Performance of the Northern X Ethics Committee

The increased longevity of humans over the past century can undeniably be attributed to the ongoing progress in medical treatments and health care as well as significant advances in slowing the aging process. (Vaupel, 2010). There have been several major medical advances in the 20th century such as the development of vaccines to combat prominent diseases such as polio, pertussis, influenza and hepatitis A and B, new classes of antibiotics which have reduced the prevalence of bacterial diseases, insulin treatment for diabetes, X-rays and other important diagnostic tools, surgical techniques such as organ and tissue transplantation and heart surgery procedures and more advanced cancer treatments (Wikipedia, 2010). Medical research is highly significant in today’s society. It serves to support and improve our current knowledge in the field of medicine, with the ultimate goal of improving patient health. Clinical trials are a necessary stage in medical research and without them many of the innovative drugs and therapies mentioned above would not have been developed. They allow cutting edge health interventions to be tested in a safe and controlled way and can also be used to improve the efficacy, safety and cost of existing therapies.

Clinical trials have several other benefits aside from the obvious health implications and act to improve our economic and social development. Participants benefit from receiving free access to new treatments and highly attentive care that subsequently reduces some of the burden on the health care system. Researchers that participate in clinical trials improve their knowledge and skills in the area, which can be applied to clinical care in general. Pharmaceutical companies make large financial contributions to pay for study sites, boosting the economy and simultaneously creating more employment opportunities. Conducting trials in New Zealand allows us to retain our own skilled workers as well as attract experienced overseas researchers (School of Pharmacy, Faculty of Health and Medical Sciences, University of Auckland, Medical Oncology Unit, Auckland Regional Blood and Cancer Service, 2010).

Although there are many benefits to performing clinical trials, many of the studies involve human participants and thus it is important to ensure that ethical practice is always upheld. All studies involving a medical or therapeutic intervention, on patients, must be approved by an ethics committee before the trial may commence. An ethics committee is a board that has been formally designated to approve, monitor, and review biomedical and behavioural research involving humans with the aim to protect the rights and welfare of the research subjects and to ensure that the final objective is to serve the community of patients in the best possible way (New Zealand Parliament, 2010).

The Health and Disability Ethics Committees (HDECs) in New Zealand were established to provide protection for participants in research in the health and disability sector. The role of the HDECs is primarily to prevent studies that pose an unacceptable risk of harm to participants and to ensure that all participants in research are aware of what their participation will involve and have given informed consent. There are seven Health and Disability Ethics Committees in New Zealand of which six are regional and consider applications for research that is to be carried out within
just one region. The seventh is a Multi Region Ethics Committee, which considers applications for research to be carried out in more than one region (Health and Disability Ethics Committees, 2008).

In 2004, the HDECs underwent several changes following an assessment by the National Ethics Advisory Committee to streamline the review of research applications. The changes included the “one study, one review” guideline which means each application will be reviewed by just one ethics committee, removing the unnecessary obstacle of duplicate reviews. The number of ethics committees was also reduced from 15 to 7 and the ethics committees are now established under section 11 of the NZ Public Health and Disability Act 2000 (Health and Disability Ethics Committees, 2008).

The overall ethical review process in New Zealand is generally well regarded (New Zealand Organisation for Rare Disorders, 2010). The standards and research protocols contribute to a sound legislative framework and thus our review system is more robust than several overseas jurisdictions and in line with the best international practice. But despite our well-respected ethics system, allocation of clinical studies is becoming increasingly competitive and New Zealand appears to be falling behind. The global clinical trials industry is worth over US $60 billion and in Australia phase I-IV trials are quoted as being worth $450 million a year, yet in New Zealand the figure is estimated at only $12-30 million (Stuff opinion article, 2010; New Zealand Herald, 2009) The main factors research companies consider when deciding where to conduct their research are cycle time, capability and cost (Merck Sharp & Dohme (New Zealand) Limited, 2010) and currently it is unclear in which of these areas New Zealand is failing to measure up.

The New Zealand Health and Disability Ethics Committees have recently been subjected to much criticism with claims they are inefficient and extremely onerous for researchers. Shaun Holt, a well-known doctor and researcher described the ethical review system in New Zealand as “a hugely complicated bureaucracy, which has lost touch with its original aims.” He goes on to say that the review system is so time consuming that the application process may take longer than the proposed study itself and that this is preventing good research and any subsequent benefits to our health and economy (New Zealand Herald, 2009).

On the 10th of February 2010, the Government Health Committee initiated an inquiry into improving New Zealand's environment to support innovation through clinical trials. The inquiry has uncovered several complaints surrounding the timelines of the ethical review system in New Zealand. The worldwide standard of best practice for application turnaround time is the UK 60 day model, which utilizes a “stop clock” system. The “clock” starts when the relevant Research Ethics Committee receives an application, however if clarification is required, a written request will be sent to the researcher and the clock is stopped while awaiting the response (Neal, 2008). In New Zealand, however, the clock is running throughout the entire review process.

This inquiry and the public debate over the ethical review process has brought to the light the fact that there is very little reliable information on how the ethics committees are in fact performing. Without this information it is very difficult to design effective
policy or monitoring systems. The inquiry sparked a lot of interest and submissions consist of highly variable opinions.

A lot of the submissions indicate issues surrounding the timelines of the ethical review system in New Zealand. A spokesperson from Merck Sharp & Dohme (New Zealand) Limited, (2010) stated that the turnaround time for applications is too slow and admitted that it is because of this that they very rarely conduct phase one research in New Zealand, preferring to do it in Belgium, US, UK or Canada where the approval process is much faster. In New Zealand it takes MSD on average 130 days to get from final trial design to the stage when the research sites are ready to start study and they assert that approximately 90% of this time is taken up in the ethical review process. The average ethics submission approval time for phase II to IV studies conducted by MSD in 2009 was 91 days in NZ, which is much slower compared to Korea and the USA which took only 29 days and under 30 days respectively.

Pharmaceutical Solutions Limited (2010) also support MSD’s view, stating that international data shows top quartile Ethics Review Committee approval times for other countries is less than 40 days whereas locally, the Multi Regional Ethics Committees takes on average 80 days for approval. The Medical Technology Association of New Zealand (2010) have a similar opinion, stating the current ethics process is slow and cumbersome and that the average approval time of 2 – 4 months is far too long when compared to the average approval time of less than 1 month in the USA.

Several of the companies that provided evidence have personal experience with the ethics committee delays. The New Zealand Cancer and Blood Research Co-ordinators Group (2010) concur that the Ethics Committees turnaround times are at an all-time low, particularly for the Multi-region Ethics Committee. The Oncology research teams have examples of ethics committee correspondence that has been outstanding for more than 12 months. Another example of extreme delays is with an application submitted by the Spinal Cord Society NZ Clinical Research Group (2010), who have been trying to obtain ethics approval for its first clinical for the past 4 years. The SCSNZ made its first application for its proposed human clinical trial in October 2006 to the Multi region Ethics Committee that was declined in February 2007. They have made several resubmissions and their application was finally approved subject to conditions that means further ethical approval processes are required in order to satisfy these conditions.

Associate Professor Richard Robson of Christchurch Clinical Studies Trust (2010) states that there are numerous examples to illustrate delays in the application approval process. After receiving a request to change an information sheet for one study, CCST responded within two working days but three weeks later were still awaiting approval from the Ethics Committee, as the application was required to be reassessed by the original committee member who reviewed it but was later unavailable. The Faculty of Medical and Health Sciences at the University of Auckland (2010) believe that although the ethical review process in New Zealand is very robust it is inefficient and they attribute the variation in timeliness to the lack of urgency or specific performance targets.
Many individuals and organizations, however, strongly support the ethics review system. Associate Professor Tim Dare (2010) says that in his experience the New Zealand Ethics Committees tend to meet the UK 60 day review timeline in all but very rare and difficult cases, even though they do not have a required approval period of their own. Most applications are considered at the meeting following their submission for review so within 4 weeks, and generally closer to two given advertised cut off dates. The outcome of the application is then communicated to researchers within a week or two of the meeting after which point delays are beyond the control of the Ethics Committee.

The Health and Research Council (2010) assert that the current system is efficient and in line with international standards, however, they acknowledge that it has several flaws and that the time to get a clinical trial up and running after ethical committee approval is longer than it should be. P3 Research Ltd (2010) also believes that the ethical review process in New Zealand works well and states that approval time normally takes 2-3 months from time of submission. In theory, Australia appears to have a more efficient system, however, in practice, New Zealand frequently offers a faster approval system at lower cost.

The current project is centred on the recent complaints surrounding the timelines of the ethical review system in New Zealand. The project focuses specifically on the Northern X Ethics Committee, one of the two ethics committees in the Northern region. It involved extracting data on the ethical review timelines from the application files at the Northern X Regional Ethics Committee with the aim of identifying where the delays are occurring and constructing reliable information to improve performance on important policy and monitoring decisions.

**Method**

Data was extracted from the Northern X Ethics Committee files and annual reports. This included the date the application was received, the date of the meeting in which the application was reviewed by the committee, the date an amendment request was sent, the date an amendment reply received, the date(s) of any further correspondence and the date of the final outcome. Only the applications that required approval by the full ethics committee were analysed, not the expedited files as they were all under the 60 day review period. All applications from 2009 (125 applications) and 2010 (132 applications) were analysed (Appendix B and C). The number of days the application spent with the ethics committee vs the number of days the application spent with the researcher was calculated using the following equation:

Number of days with Ethics committee = (number of days between day application received, day of review and day amendment letter sent out) + (number of days between resubmission and day of final outcome).

Number of days with researcher = (number of days between the day the amendment letter was sent, the day the reply was received by committee and the last day of any further correspondence).

(Appendix A)
Results

As illustrated in Figure 1 below, in 2009, 79 of the 125 (63%) applications submitted to the Northern X Ethics Committee took longer than 60 days to gain approval. In 2010, 57 of the 132 (43%) applications submitted to the Northern X Ethics Committee were under review for longer than 60 days.

Figure 1. Number of applications submitted to the Northern X Health and Disability Ethics Committee in 2009 and 2010 with a total review time of more or less than the standard 60 day period.

An analysis of the timeline break down for applications that took longer than 60 days to be reviewed was then conducted to establish where exactly the delays were occurring (Appendix A). Of all the applications in 2009 that had a turnaround time over the 60 day review period, the majority (49/79) spent less than half of that time with the ethics committee. This was also true of the applications in 2010 that were over the 60 day review period, where 37/57 spent 50% or less of the total turnaround time with the ethics committee. In 2009 only 18 of the 79 applications spent more than half of the review process with the Ethics Committee and in 2010, 19 out of the 57 applications spent the majority of their turnaround time with the Ethics Committee. Those in the other category did not have sufficient data to establish an accurate timeline break down.

<table>
<thead>
<tr>
<th>Percentage of time application was with NTX EC</th>
<th>2009</th>
<th>2010</th>
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<tbody>
<tr>
<td>≤ 50%</td>
<td>49</td>
<td>37</td>
</tr>
<tr>
<td>&gt; 50%</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Other</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>79</td>
<td>57</td>
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</tbody>
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Figure 2. Summary of applications submitted to Northern X Ethics Committee (NTX EC) that were under review for over 60 days. Table depicts the percentage of time each application spent in review with the Ethics Committee.
Discussion

The results in Figure 1 are consistent with the complaints regarding the slow turnaround time for ethical review of applications in New Zealand. In 2009, 63% of the applications submitted to the Northern X Ethics Committee were under review for more than 60 days and in 2010, 43% of the applications had a total turnaround time of longer than 60 days.

However, after further analysis it was found that the majority of applications that had a slow turnaround time spent over half of the approval process with the researcher rather than with the ethics committee as illustrated in Figure 2. In 2009, 73% of the applications that had a turnaround time over the 60 day review period with a known timeline breakdown spent less than half of that time with the ethics committee and a similar figure (66%) was found for applications submitted in 2010. Therefore the delays in approval cannot be exclusively blamed on the inefficiencies of the ethics committees.

Furthermore, there are a few simple explanations for the many of the applications that spent over half the approval process with the ethics committee. Several files were delayed due to the study number not being quoted or being misquoted (2009 applications 23, 47, 100) on the resubmitted application which drastically holds up the approval process as the ethics administration staff have to spend valuable time searching for the correct file. Some applications were sent to the incorrect address, and a common mistake was to send it to the delivery address not the PO Box that added weeks onto the approval times in some cases (2009 – application 84; 2010 application 32). Several applications were incomplete or had forms missing such as the locality assessment form in application 34, 2010. In some investigations a new principal researcher was nominated so the approval process had to be restarted (2009 application 19; 2010 applications 27, 92).

Although my findings are relatively limited, my project does indicate that the timeline data is not as bad as first thought and that the Northern X Ethics Committee does not warrant all the criticism labeling it as slow and cumbersome. With that being said, the HDECs are obviously struggling to deal with their workload and perhaps the review process is not quite as efficient as it could be.

Several of the organizations and individuals that made submissions to Health Committee inquiry also put forward suggestions to help streamline the ethics review process in New Zealand. One of the recurring themes was the idea of developing performance measures for the Health and Disability Ethics Committee’s to improve the efficiency of the approval process. Performance measures are commonplace in many other countries so perhaps New Zealand could look at adopting the UK 60 day stop clock model or a similar system. Having a set time encourages efficiency, allows performance to be monitored and permits transparency to the applicants. Performance measures could include objectives such as reducing the time from submission to meeting from the current 2 week cut off to 7-10 days and providing a response to the applicant 1-2 days after the meeting, rather than the current 1-2 weeks (Faculty of Medical and Health Sciences, University of Auckland, Medical Technology Association of New Zealand, Primorus Clinical Trials Ltd, Shaun Holt and Geoffrey Horne, 2010).
Sever al committees are burdened by an excessive workload, which impacts on the timeliness of review. The establishment of the expedited review process has been a positive step as it drastically speeds up the application process for researchers and reduces the workload for the full committees. However, it is labour intensive for the individual required to review the applications. These imbalances need to be addressed and perhaps consideration could be given to reducing the size of each of the present committees and establishing a new committee (either regional or a second multi-region ethics committee) with the saved costs and resources, especially if there are to be more research applications as a result of this inquiry. An increase in administrative staff to speed up the review process and to prevent avoidable delays due to an administrator being sick or on holiday would also be useful, however difficult to implement with the lack of available funding. (New Zealand Cancer and Blood Research Co-ordinators Group, Trans Tasman Radiation Oncology Group, Federation of Women’s Health Council, 2010).

Increasing the frequency of meetings from monthly to fortnightly for the Multi-region Ethics Committee (MREC) was another strongly supported idea. The majority of pharmaceutical sponsored studies are required to be reviewed by the MREC as clinical trials are performed in several locations. In order to attract larger scale studies to New Zealand, it is essential that the approval process for multi site studies is as simple and efficient as possible so increasing the number of meetings would allow a faster approval turnaround time and an increase in the number of studies to be reviewed. (Regional Ethics Committee, Federation of Women’s Health Council, New Zealand Cancer and Blood Research Co-ordinators Group, P3 Research Ltd, Pharmaceutical Solutions Limited, 2010). This however is not always a realistic option as committee members have other commitments and with travel and time constraints, increasing the number of meetings may result in loss of members. Perhaps options such as video-conferencing or a committee rotation system could be explored.

Another practical suggestion is to implement an electronic system filing system. Electronic submissions are standard practice in most overseas committees and can be be filed by e-mail or on memory stick/disk, as in Australia. This would eliminate the need for researchers to send an original application along with 12 copies, which can comprise of 500-1000 pages and thus is costly and time consuming to compile and post. This would also remove the potential for the items to be lost or delayed and would play a large part in reducing the expense and timeliness of the review process (New Zealand Cancer and Blood Research Co-ordinators Group, P3 Research Ltd, Primorus Clinical Trials Ltd, 2010).

An additional idea is to establish a fast-track ethics committee review process to allow choice for commercial sponsors who would be willing to pay for an expedited approval. This is likely to attract international research sponsors to set up studies in New Zealand and would be especially valuable in time critical studies such as seasonal influenza. The New Zealand Government could investigate the feasibility of privatising ethics committees as Australia and Canada have successfully done so with a resulting improvement in efficiency (Merck Sharp & Dohme (New Zealand) Limited, New Zealand Biotech 2003 Incorporated, P3 Research Ltd, Professors Shaun Holt and Geoffrey Horne, 2010). One problem with this idea is that by creating an
Ethics Committee specifically for commercial sponsors we are essentially allowing them to bypass the current ethical review system and its high ethical standards. Perhaps it would be more reasonable to implement a graduated scale of fees to be charged for ethical review and approval of clinical trial applications.

My project has several limitations with the main being the lack of data collected for analysis. Due to time constraints I was only able to look at two years of applications and only at the Northern X Ethics Committee so my results are provisional and cannot be applied to all of the Health and Disability Ethics Committees in New Zealand. My study also solely focused on the timeline issues associated with gaining ethics approval, however, the allocation of clinical trials to certain countries depends on other factors such as capability and cost and thus to improve the overall environment for conducting clinical research in New Zealand, these factors may need to be improved as well.

I recommend that a more thorough investigation into the turnaround times for all of the Health and Disability Ethics Committees in New Zealand over at least the past 5 years be conducted as little is known about how these committees are really performing and without this information it is impossible to effectively improve our ethical review process and our environment for conducting clinical trials.

From my analysis I can infer that the main reason for the extreme delays in application turnaround time appear to be due to slow resubmission response time and simple administration errors on the researchers behalf. Approval timelines are not extraordinary by international standards but further investigation into the performance of the ethics committees in New Zealand is required. Several adjustments need to be considered to improve the efficiency of the ethics review process in New Zealand. The establishment of performance based measures, an electronic submission and filing system, increasing the frequency of meetings and creating a fast track review system are all valuable suggestions and deserve deliberation. A robust and efficient ethical review system is essential before we can expect to attract a greater number of clinical trials to New Zealand.
References


Evidence

Associate Professor Richard Robson - Christchurch Clinical Studies Trust (16 April, 2010) pp 1-4.

Associate Professor Tim Dare – personal submission (Chair of the Health Research Council Ethics Committee, research interests include professional ethics) (14 April, 2010) pp 1-7.

School of Pharmacy, Faculty of Health and Medical Sciences, University of Auckland - Michelle Lockhart, Zaheer-Ud-Din Babar and Sanjay Garg (April, 2010) pp1-4.

Federation of Women’s Health Councils Aotearoa (16 April) pp1-4

Health Research Council (HRC) Sandra Reid Senior Advisor - Legal and Ethics (14 April, 2010) pp 1-8.


Medical Technology Association of New Zealand (MTANZ). Faye Sumner - Chief Executive Officer (April, 2010) pp 1-8.

Medical Oncology Unit, Auckland Regional Blood and Cancer Service - Assoc Prof Vernon Harvey, Dr Paul Thompson, David Porter (April, 2010) pp1-11

Primorus Clinical Trials – Dr Alison Luckey, Medical Director (14 April, 2010) pp 1-10.

Professor Ian Reid, Deputy Dean of the Faculty of Medical and Health Sciences, University of Auckland, on behalf of that Faculty. (April, 2010) pp1-3.

P3 Research Ltd - J Woodman, QA Regulatory Manager. (14 April) pp 1-7


Spinal Cord Society New Zealand Incorporated (SCSNZ) - Noela Vallis, President (16 April, 2010) pp 1-3.


