Article

Process error rates in general research applications to the Human Research Ethics Committee (Medical) at the University of the Witwatersrand: A secondary data analysis

P Cleaton-Jones, MB BCh, PhD, DSc (Dent), FCD

Steve Biko Centre for Bioethics, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg

Objective. To examine process error rates in applications for ethics clearance of health research.

Methods. Minutes of 586 general research applications made to a human health research ethics committee (HREC) from April 2008 to March 2009 were examined. Rates of approval were calculated and reasons for requiring revision or non-approval of the applications were grouped into eight categories.

Results. Of the applications, 37% were approved at first evaluation; minor revisions were required for 56% and major revisions for 3%, while 4% were not approved. Eventually 69% of the 586 applications were approved. Surprisingly, 28% were removed from the Committee agenda because of no response from the applicants. Of the 607 instances of process error in 369 applications requiring revision or that were not approved at first evaluation, difficulty with consent documents (55%) and missing information (43%) were the most frequent; the remaining 6 types ranged in frequency from 3% to 17%.

Conclusion. It is suggested that the process errors seen could be reduced in rate if applicants were to show a draft of their application to an HREC member or experienced researcher before submission.

Anyone who joins a health research ethics committee (HREC) soon notices that few applications for ethics clearance are approved at the first evaluation. In a recent audit of a total of 1 180 applications to the HREC (Medical) of the University of the Witwatersrand (Wits) in 2003 and in 2007, 21% were approved on first submission, 72% required minor or major revision, 5% were not approved and 2% were withdrawn.[1]

Angell and Dixon-Woods[2] recently reported on an analysis of a total of 141 letters written by UK National Health Service RECs in 4 months from July 2005 to April 2006. The initial decision rates were: approved 15%, revision needed 64%, not approved 8% and withdrawn 13%, rates similar to those at Wits.[1] The British investigators looked at what they termed process errors in the letters sent to researchers whose applications were not approved at initial submission. Four types of process errors, alone or in combination, were identified: procedural violations (74%), missing information (68%), slip-ups (44%) and discrepancies (25%).

The findings in the UK publication appeared to be similar to findings experienced with general research applications made to the Wits HREC (Medical) at an anecdotal level; this study was therefore done to objectively determine process error rates at the Wits HREC (Medical).

Methods

The policy of Wits University is that all health research under its jurisdiction must be approved by the HREC (Medical) before initiation of the research (http://web.wits.ac.za/Research/Ethics). There are two routes for applications to this committee:

- General research is submitted via the University's central Research Office.
- Sponsored clinical trials are submitted through the Ethics Division of the Wits Health Consortium, which is a private not-for-profit company within the Faculty of Health Sciences of the University.

General research applications are prepared by the investigators/researchers themselves, whereas sponsored clinical trial applications are prepared by a sponsor company or their representatives or institution specialists in collaboration with sponsor companies or their representatives and investigators/researchers.

Separate minutes of the general research and sponsored clinical trial sections of each meeting are kept. This study was limited to the minutes of the general research applications at the 11 meetings of the Wits HREC (Medical) from April 2008 to March 2009 (there is no meeting in December) under ethical clearance number M050247. The following method was used:

First, a count was made of decisions at the initial consideration of an application. Four categories were used:

- approved
- minor revision to the satisfaction of a designated member of the HREC (Medical)
- major revision – resubmission back to the full committee
- not approved.

Secondly, meeting minutes were examined for decisions on responses from applicants to requests for minor or major revision up to the May 2009 meeting, the second meeting after the initial consideration of an application. For some 20 years it has been HREC (Medical) policy to automatically remove applications from a meeting agenda if no response to its comments on these applications are received by this second monthly committee meeting.

This policy was adopted because experience showed that almost all decisions on revised applications are made by that meeting.

The minute for each application that was not approved at initial submission was then examined for reasons for the decision – this minute is what is sent to applicants. The study used the four process error categories of Angell and Dixon-Woods[2] plus four additional categories:

- procedural violation[2] – missing signatures, failure to comply with application procedures
- missing information[2] – failure to provide sufficient information to understand a proposed study
- slip-ups[2] – minor errors such as typos, incomplete sections of the application form
- discrepancies[2] – inconsistencies between sections of the application form or supporting documents
- informed consent – revision of information sheets/consent forms required
- participant confidentiality – inadequate provision for this
- study population – inappropriate choice, need for counselling owing to the nature of a study
- legal – potential incrimination or contrary to South African law.

Each application could have more than one of the categories applicable to the Committee's decision.

Results

During the study period 586 general research applications were considered by the Committee; one additional application was withdrawn before evaluation. Table I shows that 37% of applications were approved at initial submission, the bulk of applications (56%) required minor revision, 3% needed major revision, and only 4% were not approved. In due course 69% of applications were approved. According to Wits HREC (Medical) standard practice 28% were removed from the Committee agenda after two meetings beyond the submission meeting. This is done when no response to the requirement for revision or non-approval was received from applicants by that time. A later response can restore such an application to the agenda.

Table II compares the decision rates of the current study period with those in 2003 and 2007.[1] The initial decision rates in the three periods were similar, but the rate of applications removed from the agenda in the current study period was approximately 50% higher than in the preceding study periods.

Table III lists the 607 process errors identified by the Committee in the 369 applications that required revision or were not approved at initial evaluation. Two rates were calculated – the percentage of errors in each category of the 607 process errors (%PE), and the percentage of errors in each category of the 369 applications (%A). Problems with consent and missing information were the most common.

Discussion

Initial decision rates in this study are similar to those reported elsewhere, as has been discussed in a previous publication.[1] What is unusual is the high prevalence of applications removed from the HREC (Medical) agenda owing to non-response from applicants – 28% compared with 19% in 2003 and 16% in 2007. So far the reason for this discrepancy is obscure, but there are some possibilities.

- Applicants may have ignored the comments of the HREC (Medical) and done their proposed research without ethics approval. This scenario is unlikely owing to the requirement to provide evidence of ethics approval for both undergraduate and postgraduate research, for grant applications and for publication in reputable journals.
- Applicants may have discovered that the necessary funding, time or facilities to continue with the research would not be available.
- Applicants may have been so intimidated by the response of the Committee that they decided not to proceed with their proposed research. One hopes that this is not the reason.

There are many published articles on personal experiences with RECs from both applicants and committee members. Dixon-

Table I. HREC (Medical) decisions for general research applications

	Initial decision			Final decision	
	N	%		*N*	%
Approved	215	37	Approved*	404	69
Minor revision	330	56	Removed from agenda†	164	28
Major revision	19	3			
Not approved	20	4	Not approved	18	3
Total	586	100	Total	586	100

*Sum of applications approved at initial consideration and those successfully revised.

†Removed from agenda after no response from applicants – includes applications requiring minor or major revision.

Table II. Comparison of HREC (Medical) decisions for general research in three periods, 2003 (*N*=439),[1] 2007 (*N*=553)[1] and the current study (*N*=586)

	Initial decision (%)				Final decision (%)		
	2003	2007	Current study		2003	2007	Current study
Approved	27	37	37	Approved[†]	77	81	69
Minor revision	62	55	56	Removed from agenda[†]	19	16	28
Major revision	7	5	3				
Not approved	4	3	4	Not approved	4	3	3

* Sum of applications approved at initial consideration and those successfully revised.

[†]Removed from agenda after no response from applicants – includes applications requiring minor or major revision.

Table III. HREC (Medical) process errors as reasons for revision or non-approval of applications at initial evaluation

Process error categories	*N*	% of process errors (*N*=607)	% in applications (*N*=369)
Procedural violation	36	6	10
Missing information	158	26	43
Slip-ups	55	9	15
Discrepancies	27	4	7
Consent	203	33	55
Confidentiality	64	11	17
Study sample	54	9	15
Legal	10	3	3

Wood and colleagues have pointed out that much of this published work has '... come from health researchers, traditionally in the form of complaints about bureaucracy, delay and stifling of research ... systematic empirical evidence about RECs and their operation is mostly lacking. Current evidence tends to be anecdotal ...'[3]

An extensive literature search for the current study showed that published articles dealing with process errors in REC applications are few and are limited to the Social Science Research Group of the Department of Health Sciences at the University of Leicester, UK. Three of these are appropriate for the present investigation.[2-4] The current study adds to the systematic evidence of the University of Leicester Social Science Research Group.

Rates calculated in the current study show the relative frequency of the eight types of process error (%PE) within the total of 607 such errors found, as well as the relative frequency of each type within the 369 applications that required revision or were not approved at initial evaluation (%A). In contrast, the rate calculated by Angell and Dixon-Woods[2] showed the percentage of letters to applicants that listed at least one process error; this is shown as %L.

Procedural violation (6%PE, 10%A)

Many applicants do not understand that an application for ethics clearance is a legal document, but seem to consider it as a bureaucratic annoyance. General research applications at Wits are stored in the University Registry and are referred to from time to time when problems arise. Essential items are the name of the applicant (yes, people do omit this) and signatures of the applicant plus those designated by the academic entity in which the applicant is based. The latter may be the head of the entity or in large departments, for example, a research co-ordinator.

There are several reasons why the supporting signatures are required. The head of department needs to know what staff are doing, that proposed research is within the remit of the department, that the standard of the proposed investigation is of acceptable quality, and that sufficient finances are available or will be applied for. Heads are the line managers for what happens in their departments and are held responsible when a staff member does something unacceptable.

The procedural violation rate at Wits is much lower than that reported in the UK study (74%L).[2] A possible reason for this is that the application process is relatively simple, consisting of completion of a 4-page application form and submission of supporting documents if desired. In addition there are many experienced applicants available plus ready access to members of the HREC (Medical) for advice.

Missing information (26%PE, 43%A)

All researchers are intimately involved with their research. As a result, both novice and experienced researchers fail to appreciate that an outsider to their research may lack information necessary to understand what is to be done. There needs to be sufficient information in an application to enable a broad understanding of what is proposed. A way to ensure this is to show a draft to someone not involved with the research, ideally an HREC (Medical) member, and have them say what they understand. Attachment of a detailed research plan helps – sometimes such plans are referred to but not provided with the application. When a designated member of the HREC (Medical) discusses a required revision with an applicant, it is frequently amusing to see the person discover just how cryptic the application was. The missing information rate identified in this study is two-thirds lower than that in decision letters in Britain (68%L).[2]

Slip-ups (9%PE, 15%A)

Everyone makes slip-ups, but this should be avoided as much as possible when completing application forms. Minor errors such as typographical errors are correctable with spell-checking today. Failure to specify age of participants, for example, will certainly delay an application when age of legal consent has to be considered. Numbers of participants (sample size) give an idea of the scope of a study – numbers may be too small for a particular type of study, but adequate for another type. A particular annoyance for HREC members is when sections such as 'Objectives of the study' contain the words 'See attached'.

Double-checking an application form is a useful habit for researcher/applicants to develop. Application forms for ethics clearance, grants and prizes are not drawn up to annoy applicants; they provide valuable information to help committees to make decisions.

Incomplete sections in the application forms are a common cause for negative decisions. Ability to complete application forms for ethics clearance, grants, awards and so on is a basic skill that researchers need to develop; having a personal check list helps. The slip-up rate in the British study was approximately three times higher than in the present audit (44%L).[2]

Discrepancies (4%PE, 7%A)

Inconsistencies between sections of the application form and supporting documents indicate sloppiness to HREC (Medical) members. This is often due to 'cutting and pasting' from one document to another. Common examples of discrepancies in application forms are variations in study areas, age of participants and tests to be done. When there are multiple discrepancies in an ethics application form it raises concern about the standard of the research itself. The low discrepancy rate in this study does suggest some checking of the applications prior to submission.

Consent (33%PE, 55%A)

Inadequate informed consent was the most frequent problem seen in the study. Typical inadequacies are:

- coercive documents of the 'I want, you will' variety that imply automatic enrolment
- inadequate explanation of expectations of both investigator and participant
- poor language filled with cryptic jargon that even members of the HREC (Medical) have difficulty understanding
- lack of respect for the autonomy of a potential participant, which includes no greeting of the person being approached and no introduction of the researcher
- lack of understanding of the legal requirements for consent in South Africa – minors, relatives, caregivers, physical or mental state
- failure to include a voluntary withdrawal clause without penalty.

To avoid these difficulties, the HREC (Medical) has a template on the University and Wits Health Consortium websites which outlines the issues pertinent to adequate informed consent. In spite of this, inadequate consent is still common.

Participant confidentiality (11%PE, 17%A)

Many studies are innocuous and without risks to participant confidentiality, but others have serious risks of disclosing confidential information.

- Researchers often use phrases such as '... your information will be kept confidential ...' without explaining what this means. For example, a statement such as. '... your name will not be recorded in any study reports, so no one will be able to identify information as yours ...' gives an idea of measures that will be put in place to protect participant confidentiality.
- Researchers often promise anonymity, then proceed to record names, addresses, hospital numbers, dates of birth and suchlike on the data sheets – completely the opposite to what was implied in the participant information sheet. Particular identifiers are date of birth instead of age and employment level in a small group that permits identification of a person.
- Focus groups, in which a group of research participants discuss concepts initiated by a reaearcher/facilitator, are a common technique used in qualitative research. Many researchers promise absolute participant confidentiality, but this is an empty reassurance – there is no absolute confidentiality in a focus group; participants may freely discuss their participation in the research.

Study population (9%PE, 15%A)

Problems seen in applications under this heading include:

- Inappropriate choice of the target study population by an inexperienced investigator. HRECs have experienced researchers as members who may advise an applicant as to the appropriate study population for the suggested research.
- Studies may cause psychological discomfort to participants, or worse require participant counselling, and a researcher has not considered this.

- A researcher may be inappropriate for research in a particular study population. For example an undergraduate student may be too inexperienced for a certain population, while a qualified health care worker may be suitable.

Legal (2%PE, 3%A)

This was the least common process error in the study. Competence to consent with regard to age or mental or physical state is included in the consent section above.

Potential incrimination of a researcher or a participant in certain types of research is seen from time to time. For example, investigation of an illegal activity may be proposed in which researchers promise confidentiality to a participant without realising that they may have a legal obligation to provide information that may be used to the detriment of themselves and their research participants. Researchers do not share the legal confidentiality of a lawyer and client.

In South Africa there is a statutory duty on health care workers to report child abuse and sexual offences, something that may be discovered in a research study. Applicants may not understand this obligation or know how to manage such cases.

In rare instances it may even be unsafe for a researcher to do a particular investigation, for example in areas in which there is civil unrest or high crime rates.

Conclusion

This study has shown the types of process errors seen over 1 year in applications for ethics clearance to the Wits HREC (Medical). The author believes that discussion of an application draft with a member of the HREC or an experienced researcher before submission is likely to increase the rate of application approvals at initial evaluation, thereby reducing applicant frustration over delays in starting a project. Personal discussion with department heads has also suggested that they should not permit submission of substandard applications. However, several department heads have said that in the interests of good departmental interpersonal relations, they prefer to have the HREC (Medical) act as the screener rather than themselves.

One may add to these points that committees such as the Wits HREC (Medical) should ensure that their standard operating procedures and application forms are comprehensive and helpful and that templates are available to help with drafting informed consent documents. Finally, cut-off dates for response to comments from committees may be useful.

Many thanks to the hard-working HREC (Medical) Secretariat staff in the Wits Research Office and the Ethics Division of the Wits Health Consortium that keep the Committee functioning.

References

1. Cleaton-Jones P, Vorster M. Workload of a South African university-based health research ethics committee in 2003 and 2007. *South African Journal of Bioethics and Law* 2008; 1: 38-43.
2. Angell E, Dixon-Woods M. Do research ethics committees identify process errors in applications for ethical approval? *J Med Ethics* 2009; 35: 130-132.
3. Dixon-Woods M, Angell E, Ashcroft RE, Bryman A. Written work: the social functions of research ethics committee letters. *Soc Sci Med* 2007; 65: 792-802.
4. Dixon-Woods M, Angell E, Tarrant C, Thomas A. What do research ethics committees say about applications to do cancer trials? *Lancet Oncology* 2008; 9: 700-701. http//www.thelancet/oncology (accessed 7 August 2009).