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Recurring themes arising during medical research ethics committee review.

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Recurring Themes Arising During Medical Research Ethics Committee Review

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Abstract

A standard application form for the ethical review of health-related research studies has recently been adopted by many Irish medical research ethics committees. In order to assess the impact of the new form, we reviewed all comments made by the Beaumont Hospital Ethics Committee during two six-month periods, immediately prior to adoption of the new form (2010), and soon afterwards (2011). Neither volume nor comment type differed significantly between the two observation periods. Participant documentation (information leaflets and consent forms) accounted for the largest proportion of comments (2010; 44%, 2011; 37%). Other common areas prompting queries were study administration (7%), design (12%) and procedures (13%), participant selection and recruitment (8%), and lastly data protection (9%). Because of these findings, the standard operating procedures of the committee have been revised – use of provided template participant documentation is strongly encouraged, and a "Recurring Review Themes" checklist is highlighted to all applicants.

Introduction

All clinical research projects are required to undergo ethical review. Until 2010, in Ireland, each hospital medical research ethics committee (REC) had its own application form. This was seen to act as a potential impediment to research.[1] Of particular concern were projects involving multiple research sites, where researchers were required to complete a number of different forms for the one multi-centre study. Hence in 2009 a consultation group was formed, including representatives from many of the RECs across Ireland, with the aim of designing a standard application form that could be adopted by all RECs. The form was designed to be used for the ethical review of health-related research studies that were not clinical trials of medicinal products for human use as defined by the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations, 2004, (Statutory Instrument 190 of 2004). The form was finalised in late 2010,[2] and adopted for use by Beaumont REC at that time. This audit had two purposes: to assess the volume and types of comments made during committee review and, to assess if the changeover to the new standard application form had any impact on the volume or type of comments made.

Methods

All clinical research studies, except clinical trials of medicinal products, reviewed by the Beaumont Hospital (Medical Research) Ethics Committee between January and June 2010, and between January and June 2011, were included in this audit. The type of study, the study intervention and level of the principal investigator were recorded for each application. All comments made by the committee are documented in the monthly meeting minutes. In order to optimise consistency and so as to avoid bias, comments from 2010 and 2011 were collected and analysed according to month order i.e. January comments for both 2010 and 2011 were analysed first followed by February comments for both 2010 and 2011.

Each comment was classified according to the following criteria; Category - most categories were derived from the section headings of the new standardised application form: general study and administrative details; study design and descriptors; study participants; informed consent; inclusion of vulnerable groups; research procedures; data protection; human biological material; radioactive material; medical devices; indemnity; cost and resource issues; other ethical issues; and participant documentation. Nature of comment; Requests for a change to the application or participant documentation, or for further information or clarification; Level of importance of comment; major / intermediate / minor. Qualitative data was also extracted by recording a short summary of each comment.

The above data was entered into a spreadsheet and underwent both qualitative and quantitative analysis. Wilcoxon rank-sum (Mann Whitney) tests were used to test for between year differences in the volume, category, nature or level of importance of the comments.

Table 1 displays requests for further information and for changes during 2010 and 2011, according to category and level of importance (minor, intermediate, major)

	Requests			
	2010		2011	
	Further Information	Change	Further Information	Change
General Details	23 (0,5,18)	8 (5,3,0)	8 (1,1,6)	21 (4,6,11)
Study Descriptors	8 (5, 3, 0)	18 (8, 2, 8)	35 (3, 14, 18)	24 (3, 4, 17)
Study Participants	17 (6, 7, 4)	12 (1, 7, 4)	35 (9, 16, 10)	7 (3, 1, 3)
Informed Consent	10 (2, 1, 7)	4 (0, 2, 2)	10 (0, 7, 3)	2, (0, 0, 2)
Vulnerable Groups	8 (0, 7, 1)	3 (0, 1, 2)	8 (3, 4, 1)	2 (0, 1, 2)
Research Procedures	28 (1, 16, 11)	8 (0, 4, 4)	62 (2, 45, 15)	17 (2, 6, 9)
Data Protection	21(5, 6, 10)	17 (3, 10, 4)	28 (2, 16, 10)	18 (8, 3, 7)
Biological Material	5 (0, 3, 2)	5 (2, 3, 0)	7 (1, 3, 3)	5 (1, 2, 2)
Medical Devices	0 (0, 0, 0)	2 (0, 0, 2)	1 (0, 0, 1)	0 (0, 0, 1)
Indemnity	2 (0, 0, 2)	3 (1, 0, 2)	10 (0, 1, 9)	4 (0, 1, 3)
Cost & Resources	10 (0, 5, 5)	2 (1, 1, 0)	15 (1, 8, 6)	2, (1, 0, 1)
Other	1 (0, 0, 1)	3 (0, 1, 2)	1 (0, 1, 0)	5 (2, 3, 0)
Participant Documentation	19 (4, 8, 7)	170 (86, 51, 14)	22 (9, 10, 3)	199 (84, 69, 24)
Total	152	236	242	285

Data as total number of queries (minor, intermediate, major)

Results

Eighty-six ethical review applications were analysed in total, 52 from 2011 and 34 from 2010. This represented all applications considered at full committee meetings (other than clinical trials of medicinal products under S.I. 190/2004) between January and June of those two years. The majority of applications were submitted by medical consultants, accounting for 54% of the total (n=47). Surgical consultants accounted for 10% (n=9), as did

non-consultant hospital doctors (NCHDs) and laboratory scientists. Paramedical staff and other allied health professionals made up 9% of submissions (n=8). Four studies were sent back for a complete rewrite of the protocol, application form and patient documentation prior to resubmission for ethical review – two from each six-month period.

There were in total 915 queries made by the REC concerning the 86 applications. Between January and June 2010, 409 comments were made concerning 34 applications – 173 were requests for further information (mean±SD per application; 5.1±4.5), and 236 were requests for changes to the protocol or participant documentation (6.9±6.1). During the same period in 2011, 527 comments were made concerning 52 applications (further information requests; n=242, 4.7±3.9, and change requests; n=285, 5.5±4.6,). Two-sample Wilcoxon rank-sum (Mann-Whitney) tests showed no significant difference in numbers of comments per application, category type, nature of comment, nor comment level of importance, between the two periods.

Table 1 shows the volume, nature and level of comments made in each category for each period. It is clear that in both 2010 and 2011, 'Participant Documentation' accounted for the greatest proportion of comments – 170 out of 388 in 2010 (44%) and 199 out of 527 in 2011 (38%). It can also be seen that the other areas prompting a large number of comments were general study details and administration (7%), study design and descriptors (12%), study research procedures (13%), participant selection and recruitment (8%), and lastly data protection (9%). These 5 categories alongside participant documentation accounted for 88% of all queries.

It was noted that within each of the six categories accounting for greater than 5% of comments, there were common themes or sub-categories. The 6 categories and any sub-categories that prompted at least 1% of the total comments, along with the most common queries or required corrections are illustrated in Figure 1. This figure forms the basis of a checklist provided to applicants to this committee, aiming to reduce committee queries and comments through highlighting our previous most common comments, queries and requests for changes.

Recurring Review Themes and Comments: A Checklist for Applicants

General Study Details/ Administration *(n=60, 7%)*	Study Investigators (n=22, 2%)	Is a Beaumont Hospital consultant involved?
		Ensure the principal investigator is consistent throughout the application
		Include an expert co-investigator if necessary
	Queries about Irish Medicines Board (IMB) issues (n=6, 1%)	Is the application for a clinical trial? (If so, a different application applies)
Study Descriptors *(n=106, 12%)*	Statistical Analysis (n=26, 3%)	Provide details of sample size
		Provide a power calculation
	Justification for elements of the study (n=13, 1%)	Justify the outcome measures
		Is the timeframe practical?
Study Participants (Recruitment & Selection) *(n = 71, 8%)*	Inclusion / Exclusion Criteria (n=18, 2%)	Ensure consistency throughout the application
		Are all the criteria justified?
	Recruitment (n=21, 2.3%)	Comment on the feasibility of recruiting adequate numbers
		How will participants be recruited?
Research Procedures *(n=115, 13%)*	Provide more details (n=35, 4 %)	What procedures will participants undergo?
		Justify use of procedures
	Clarify what is part of routine care and what is not (n=18, 2%)	What exactly does the study involve, and how is it separate from the treatment patients already receive?
	Queries regarding aspects of treatment (n=15, 2%)	Provide specifics of what is involved if the research study is also part of the participant's treatment
Data Protection *(n=84, 9%)*	Data Access (n=10, 1%)	Will medical records be accessed?
		Who will be accessing the data?
	Confidentiality (n=11, 1%)	Will identifiable data be collected?
		Will data be anonymised or coded?
	Data Storage (n=19, 2%)	Where will data be stored?
		Will data leave the hospital?
		Will data be sent abroad?
Participant Documentation *(information leaflets, consent forms, questionnaires, and any other documentation provided to the participants)* *(n=369, 40%)*	Clarify information in patient documentation (n=110, 12%)	State if a procedure is part of the participant's standard care or if it is an additional procedure for research purposes
		State who has access to data collected
	Additional information required (n=59, 6%)	Include contact details of investigator(s)
		State risks of participating
		State what will happen to data collected
	Grammar / Formatting (n=37, 4%)	Correct typos
		Correct inappropriate use of headings
		Adjust font size
		Adjust layout
	Missing documents (n=10, 1%)	Provide information leaflets specific to next-of-kin, parents etc.

Figure 1: The most common comments made by Beaumont Hospital (Medical Research) Ethics Committee, in response to 86 submitted application forms and participant documentation during two six-month periods in 2010 and 2011, are grouped according to category and sub-category. Numbers of comments, and the percentage of the total number of comments (n=915) in each category and sub-category are indicated. This figure forms the basis of a checklist provided to applicants to this committee, aiming to highlight common comments, queries and requests for changes.

Discussion

While adoption of a standard application form for the ethical review of health-related research studies by the majority of medical research ethics committees country-wide is a welcome initiative towards streamlining the review process, this audit clearly demonstrates that it had little or no impact on the volume or nature of comments made by the Beaumont Hospital (Medical Research) Ethics Committee. The second major finding of this audit was that a very limited number of areas accounted for a very high proportion of comments – queries concerning participant documentation prompted 40% of comments, and five other categories (general study details and administration, study design and descriptors, study research procedures, participant selection and recruitment, and data protection) were responsible for a further 48% of all queries. As a consequence of these findings, the standard operating procedures of the Beaumont Hospital (Medical Research) Ethics Committee have been revised. Firstly the table of recurring review themes and comments is provided as a checklist to all investigators intending to submit an application to the REC. Secondly use of provided template participant information leaflets and participant consent forms in drafting the participant documentation is strongly encouraged.

Our findings are likely to be generalisable to other Irish RECs reviewing clinical studies and using the standard application form – it is to be

anticipated that the same common issues are raised by many committees. Hence we have made our checklists and template participant documentation freely available to all on our website www.beaumontethics.ie/application/index. It is hoped and anticipated that through identifying and highlighting the common sources of REC queries to future applicants, that completion of the application form and participant documentation will be improved, and that fewer comments will be raised by the REC. If this does occur, applicants will gain ethical approval with a lesser number of document adjustments, the workload of REC members could be considerably reduced, and the timelines of the review process would be likely to shorten. This question will be the subject of a future audit.

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