Integrative Assignment 1

Candidate: 13027

Community Health Sciences BMedSci

Hand in Date: 09/01/2006

Word Count: 2,982

"Medical research in the U.K. is being suffocated by excessive governance and ethical review"

(Guidance for BMedSci Students, Tutors and Examiners Booklet 2005; 5)

Contents: **Page**

"Medical research in the U.K. is being suffocated by excessive governance and ethical review"

This report will explore and focus on the recent overhaul and complete reform of the face of research ethics in the UK (United Kingdom).[1] Researchers and research ethic committees have been waiting for these changes for a considerable amount of time but will they increase quality of research or the quantity of it. This report also will try to examine whether the new changed aid in the safety and dignity of participants or hinder these in favour of interesting research protocols.

History of UK's Research Ethics

The first signs of a "centralised" research governance system of ethics occurred in 1991. These were however set up as local branches known as LREC (Local Research Ethics Committees) and were involved in the regulation of research in their respective local NHS establishments.[1,2] They are funded by local health authorities and made up by twelve members consisting of medical professionals to lay persons.[3] There seemed to be no standardising of directives between each LREC and hence led to inconsistencies in approving research proposals, especially multicentre trials.[4]

This led to an uprising in researches complaining about the procedures in place which inevitably led to calls for a reform. The main concern was that for a multicentre approval the application was time consuming and was surrounding with "red tape" and bureaucracy which hindered the advance of research itself.[5,6,7] This called for one regulatory body in the UK to have the final approval, if granted this meant that the approved research protocol could take place across a number of European countries without further criticisms. Thus in 1997 the advent of MREC (multicentre research ethics committees) took place. This meant that multicentre applications instead of being scrutinised by many LRECs, will be considered by one MREC.[2]

However one aspect of research MRECs failed to consider are local issues. This resulted in a research protocol being submitted to LRECs for consideration on the impact of the research in their local communities.[8] The chief medical officer introduced "pertinent local issues" as a bid to clarify and decrease time delays in determining community considerations.[4,9] This brought some light to standardising approval methods, although other problems remained. It became necessary for multiple research applications to be submitted to each LREC and again the original problem of inconsistencies and bureaucracy hindering research began to emerge. In some cases LRECs reviewed not only the local issues but ethical ones also and if noticed it would write to a MREC which were often too busy to reply and hence the protocol would be rejected.[10]

Research ethics committees have been accused of making researchers work increasingly arduous. Five different research groups recorded a range of problems with ethic committees including distorting designs, delaying research protocols and prohibitive scientific advances.[11,12,13,14,15] Sometimes the paperwork involved in one aspect of ethics such as confidentiality resulted in production of long application forms which the lay public find difficult to digest and understand, hence resulting in lowered response rates.[13]

Researchers continued to argue against the increased work that was placed on them to deal with these multiple ethical reviews and felt that ethical committees not only delayed their research but prevented scientific advances in helping the population as a whole.[16] This forced a major review in 2001 in which governance arrangements replaced directives of 1991 and 1997. Various legislative reforms continue to occur including the 2004 clinical trial regulations.[17]

The "Warner Report"

In view of these continuing changes in policy and burdensome nature of research ethics committees, Lord Warner, in late 2004 a junior health minister arranged for an independent ad hoc advisory review of all NHS research ethics committees in health and social care.[18]

Group members examined aspects concerning remit, administration, operation, and workload of ethics committees in England. Their main tasks were to explore the presence of unnecessary regulations that hinder future research approvals. Other objectives of this group were to find solutions to any limiting factors that are existed in the governance process, to submit recommendations in reducing the time required for protocol processing while still adhering to the rights, dignity and safety of research participants. Also aims of strengthening the system, structures and ensuring efficient processing of information and the adequate training of users and committee members needed to be achieved.[19]

The main conclusion reached by the group, which were published in June 2005 was that NHS research needed to be more efficient and punctual. It was stated that in order to achieve these vital factors the committees must be focused on ethical issues and that the scientific responsibilities of protocols must be placed on different governance body. This meant that patient surveys, the suitability of staff involved and the adequacy of research sites can be resolved outside research ethics committees. The Central Office for Research Ethics Committees which is involved in the training of members, support and management was said to require further administrative support. The most vital result argued that the whole process of ethical approval was surrounded by the constraints of bureaucracy. The review brought to light the importance of standardization across all of Europe and within the UK which must include a simplified research governance framework. The examination further described the presence of too many committees and hence led to the inconsistencies experienced by multicentre trials. The solution was said to reduce committee numbers but to increase the frequency of meetings and to pay members and chairs of the committees for a better service. [18,20]

Digestion of the "Warner Report"

No doubt all the alterations suggested are very welcomed by the research community on the whole but whether they actually work remains to be seen. The recommendations for change may lead to some flaws not anticipated by the report.

Perhaps the increased number of committees does result in further inconsistencies in protocol approval. However the intended alterations would mean professionalising committee members. No evidence is given to suggest that increased frequency of meetings and paying the members would reduce cost, increase consistency and effectively increase efficiency. It remains to be seen that the members already in committees would accept these changes. Indeed it may result in a loss of the members that cannot spare longer hours or greater work loads or who have been serving out of public dedication and not for financial gain.[4]

The report seemed to have not resolved the distinction between the scientific review and the ethics behind a protocol. Its' bid to separate science from ethics could be hindered by the laws that bind the two eternally. The aspect of ethical review after scientific independent peer review could be flawed as increased alteration in ethics of a protocol may inadvertently alter the scientific aspects of it also. Another factor is that independent peer review could be biased to the point where it is done by individuals who have done research themselves and who obviously the favour the advent of interesting research.[21,22]

The report in the whole is in good nature and it does follow the trend of concluding that more reform is needed again. The time allocated for the report and the narrow references used in it may have affected the ability to thoroughly review UK's ethical legislations.[21] However the reform seems to be in deregulation rather than the previous increased legislations and maybe just another bandage for a gun shot wound.

What happens now?

Continuing reforms of NHS brought with it the research governance strategy for England published by the Department of health in 2000.[1] This new Research Governance Framework together with the changes in research ethics committees has been the largest reconstruction of research governance since post war 1960s.[23]

The reform means from April 2004, research undertaken in care organisations must have a sponsor, this signifies how commercial interests have molded the way research ethics is viewed.[24]

This is a bid to take advantage of the talents of researchers and their potential research material to encourage commercial gain and possible improvements of the NHS.[25] The increased legal issues of using human subjects or human materials for research means that this vast commercial potential in the NHS goes unused. New Human Tissue Bill, Human Rights Act 1998 and Data Protection Act 1998 all promote strict restrictions in research that contain humans.[26]

Therefore, the main idea behind the sponsor apart from financial gain is that the NHS remains a care organisation. This means it must ensure that all research on it's patients, staff, their private data any other materials that could be traced is carried out according to the framework stated. Having a sponsor would further achieve the goal of adhering to governance protocols, especially if the trust itself is its' own sponsor. In all cases it is important to carry out an independent scientific review, which means all research has to be approved by the relevant governing body of the site. Conflicts of interest could arise when the trust is conducting internal research on its' own patients, hence a system of internal independent review must be in place. [24]

The new European Union clinical directive introduced from May 2004 will mean that ethics committees will need to have better communication and a more centralized structure overseen by

an organisation known as the Central Office for Research Ethics Committees. After May 2004, sole responsibility of all UK Ethics Committees will be with the Central Office.[27]

Scientific quality, consent process and above all the safety of research participants have been the dominant aspect of research ethics committees in the past.[28] The fact that the new scheme would be the review of scientific aspects of the protocol by a sponsor or care organisations means the new breed of ethics committees will discuss safety and very vaguely defined ethics only.[24]

The main aim since the birth of the Declaration of Helsinki has primarily being the safety of the research participants above all else.

"*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".*[29]

The factors found addressed in the "Warner Report" such as delayed approval times and inconsistencies of decisions made are all acceptable if the fundamental above rule is adhered to. The new governance arrangements have aimed to target committee members which sometimes lacked guidance, funding, communication between committees and poor training.[30] The independent ethics committee should be better guided and at the same time reduction of bureaucracy to hinder ethical research must be prevented, though not enough for flaws of ethical judgment to leak through to an extent of affecting research participant safety. It is finding the balance between these factors that is most important and the most difficult aspect of research ethics.[31,32]

The introduction of the European directive is a bid to stop the competition between ethical aspects and good clinical practice and instead seek to bind the two. The "good clinical practice" guidelines produced by the International Conference of Harmonisation were also based upon good ethical practice and the Declaration of Helsinki.[33] The identification of the need to decrease

legislation was also apparent in the article which was equally concerned with facilitating research and the ethics of projects concerned.

The aim on the whole is to ensure that Europe remains an attractive location for interesting and financially motivated research. Sponsored and multicentre clinical trials will be of most benefited by the new directives.[4]

"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."[34]

The governance of the research ethics committees will no doubt build on the above directives and it is hoped that it will produce better consistency. It is interesting to see however that this directive is an internal medical professional orientated bid and no lay or public input has gone into the formation of it. The public reluctance of scientific research is perhaps the stimulant of this nature of ethics committees that has decided to conduct private meetings.[35,36] Also, no requirements or directives are in place about informing research subjects on decisions made in these meetings.[24]

"*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."*[4]

If read between the lines this may suggest the subtle way of stepping away from considering safety to the research participant as the major factor in approving a protocol. Rather, it seems to dictate that ethics committees should balance this with the importance of the advances in medical science. This together with many new governance provisions increasingly inhibits the following the fundamentals of the Declaration of Helsinki stated above. Inevitably the placing of research participant's safety as the dominant concern of research ethics committees is well and truly under attack.[4,21]

The Separation of Scientific Review

The original guidance to LREC representatives dictated that committees should judge protocols in three different approaches.[1]

"Patient welfare involved a duty-based approach, patient dignity a rights-based approach, and scientific validity a goal-based approach."[4]

The new framework would mean the much of the latter will be lost. The clinical trials directive has focused the committees into validating the clinical trial and the trial design only. This has been a new step backed by the "Warner Report" in reassuring the lay members of the committee that thorough independent review has already been passed on the protocol before being subjected to ethical review.[19] Essentially, this suggests that the study design, control criteria, monitoring, withdrawal and inclusion criteria, benefits and risks, review of the research site and the arrangements to report the research will all be recorded and presented before ethical review takes place. However if the ethics committee are not satisfied with the prior review then they can ask for a resubmission but cannot conduct a scientific review themselves.

"*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".*[4]

Here in lies a fundamental difference in the new framework and does not stem from the European directive nor does it come from the research governance framework. This means the review process would be more difficult as sometimes ethical and scientific reviews are hard to separate for reasons mentioned earlier in this article, hence decisions made by committees could become more controversial than ever before.

Community Considerations

In the past much conflict resulted in the presence of differing view between MRECs and LRECs, especially when it came to community considerations. The new directives state that multicentre research ethics will review protocol if more than five sites are involved. Furthermore local research committees at each site will be asked to review the protocol further, using strictly defined locality issues. Good communication between the MRECs and LRECs is a vital element for this scheme to work as they each must know what changed the other has made.[4]

The introduction of time limits in the UK protocol review has hastened the review process and although this would mean more cases are dealt with sooner, it may affect the safety of participants if matters are rushed. It also means that local issues require meetings in short notice, hence sometimes only few members can be present in short notice. This may decrease the diversity of views and could be seen as being unethical practice.[37]

Personal Conclusions

On the whole the latest revisions in guidance for the research ethics committees have been long awaited by researches. It was expected to stop the down regulation of research and encourage researchers to continue to produce work. The good that has come out of it has certainly been comprehensive and will benefit researchers and ethics committees in many ways mentioned above. Also the objectives of the latter is much better defined and regulated.

Conversely has this bid to increase research in a bid to improve scientific advance affected the public safety? Not only have some flaws regarding the safety of research participants identified in this report but also potential flaws regarding the design and quality of research that is being approved. The fact remains that it is highly ironic that the public view as a whole is not considered in forming these new directives. In fact the public view has never being considered in this aspect of research ethics which is in place to protect those who do not know its rules, regulations or its governance protocols. The recent vogue of public involvement in every aspect of medicine makes this self governance of research ethics by medical professionals is even stranger.

To answer the question stated at the start of this report, this recent change in ethical directives is a step away from the principles announced in the Declaration of Helsinki and it is addressing the issue of quantity of research not the quality of it. It is important to understand in the future that more change is needed and it will continue to happen. However as the new tide of directives continue to come it's time to recognise that ethics remain at most a human response to conflicting social opinions. It is impossible to form a directive to every foreseeable ethical circumstance, so at the end it is up to the people to decide their own fate and increased governance will not have the final say.

---

[1] Department of Health. **Local research ethics committees.** London: DoH, 1991 (HSG(91)5).

[2] Department of Health. **Ethics committee review of multi-centre research: establishment of multi-centre research ethics committees.** London: DoH, 1997 (HSG(97)23).

[3] Department of Health. **Research governance framework for health and social care.** London: DoH, 2001.

[4] Cave E, Holm S. **New governance arrangements for research ethics committees: is facilitating research achieved at the cost of participants' interest.** *Journal of medical ethics* 2002; 28: 318

[5] See Penn ZJ, Steer PJ. **Local research ethics committees; hindrance or help**? *British Journal of Obstetrics and Gynaecology* 1995; 102:1–2;

[6] Garfield P. **Cross district comparison of applications of research ethics committees.** *British Medical Journal* 1995; 311:660–1.

[7] Harries UJ, Fentem PH, Tuxworth W, *et al*. **Research ethics committees: widely differing responses to a national postal survey.** *Journal of the Royal College of Physicians of London* 1994; 28:150–4.

[8] Tully J, Ninis N, Booy R, *et al*. **The new system of review by multicentre research ethics committees: prospective study.** *British Medical Journal* 2000; 320:1179–82.

[9] Stacey TE. **How should an LREC handle an MREC approved application: interim guidance [circular letter to all LRECs and MRECs]** 1998; 28:1–3.

[10] Alberti KGMM. **Multicentre research ethics committees: has the cure been worse than the disease?** *British Medical Journal* 2000; 320:1157–8.

[11] Ward HJT, Cousens SN, Smith-Bathgate B, Leitch M, Everington D, Will RG, Smith PG. **Obstacles to conducting epidemiological research in the UK general population**. *British Medical Journal 2004;* 329: 277 – 279.

[12] Jones AM, Bamford B. **The other face of research governance.** *British Medical Journal 2004;* 329: 280 – 281.

[13] Wald DS. **Bureaucracy of ethics applications**. *British Medical Journal 2005;* 329: 282 – 284.

[14] Jamrozik K. **Research ethics paperwork: what is the plot we seem to have lost?** *British Medical Journal 2004;* 329: 286 – 287.

[15] Parker M, Ashcroft R, Wilkie AOM, Kent A. **Ethical review of research into rare genetic disorders**. *British Medical Journal* 2004; 329: 288 – 289.

[16] Foster C. **Why do research ethics committees disagree with each other?** *Journal of the Royal College of Physicians of London* 1995; 29:315–18.

[17] The Medicines for Human Use (Clinical Trials) Regulations 2004. SI 1031. London: HMSO, 2004.

[18] Department of Health. **Report of the ad hoc advisory group on the operation of NHS research ethics committees. London: DoH, 2005.** *Available;* URL:http://www.dh.gov.uk/assetRoot/04/11/24/17/04112417.pdf (accessed 02 January 2006).

[19] Mayor S. **Advisory group to review NHS research ethics committees.** *British Medical Journa*l 2004; 329:1258.

[20] Edwards SJL, Ashcroft RE, Kirchin S. **Research ethics committees: differences and moral judgement.** *Bioethics* 2004; 18: 408-27.

[21] Ashcroft RE, Newson AJ, Benn PMW. **Reforming research ethics committees** *British Medical Journal 2005;* 331: 587 – 588.

[22] Tinker A, Coomber V. **University research ethics committees: their role, remit and conduct.** *London: King's College London* 2004.

[23] **Geneva Conventions.** *Available;* URL: www.globalissuesgroup.com/geneva/texts.html (accessed 03 January 2006).

[24] Kerrison S, McNally N, Pollock AM. **United Kingdom research governance strategy.** British Medical Journal 2003; 327:553-556.

[25] Poste G. **In: House of Lords Select Committee on Science and Technology. Human genetic databases: challenges and opportunities.** *4th report*. London: Stationery Office, 2001: paragraph 6.2 (HL 57).

[26] Jacobson PD. **Regulating health care: self regulation to self-regulation?** *Journal of Health Politics* 2001; 26: 1165-77.

[27] McNally N, Kerrison S, Pollock AM. **Reforming clinical research and development in England.** *British Medical Journal* 2003; 327: 550-3.

[28] Savulescu J. **Two deaths and two lessons: is it time to review the structure and function of** research **ethics committees?** *Journal of Medical Ethics* 2002; 28: 1-2.

[29] **World Medical Association**. *World Medical Association Declaration of Helsinki—ethical principles for medical research involving human subjects*. Adopted by the 18th WMA General Assembly Helsinki, Finland, June 1964 and amended by the 29th WMA General Assembly, Tokyo, Japan, October 1975; 35th WMA General assembly, Venice, Italy, October 1983; 41st WMA General Assembly, Hong Kong, September 1989; 48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996, and the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000: **article 5**.

[30] Freedman B. **Multicenter trials and subject eligibility: should local IRBs play a role?** *IRB: Review of Human Subjects Research* 1994; 16:1–6.

[31] Eichler H-G. **Hazards of misguided ethics committees.** *Lancet* 1995; 346:1115–16.

[32] Hotopf M, Wessely S, Norman N. **Are ethical committees reliable?** *Journal of the Royal Society of Medicine* 1995; 88:31–3.

[33] **International Conference on Harmonisation of Technical Requirements for Regulation of Pharmaceuticals for Human Use.** *Tripartite guideline for good clinical practice*. Geneva: International Federation of Pharmaceutical Manufacturers Association, 1996.

[34] **Directive 2001/20/EC of the European Parliament and of the Council of 2001 April 4**. **Article 7**. On the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. *Official Journal of the European Communities* 2001; L121:34–41.

[35] Ayres I, Braithwaite J. **Responsive regulation: transcending the deregulation debate.** Oxford: OUP, 1992.

[36] Ashcroft R, Pfeffer N. **Ethics behind closed doors: do research ethics committees need secrecy?** *British Medical Journal* 2001; 322: 1294-6.

[37] Barber SG. **Ethical ethics committees?** *Journal of Medical Ethics* 2000; 26:142.