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 project, there is very little research on the prevalence or types of IRB stipulations required of investigators. In a British project, 24% of research submissions 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.

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%), χ² (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.
The stipulations of one institutional review board 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 differences between group differences were found are listed in table 2. Consistent with the frequency data, it can be seen that pharmaceutical 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 pharmaceutical 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 pharmaceutical 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.

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 overview 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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