

BRIEF REPORT

The stipulations of one institutional review board: a five year review

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Objectives: This study was designed to explore the prevalence and types of stipulations (such as clarifications or changes) required of investigators by the institutional review board (IRB) of one institution over a five year period.

Design: Stipulations to research proposals (n = 124) were documented from the minutes of the IRB meetings.

Setting: Community hospital.

Participants: IRB submissions.

Main measurements: Number and type of IRB stipulations.

Results: Nineteen research submissions (15.3%) were approved without any stipulations. For the remainder, the majority of stipulations related to consent forms (74.2%).

Conclusions: Consent forms appear to be at highest risk for IRB stipulations. Being aware of high risk areas before submission of research proposals may reduce the frequency of stipulations required of investigators.

Institutional review boards (IRBs) have the responsibility to protect human subjects who are participating in research protocols. In this role, IRBs review research submissions and indicate in writing the changes (that is, the “stipulations”), if any, which are required to undertake the research project. There is very little research on the prevalence or types of IRB stipulations required of investigators. In a British study,¹ Kent found that 24% of research submissions were approved without stipulations; stipulations were primarily related to requests for further information, design queries, changes in information sheets provided to participants, and changes in the consent procedure. Olsen and Mahrenholz² found that 46% of nursing protocols were approved without stipulations whereas 8% were not approved at all; stipulations related to the consent form (43%), the need for additional information (31%), and inadequate explanation to candidates of the potential benefits of participation (22%). In summary, available studies exploring the prevalence and types of IRB stipulations are few in number and limited with regard to the ability to generalise findings. The following pilot study was designed to audit, in a single US institution, the prevalence and types of stipulations required by an IRB.

METHOD

The setting for the IRB is a 486 bed suburban Midwest hospital in the United States with several affiliated inpatient and outpatient facilities. This IRB is well established, including having the same chairperson for the past eight years. All reviews of research submissions by the IRB, both pharmacological and non-pharmacological, including all stipulations, are recorded in the minutes of the IRB meetings. During the study period of five years, the same staff assistant has recorded the minutes of these meetings.

Following consultation with the IRB staff assistant to informally explore the most common types of IRB stipulations, we developed a data collection sheet to record stipulations. A single investigator then reviewed all of the IRB minutes over a five year period, noting all stipulations. Because of some unanticipated types of stipulations, we revised the data collection sheet midway through the project. The final data collection sheet included the major categories (and subcategories) for stipulations shown in the box.

Questions regarding the categorisation of some stipulations were resolved by the review of the unassigned stipulation with a second investigator; subsequent assignment was based on mutual agreement between the two investigators. In addition, we classified each IRB submission according to pharmacological versus non-pharmacological research. The IRB of the institution approved this project.

RESULTS

Overall frequencies of stipulations

Of the 124 IRB submissions examined, 105 (84.7%) were given at least one stipulation. Table 1 lists the major categories of stipulations that were examined, along with the number and percentage of all submissions that were given at least one stipulation in a given category, and the descriptive statistics for the number of stipulations given for the category. Stipulation subcategories with a mean of greater than one are also included in table 1.

Note that the consent form was the major category most likely to receive at least one stipulation (n = 92, 74.2%), followed by the study protocol (n = 23, 18.5%). For each of the remaining categories, less than 10% of submissions were given at least one stipulation.

The mean (standard deviation) number of stipulations per consent form was 17.22 (19.48). When the 19 submissions that were not given any stipulations are excluded, the mean number of stipulations given for the consent form category increases to 20.47 (19.62). No other major category averaged more than one stipulation per submission.

Stipulations by study type (pharmacological v non-pharmacological)

We next examined whether the type of research study that was submitted (pharmacological (n = 60) or non-pharmacological (n = 62)) had any impact on the types and/or rates of stipulations given. (It should be noted that the study type could not be determined for two submissions.) In examining this, we found that pharmacological study submissions were significantly more likely to be given at least one stipulation for consent forms (n = 58, 96.7%) compared with non-pharmacological submissions (n = 32, 51.6%), χ^2 (1, n = 120) = 28.06, p < 0.001. However, compared with non-pharmacological studies (n = 20, 32.3%), pharmacological studies (n = 3, 5.0%) were significantly less likely to be given a stipulation for the study protocol,

Stipulations

Consent form

- Typographical errors; Spelling; Grammar; Format; Phrasing; Jargon; Clarify costs; Clarify risks/benefits; Clarify protocol/procedures; Clarify patients' rights overall; Confidentiality; Right to refuse/withdraw; Other.

Study protocol

- Protocol design; Risks inherent to the study; Patient screening/baseline labs; Typographical errors; Spelling; Grammar; Format; Phrasing; Jargon; Clarify costs; Clarify risks/benefits; Clarify protocol/procedures; Clarify patients' rights overall; Confidentiality; Right to refuse/withdraw; Other.

Research measures/forms/surveys

Application to the IRB

Site participation letter

Other

χ^2 (1, n = 124) = 14.81, $p < 0.001$. Significant differences were not found between the two submission types on any other major category.

Finally, we examined the mean number of stipulations given in each category by study type. It should be noted that using a Bonferroni correction, we set the alpha level for statistical significance to 0.003 to control for the large number of statistical tests (that is, one way ANOVAs) that we set out to conduct. This alpha level was obtained by dividing our preferred alpha of 0.05 by the number of ANOVAs performed within each category, which were 14 and 15 respectively for consent form and study protocol. Also, as the data were negatively skewed, we transformed the raw data into square roots and re-ran analyses. Results were identical to those obtained for the raw data; for clarity, only the results from the analyses with the raw data are reported. Overall, non-pharmacological submissions were given significantly more stipulations (mean = 0.61, SD 1.08), on average, than were pharmacological submissions (mean = 0.07, SD 0.31), $F(1, 120) = 14.28$, $p < 0.001$. Table 2

Table 1 IRB submissions (n = 124) given at least one stipulation, and descriptive statistics for number of stipulations given per submission by category

Stipulation category	Number (%) of submissions with at least one stipulation	Number of stipulations Mean (SD)	Range
Consent form	96 (74.2%)	17.22 (19.48)	0–109
Grammar	58 (48.3%)	2.33 (4.29)	0–29
Format	72 (60.0%)	2.35 (3.99)	0–24
Phrasing	74 (61.7%)	4.73 (5.90)	0–30
Jargon	51 (42.5%)	1.65 (2.92)	0–14
Clarify risks and benefits	68 (56.7%)	2.53 (3.29)	0–14
Clarify protocol/procedures	72 (60.0%)	2.51 (2.56)	0–10
Study protocol	23 (18.5%)	0.34 (0.84)	0–4
Research/measure/forms/surveys	5 (4.0%)	0.05 (0.25)	0–2
Application to the IRB	4 (3.2%)	0.03 (0.18)	0–1
Site participation letter	10 (8.1%)	0.10 (0.37)	0–3
Other	9 (7.3%)	0.10 (0.37)	0–2

Table 2 Comparison of mean number (SD) of stipulations given in each category by IRB submission study type (pharmacological v non-pharmacological)

Stipulation category	Pharmacological (n = 60)	Non-pharmacological (n = 62)	F Value
Consent form	25.07 (20.21)	8.40 (13.54)	27.52
Spelling	0.57 (1.65)	0.07 (0.43)	9.50
Grammar	3.55 (4.31)	1.03 (3.99)	10.81
Format	3.27 (4.40)	1.05 (1.54)	13.15
Phrasing	6.50 (6.19)	2.72 (4.94)	13.34
Clarify risks and benefits	3.80 (3.56)	1.16 (2.32)	22.55
Clarify protocol/procedures	3.33 (2.77)	0.88 (1.46)	35.80
Study protocol	0.07 (0.31)	0.61 (1.08)	14.28

All F values are statistically significant at $p < 0.003$.

presents the mean number (and standard deviation) of stipulations given for only the categories on which significant differences were found between the two study types, as well as the associated F values. Only subcategories for which significant between group differences were found are listed in table 2. Consistent with the frequency data, it can be seen that pharmacological study submissions were given significantly more stipulations per submission for consent forms, whereas non-pharmacological submissions were given more stipulations for study protocols. No significant differences were found to exist between pharmacological and non-pharmacological study submissions on any of the other categories.

DISCUSSION

These data suggest that there are particular areas of the research submission that are likely to receive IRB stipulations. Indeed, the consent form appears at most risk for stipulations, particularly the clarification of risks and benefits to participants. In comparing pharmacological versus non-pharmacological research, consent forms remain a predominant concern for the former whereas study protocols remain a predominant concern for the latter.

Given these identified probabilities for IRB stipulations, investigators have the opportunity to prepare for and possibly avoid stipulations. Strategies include more careful investigator review of these specific areas before submission and/or a checklist review of all items to be covered in the consent form. Some institutions provide specific training for investigators in stipulation risk areas.³

The limitations of this study include the review of IRB stipulations in a single institution, a very limited sample size (the activity rate is relatively low compared with other US and UK IRBs), and the decision making around the categorisation of particular stipulations. However, research overviews of IRB stipulations in the literature are few in number. These data might be confirmed by review of submissions of a more active IRB with, given our findings, more focused or specific data collection (that is, consent form stipulations). Regardless, individual institutions may want to consider conducting audits of their IRB stipulations and design training programmes or materials to reduce their frequency. Both IRBs and investigators will likely appreciate any information or training that will reduce their mutual workloads.

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