

Workload of a South African university-based health research ethics committee in 2003 and 2007

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Objective. To compare workloads of a university-based health research ethics committee (medical) for 2003 and 2007.

Methods. Minutes and database records of all applications processed by the committee in 2003 and 2007 were examined.

Results. General research applications increased from 439 to 553 in 2007 while clinical trial proposals declined from 102 to 86. Some 60 - 70% of applications required revision; 77 - 81% of general research applications and 86 - 97% of clinical trials were eventually approved.

Conclusion. The workload puts an increasingly heavy burden on committee members and support staff.

A health research ethics committee (REC) to deal with medical research involving humans was established at the University of the Witwatersrand, Johannesburg (Wits), in October 1966, 4 months after publication of the seminal article on ethics and clinical research by Beecher.¹ This committee, the first in South Africa, has functioned continuously ever since. From 1966 to 2002 it was known as the Committee for Research on Human Subjects (Medical) and subsequently as the Human Research Ethics Committee (Medical) (HREC(M)). The Committee has United States Federal Wide Assurance (FWA No. 00001223) and has applied for registration with the newly formed National Health Research Ethics Council in South Africa; it is informally accepted by the South African Medical Research Council (MRC) and the Human Sciences Research Council (HSRC). There are two other RECs at the University, one dealing with research in the humanities (since 1988) and the other with research involving animals (since 1975).

In time other South African universities and the Medical Research Council established RECs during the 1970s and 1980s, followed by the South African Medical Association and the pharmaceutical industry in the 1990s and the Human Sciences Research Council and the Department of Health in the new millennium.

Regarding health research, the policy at Wits is that all such research must be approved by the HREC(M) (<http://web.wits.ac.za/Research/Ethics>). There are two routes for applications to the HREC(M). 'General' research is submitted to the University's central Research Office to a full-time administrator who services the committee aided, when required, by a part-time staff member who attends to the other two committees. The administrator collates application documents, circulates them to the HREC(M) members, keeps minutes of the general research part of the monthly meeting, handles queries, maintains the master database and prepares clearance certificates for the Chairs to sign.

Applications for sponsored clinical trials are submitted to the Ethics Division of the Wits Health Consortium (WHC), which is a private 'not for profit' company within the Faculty of Health Sciences of the University. Here four full-time members of staff

manage the extensive documentation required by Good Clinical Practice for the University, the Medicines Control Council, and international bodies. They maintain the sophisticated database and tracking system, service a Protocol Review Committee and keep minutes of the clinical trial section of the monthly HREC(M) meeting. Standard Operating Procedures are at <http://www.witshealth.co.za/ethics>. About 10 days before an HREC(M) meeting, a Protocol Review Committee (PRC) within the WHC Ethics Division examines the science and safety of a proposed clinical trial and whether this may be carried out in the State-funded academic hospitals attached to the University (these hospitals have representation on this committee). The findings of the PRC are provided at the HREC(M) meeting.

The HREC(M) consists of 33 members, 28 from within the University and five from external institutions (two are from a neighbouring university, one is from a local church and two are from private sector entities). The members, all of whom are appointed in their personal capacity, encompass the following disciplines: anaesthesiology, bioethics, dentistry, education, bioethics, gynaecology, immunology, internal medicine, law, neurology, nursing, occupational health, paediatrics, physiology, physiotherapy, psychiatry, psychology, public health, radiation oncology, religion, speech therapy, social work and surgery. There is one Chair and four co-Chairs, all of whom have equal decision-making powers. Coincidentally, one member serves on the RECs of the MRC, Palliative Care Society and Health Professions Council of South Africa Human Rights and Ethics Committee and is Deputy Chair of the National Health Research Ethics Council, and two are on the Ethics Committee of the HSRC, one of whom is the Vice-Chair. Length of HREC(M) experience ranges from a few months to 34 years with over half the members having at least 10 years of experience. Formal qualifications in bioethics are held by four members with two more completing postgraduate courses.

Monthly meetings are held from January through November on the last Friday of the month from 12h30 until the agenda is completed, usually around 17h30. Applications submitted by the 7th

of a month are considered in the same month. Applicants for general research (all research except sponsored clinical trials) have to provide 23 hard copies of a completed four-page application form as well as informed consent documents; they are advised also to submit four copies of a full protocol, but this is optional. Applications for sponsored clinical trials provide the 23 copies of the application form plus four copies of the extensive documentation required by the national regulating authority, the Medicines Control Council (MCC), the equivalent of the United States Food and Drug Administration.

About 2 weeks before a meeting members confirm by email who will be attending, after which one of the Chairs assigns two members to assess each application in depth; however, all members receive copies of all application forms and informed consent documents. By mutual arrangement, the Chairs share the workload so that each application is also assessed by a Chair. For retrospective clinical record reviews or secondary data analysis one Chair and one member provide a written summary assessment at the meeting, subdivided into those requiring discussion and those that may be approved at once if HREC(M) members agree – this speeds the meeting.

The monthly REC meeting is run in two sections. In the first, sponsored clinical trials are considered and serviced by staff from the Ethics Division of the WHC. This part of the meeting is closed except to HREC(M) members plus applicants and sponsors of a particular trial who may attend, or be asked to attend, when their application is considered. In the second part, general research is considered serviced by the University's Research Office. One hour of this section of the meeting is open to anyone who wishes to attend and is accredited with the Health Professions Council of South Africa for the compulsory continuing education ethics points required for maintenance of a clinical licence. In addition, any applicant may request to attend, or be requested to attend, for the consideration of their application. At the meeting the assessors verbally report on the applications they have evaluated, after which discussion is open to the committee.

Throughout the research ethics committee world there are complaints that committee workloads are high and increasing. While there is some published information from the developed world about this, there is a lack of publications from developing countries.

This paper evaluates the workloads of the longest established HREC(M) in South Africa for the years 2003 and 2007.

Methods

After clearance of the protocol by the HREC(M), information from the minutes of the HREC(M) meetings and database of the Ethics Division of the WHC was obtained and placed into a SAS data set for analysis with SAS for Windows (Version 9.1 SAS Institute Inc., Cary NC, USA).

The fate of each application was examined and classified into:

- Approved – either at the first consideration or after revision.
- Minor revision – here an HREC(M) member is assigned to help an applicant rectify minor points. Approval is given once acceptable modifications have been made.

- Major revision – the application needs to be resubmitted to the full HREC(M) after extensive changes.
- Not approved – the application is not acceptable.
- Withdrawn – an applicant chooses to withdraw the application.
- Removed from the agenda – if after 3 months no revision has been submitted by an applicant it is taken off the agenda. It may be replaced on request.

Results

General research

There was a 26% increase in total applications from 439 in 2003 to 553 in 2007. The percentage of applications from graduates increased from 75% in 2003 to 90% in 2007 with an accompanying decrease in applications from undergraduates from 25% to 10%. The numbers of applications per month for the two years examined are shown in Fig. 1. In both study years a typical number of applications considered at each meeting was between 40 and 50 with a peak of 72 in March 2007. The beginning and end of the year were the busiest times.

The outcomes of the general research applications are shown in Table I. At the initial HREC(M) meeting a quarter to a third were approved at once, around 60% required minor revisions, and approximately 10% needed major revision and resubmission or were not approved. Ultimately some 80% of applications were approved but almost 20% were removed from the agenda due to inaction by applicants.

Clinical trials

In 2003 applications for 102 clinical trials were processed compared with 86 in 2007, a reduction of 16%. The numbers of applications per month are shown in Fig. 2. The pattern of applications was erratic from January through July, but thereafter the numbers in 2003 and 2007 showed some parallels.

Outcomes of applications are listed in Table II. A striking feature is that 17% of applications in 2003 required major revision or were not approved compared with no such decisions in 2007.

Discussion

A great deal has been written on guidelines for research ethics committees (known as Institutional Review Boards (IRBs) in some countries) to follow in their functioning, but there is little on workload.

Background

The University of the Witwatersrand, with a current total student enrolment of 25 000 was established in 1922. It has five Faculties containing 37 Schools and more than 30 research entities. The Faculty of Health Sciences comprises Schools of Anatomical Sciences, Clinical Medicine, Oral Health Sciences, Pathology, Public Health, Physiology and Therapeutic Sciences. In most years 400 undergraduate and 60 postgraduate degrees are awarded and there are some 500 health specialists in training (see web.wits.ac.za/Academic/Health/Faculty/History.htm).

In keeping with the research ethics policy of the University the HREC(M) deals with health research and some social science re-

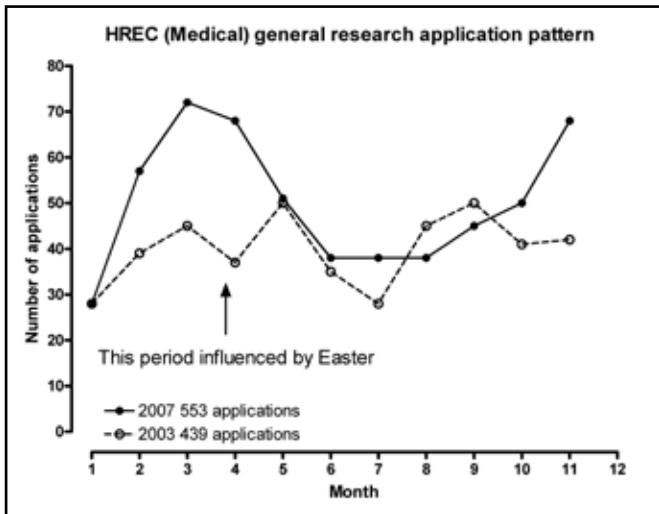


Fig. 1. General research application numbers by month of application.

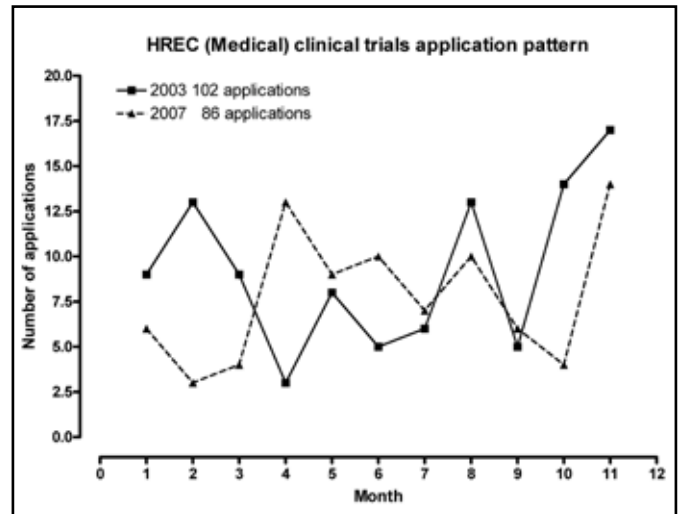


Fig. 2. Clinical trial application numbers by month of application.

TABLE I. HREC(M) DECISIONS FOR GENERAL RESEARCH

	Initial decision					Final decision			
	2003		2007			2003		2007	
	N	%	N	%		N	%	N	%
Approved	118	27	205	37	Approved	339	77	451	81
Minor revision	270	62	307	55					
Major revision	32	7	27	5					
Not approved	19	4	14	3	Not approved	17	4	14	3
Withdrawn	0	0	0	0	Removed from agenda	83	19	88	16
Total	439	100	553	100	Total	439	100	553	100

TABLE II. HREC(M) DECISIONS FOR SPONSORED CLINICAL TRIALS

	Initial decision					Final decision			
	2003		2007			2003		2007	
	N	%	N	%		N	%	N	%
Approved	14	14	6	7	Approved	88	86	83	97
Minor revision	66	65	77	90					
Major revision	8	8	0	0					
Not approved	11	11	0	0	Not approved	11	11	0	0
Withdrawn	3	3	3	3	Removed from agenda	3	3	3	3
Total	102	101	86	100	Total	102	100	86	100

search carried out in health establishments or dealing with health. All applications are evaluated by the full HREC(M); occasional expedited approval by an *ad hoc* decision of at least two Chairs is

limited to 'provisional approval' of a project with good reason to begin and a sound balance of benefits and risks but is subject to ratification by the full HREC(M). A waiver from ethics review

may be granted by an HREC(M) Chair for research not involving humans – for example when the research uses only microbial cultures or commercial cell lines or is desk-top analysis of public domain material.

In common with elsewhere the workload of HREC(M) members is additional to their normal duties and consists of detailed assessment of up to 10 protocols per monthly meeting, handling of queries, assisting applicants to write or rectify applications, and occasionally serving on *ad hoc* subcommittees. The latter deal with quality assurance reports on research sites produced by an independent auditor. Chairs have the same duties but in greater volume.

Both international and local research ethics guidelines state that monitoring of ongoing research is a responsibility of research ethics committees. Sponsored clinical trials adhering to Good Clinical Practice norms are monitored through twice-yearly reports and, from time to time, on-site quality assurance inspections by an independent auditor appointed by the HREC(M). An unsolved problem is monitoring of general research, due to the high numbers of projects and movement of applicants. It can be estimated that some 1 500 projects need to be monitored annually (500 new projects per year which last for say 3 years), plus the additional new projects, which is an enormous workload. Currently a single-page list of projects completed or ongoing in the year, plus a declaration that all have ethics approval which has been adhered to, is what is being used.

Should an applicant find the outcome of an application unsatisfactory an appeal is made to the HREC(M) for reconsideration. Should the appeal outcome be unacceptable, an applicant may approach the Deputy Vice-Chancellor (Research), who may arrange an outside re-assessment. Should a grievance be declared between an applicant and the HREC(M) the National Health Research Ethics Council may be involved in arbitration.

What is not often realised by applicants is that while health researchers in South Africa must adhere to a moral requirement to obtain informed consent, they also have a legal obligation, since informed consent is entrenched in the Bill of Rights (Section 12(2)(c) of the South African Constitution² and the National Health Act requires ethics approval of human health research.³

Change in workload at Wits

The reason for the increase in general research workload is unclear but may be due to an increasing emphasis on staff research by the University. Why there is a reduction in clinical trials is also obscure. Perceptions are that sponsors may be shifting to other countries for reasons of cost and because of slowness in processing projects through the Medicines Control Council. A pleasing change has been the improvement in quality of applications and often discussion of a proposed clinical trial with the REC before submission of an application. These are the reasons why no clinical trials were refused in 2007.

Reported workloads elsewhere

Australia

In order to see what Australian RECs might learn from Western European and US experience Frew⁴ visited eight institutions, two each in England, France, the Netherlands and the USA; he estimated the number of new applications per year as 300 - 400

per institution. Millar⁵ stated that two major teaching hospitals in Perth review 100 applications each per annum at one of which REC members have to look at 50 - 100 pages for each monthly meeting. Dodds,⁶ on the other hand, maintained that anecdotal evidence suggested 500 pages of reading per meeting and 764 applications per annum at an un-named institution.

Finland

A total of 666 applications at two university hospitals in Finland for the years 1992, 1994, 1996 and 1998 were studied by Keinonen *et al.*⁷ Of these 55% were approved, 14% were approved with advisory comments, 22% were amended, 5% were pending and 3% were not approved. The main problems were with participant consent and study design.

France

Ducullier *et al.*⁸ reported their findings from a retrospective cohort of 976 protocols seen in 1994 in 25/48 French RECs. Of the protocols 31% were approved without modification and 57% needed modification (19% required a second modification). Forty-six per cent of the modifications were to information/consent documents. The mean workload per REC per year was 39 new protocols, 39 revisions and 37 amendments. Each new protocol required 6 hours for the expert panel at the initial consideration and then 3.25 hours per revision. Administrators spent 4.5 hours initially, 4.5 hours per revision and 3.5 hours per amendment.

Japan

REC meetings in 80 medical schools and general hospitals with more than 300 beds from 1996 to 2002 increased in frequency accompanied by increasing workload and responsibility.⁹ Medical school REC meeting frequency per years increased from 3.6 to 7.7 while cases discussed at each meeting increased from 5.7 to 51.2.

Spain

Dal-Re *et al.*¹⁰ evaluated 100 clinical trial applications at 50 hospitals in 25 cities in Spain. Three per cent were not approved and 97% were approved, just over a third of which had modifications. Mean committee size was 12 members.

United Kingdom

A questionnaire as well as local research ethics committee reports in the UK between 1991 and 1995 were used by Nicolson¹¹ to determine workloads. Replies obtained from 209 of 255 possible responders showed that applications processed ranged between 9 and 447 per Local Research Ethics Committee (LREC); the highest numbers were in 12 teaching hospitals, which had >250 applications each. Mean numbers of applications increased steadily, as follows: 1991 – 57, 1992 – 73, 1993 – 102, 1994 – 107 and 1995 – 123, indicating a doubling over the 5-year period. Average committee membership numbered 11, three of whom were lay members. Most amendments were to information sheets.

Boyce¹² studied 353 applications for 38 scheduled meetings of London multi-centre RECs during 1997 - 2000. The median number of committee members was 14 (range 11 - 16). There were some 10 applications per meeting (range 3 - 14), four of which were new (range 0 - 8). Four per cent were approved at the first meeting, 62% received conditional approval, 29% were deferred and 5% were not approved. In 85% of applications there were problems with information sheets and in 50% with study design. Only one decision required a vote, the rest were decided by consensus.

United States of America

Wagner *et al.*¹³ surveyed 109 IRBs at Veteran's Affairs hospitals in the US; response rates were 73% for administrators and 59% for chairs. They termed all types of protocol reviews, including amendments or re-certifications, as actions. Sixty-seven IRBs were arbitrarily classed as small ($N=22$, mean support staff 2.3), medium ($N=22$, mean support staff 2.6) or large ($N=23$, mean support staff 5.6). Actions handled by the three categories and their estimated average costs were small 52 (3 - 151) US\$2 781, medium 431 (172 - 826) US\$416, and large 2 676 (1 637 - 3 399) US\$187. Costs were highest when there were less than 150 actions.

According to Brown *et al.*¹⁴ the IRB at the University of Texas Health Science Center at San reviewed 850 new or renewal applications each year at a cost of approximately US\$100 000 or about US\$100 per application.

Meaning of the study – workload itself

This article shows the heavy and increasing workload of the HREC(M) on which we serve. It also indicates a lack of published information on the experiences of other RECs. What is available is reported in many ways but, we believe, with a common thread of increasing load and costs.

What should a workload be? This question is like the proverbial 'how long is a piece of string' ... as long as it needs to be. The only recommendation found is in the standard operating procedures of the UK National Research Ethics Service which states that RECs should have at least 10 meetings per year, each of which should have not less than 5 and not more than 10 applications for discussion.¹⁵ In our circumstances this is unrealistic since applicants would wait many months to have a proposal reviewed.

Is our workload likely to increase? Certainly, for several reasons. Firstly, at a local level the total number of applications considered by the HREC(M) increased by 18% from 541 in 2003 to 634 in 2007. Secondly, the strategic plan of our university requires an increase in research to be a 'research-driven' university.¹⁶ Thirdly, at a national level, because of forthcoming changes in requirement for training clinical specialists, the HPCSA and the Colleges of Medicine will implement a requirement that a research project must be completed for specialist registration; it is estimated that this may increase applications to the HREC(M) by about 200 per year. The heavy workload, in turn, could negatively affect quality of review.

Is one solution to increase the number of RECs in an institution to decrease workload per meeting? At first glance this is appealing, but such an action will increase strain on support staff, probably requiring hiring of more people, thereby increasing costs to an institution. Also, there is the problem of finding members to serve on RECs; the work must be done over and above normal service and teaching loads, which are high. The reason for having a large committee (33 members) at our university is to ensure an adequate attendance at meetings – usually 12 - 18 – given the heavy workload of members. Also, the larger the number of members attending a meeting the lighter will be each individual's detailed assessment load.

Obtaining diversity of skill and demographic representation is also difficult in spite of numbers of faculty staff wanting to serve on the committee. Representation is not just a local problem. Camp-

bell *et al.*¹⁷ described 2 898 faculty members on IRBs at 121 4-year medical schools in the USA. Of these 73% were male, 84% white (non-Hispanic), 4% Asiatic and 5% from under-represented minority groups, while 76% were medical graduates.

If the number of RECs is increased to cope with increasing application numbers there will be a concomitant need to increase support staff servicing the committees, which in turn will increase costs to the employing institution.

Another option might be to reduce the research types required to be approved by the HREC(M). This is not feasible, because institutions must comply with local and international ethical and legal requirements.^{3,18-21}

What has helped reduce load on the four full-time academics who are HREC(M) co-Chairs at our university is that the Chair is a semi-retired academic who has been retained for three mornings per week for ethics consultation. A visit by one of the authors (PC-J) to the REC secretariat in the medical faculty of McGill University in Montreal found that a semi-retired Vice-Chair is active in the same way for the same reason.

Ideally members serving on RECs should have some relief from other duties to facilitate review of applications, which are becoming more complex as well as more numerous. This route was followed by Johns Hopkins University, where the IRB (REC) functioning was restructured following the death of a healthy volunteer in a clinical study.²²

Meaning of the study – decisions made

The rates of approvals, revisions and non-approvals of general research made by the HREC(M) follow the same trends as in Finland,⁷ France,⁸ Spain¹⁰ and the UK.¹² What is as yet unknown is why 16 - 19% of applications are removed from the agenda without a firm conclusion. Perhaps applicants are discouraged by having to revise applications, perhaps they leave the institution, or maybe some research is being done without ethics approval.

A pleasing observation is that no clinical trial applications were rejected in 2007 compared with 11% in 2003. This is probably due to more active discussion by applicants, clinical research organisations and sponsors with Chairs before submission applications plus clear standard operating procedures available on line (see www.witshealth/ethics).

Conclusions

This paper has shown an increasing workload for the HREC(M) of the University of the Witwatersrand between 2003 and 2007, with the likelihood of more increase. This trend follows international patterns. Since it is a legal requirement in South Africa for research involving humans to have ethics review in advance,³ institutions will have to adapt to suit their individual circumstances.

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