically before and expressly above paragraph 1.1, is worrying. Though subtle, the wording marks a step away from protection of the research participant as the factor of paramount importance and instead asks the ethics committee to balance this with the furtherance of medical science. A number of provisions in the governance arrangements limit the remit of ethics committees and make it potentially more difficult for research participants to be given paramount protection.

APPLICATION OF 'RECOGNISED ETHICAL STANDARDS'

In paragraph 2.1—for example, it is stated that research ethics committees should provide independent advice to relevant parties as to the extent to which proposals comply with recognised ethical standards. Taken literally, researchers might have a legitimate complaint if ethics committees rule that a protocol is unethical and the committees have not applied recognised ethical standards to back up their advice.

Perhaps ethics committees should have trained ethicists as members so that in any novel situation (where there are no recognised standards to apply) they can nevertheless apply philosophically relevant standards. This is unlikely to be the required outcome of the arrangements as there is no mention that ethicists should be included on the committee or that training should radically improve members' understanding of moral philosophy. Otherwise, paragraph 2.2 might imply that Department of Health ethical guidelines should always be considered and applied. Ethics committees would welcome comprehensive guidance on every aspect of health care research. There would, however, be little need for the humble ethics committee if that ever became the reality. Research is constantly evolving and changing and ethics committees must be prepared to deal with novel situations for which there is limited ethical guidance. Rarely are ethical standards absolute. Ethics committees will have to give advice where ethical standards are in the process of being developed and debated. Consequently a researcher could argue that a standard promotes his research and the ethics committee could quote standards that render it unacceptable.

PROHIBITION ON LEGAL INTERPRETATION

The arrangements create some confusion in relation to the ethics committees' required knowledge and application of law. Paragraph 2.6 states that: "Research ethics committees should have due regard for the requirements of relevant regulatory agencies and of applicable laws", but that "it is not for the [research ethics committee] to provide specific interpretation of regulations or laws, but it may indicate in its advice to the researcher and host institution where it believes further consideration needs to be given to such matters". This is likely to cause confusion, as having due regard to regulations and laws necessarily involves an element of

interpretation. As HLA Hart's famous example shows, even an apparently simple legal statement like "No vehicles are allowed in the park" require interpretation to be applied.19 A car is clearly a vehicle, but what about motorcycles, bicycles or skateboards? Further, it might be argued by researchers that ethics committees have no power to withhold approval on the basis that the trial is in some way illegal, as the arrangements only allow them to indicate a need for further consideration. The law represents a minimum standard of conduct which ethics complements and builds upon. The essence of the arrangements is to ensure that ethics committees are mindful of legal principles but are not hindered by the necessity to get involved in minute interpretation. Yet, this provision has the potential to be abused by limiting the remit of the ethics committee to matters free of any legal interpretation.

PROHIBITION ON SCIENTIFIC REVIEW

A similar situation has developed in relation to ethics committees' consideration of scientific aspects of research. The original guidance to local research ethics committees, (HSG(91)5),4 required committees to look at protocols on the basis of three different approaches. Patient welfare involved a duty-based approach, patient dignity a rights-based approach, and scientific validity a goal-based approach. It seems that much of the latter element is to be lost.

Article 6 of the clinical trials directive provides that the research ethics committee is responsible for determining the relevance of the clinical trial and the trial design. This has been interpreted for the purposes of paragraph 9.13 of the governance arrangements so as to demand that research ethics committees are "adequately reassured" about the appropriateness of study design, risks and benefits, use of controls, criteria for withdrawing participants, adequacy of the monitoring arrangements, research site, and manner in which the research will be reported. By virtue of paragraph 9.9, however, it seems that the means of reassurance is not through review of the protocol, but through assessment of prior review by experts in the relevant research methodology. If the ethics committee is not satisfied that the prior review is adequate, paragraph 9.10 allows them to require resubmission. The requirement that ethics committees do not review scientific aspects of the protocol does not come from the European directive. Neither does it come from the research governance framework which states that: "All proposals for health and social care research must be subjected to review by experts in the relevant fields able to offer independent advice on its quality". This does not preclude scientific review by the research ethics committee. So it is a novel means of dealing with the scientific aspects of the protocol and it is likely to be problematic. Not only might it be difficult for the committee to separate the scientific review and the process of review, but there are different schools of thought within the field of research methodology which may make the review of process more difficult and controversial than it first appears.

LOCALITY REVIEW

In relation to multicentre research (involving five or more sites), the multicentre research ethics committee will review the ethics of the protocol. In parallel, each local research ethics committee will look at carefully defined locality issues. This presents potential difficulties in that the committee may require access to the reviewed protocol. The local research ethics committee might need to know what changes the multicentre research ethics committee has demanded in order to properly assess locality issues.

Time limits have recently been placed on the review process in the UK with the result that expedited review of local issues in multicentre trials takes place occasionally with as few as two local research ethics committee members. Some commentators believe this to be unethical.20 It potentially reduces the protection afforded to research participants. Nevertheless, the governance document leaves each committee to make its own arrangements for expedited review and does not expressly limit its use to cases of “locality issue” review.

The revision of guidance to ethics committees has been long awaited. The result is comprehensive and will benefit researchers and ethics committees in a number of ways. The function of ethics committees is better defined. Their funding and training requirements are secured. The benefits are marred, however, by an underlying emphasis on facilitating research to the extent that there is potential for it to adversely affect the interests of individual research participants. Though in total accordance with the clinical trials directive, this marks a small but significant step away from the principles ensconced in the Declaration of Helsinki.

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