

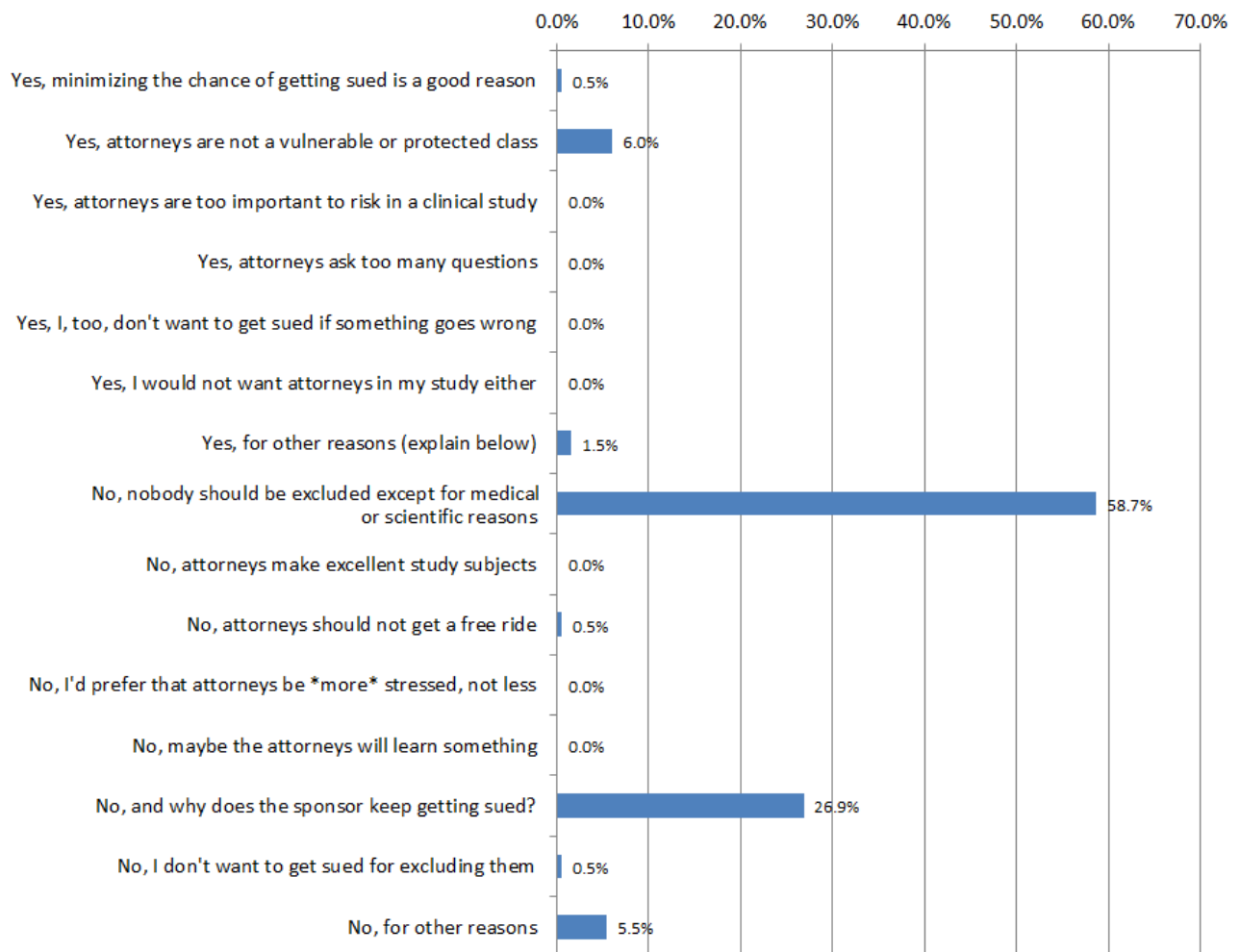
Clinical Research Ethics Question of the Month: No Attorneys?

By Norman M. Goldfarb

You are a member of an IRB reviewing a Phase 2 study for cardozamine, a new drug for treating stress. One of the exclusion criteria in the protocol is: “Educated or employed as an attorney.” The cover letter on the application explains that the study sponsor has been sued on three occasions by attorneys who were study subjects, and it does not want it to happen again. You have no other information to make your decision and no clever way to dodge it. Will you vote to approve the study with this exclusion criterion?

Results

Question 1. Will you vote to approve the study with this exclusion criterion?



Of the 201 respondents, 8% would approve the protocol and 92% would not.

Question 2. What profession(s), if any, could rightfully be excluded from certain clinical studies?

Respondents identified the following professions as problematic for certain studies for medical or scientific reasons:

- Health professionals with knowledge that could bias their perceptions, behavior, patient-reported outcome data, or retention in the study
- People whose profession could make them vulnerable to possible side effects, e.g., sun sensitivity for life-guards or reaction speeds for bus drivers.
- People, e.g., radiology technicians, whose profession could confound study results
- People whose profession could make it difficult to complete the study without significant protocol deviations, e.g., flight attendants.
- People whose profession requires very atypical physiological or mental characteristics, e.g., Olympic athletes

Discussion

Legitimate Reasons for Exclusion

The Belmont Report's principle of justice prohibits excluding — or targeting — study participants for other than scientific or medical reasons. Survey respondents identified four such scenarios above.

No respondents suggested excluding people who are too valuable to society to risk in a dangerous clinical study, e.g., the head of state. Of course, bioethicists can disagree on the value of certain heads of state.

No respondents suggested excluding possible study participants who could be dangerous to the study team, e.g., professional criminals. However, such people could be excluded based on workplace safety laws.

U.S. federal protected classes prohibit discrimination based on race, color, religion or creed, national origin or ancestry, sex, age, physical or mental disability, veteran status, genetic information, and citizenship (but not profession). The term "protected class" does not appear in the relevant human subjects protection statutes, regulations or guidances. However, it would be an ethical leap for an IRB to approve a protocol that discriminates against a protected class (although age could be an exception in some studies).

It is unknown how many survey respondents are attorneys or have been involved in litigation. People who have been involved in litigation are more likely to be sympathetic to the sponsor's concerns.

Regulations and Ethical Guidelines

Relevant sections of the Code of Federal Regulations (21 CFR 50, 21 CFR 56, 45 CFR 46) and related FDA guidances do not discuss the broad principle of justice. Instead they focus on protecting "vulnerable categor[ies] of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons." (45 CFR 46/107) Attorneys, based on their training and experience, are relatively unlikely to qualify as vulnerable.

However, IRBs are not obligated to approve any protocol that does not violate a specific regulation. They also have the duty and authority to weigh ethical considerations in their deliberations.

The go-to ethics document in the U.S. for this situation is, of course, the Belmont Report, which includes the following passages:

An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly... What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally.

For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied.

[T]he principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects.

Justice is relevant to the selection of subjects of research at two levels: the social and the individual. Individual justice in the selection of subjects would require that researchers exhibit fairness: thus, they should not offer potentially beneficial research only to some patients who are in their favor or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons.

One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may continually be sought as research subjects, owing to their ready availability in settings where research is conducted. Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition.

In other words, the Belmont Report (a) argues for fairness in general, (b) explicitly envisions legitimate distinctions (specifically including "position"), and (c) focuses on the protection of the vulnerable. The ethical question of whether attorneys can be excluded from a clinical study thus boils down to whether the sponsor has a legitimate reason for the exclusion. To make this determination, the IRB should inquire into the circumstances of the sponsor's previous litigation experiences. It might learn that the sponsor has a legitimate issue. At one extreme, a group of attorneys might have targeted the sponsor with frivolous litigation because the CEO of the company is a member of a vulnerable population. At the other extreme, the sponsor might be a bad actor who should be reported to the FDA and forever banned from clinical research.

Next Month's Question

You are the chairperson of an IRB overseeing a study comparing three diabetes drugs. Some of the study participants have been talking about the study on social media. The sponsor believes their posts have affected study enrollment, adherence and retention. She wants your advice on how to deal with this problem ethically... Read the full question and give us *your* answer at: <https://www.surveymonkey.com/r/66TMYWM>.

Please send your ethical conundrums to ngoldfarb@firstclinical.com.

Author

Norman M. Goldfarb is Managing Director of First Clinical Research LLC, a provider of clinical research best practices information services. Contact him at 1.650.465.0119 or ngoldfarb@firstclinical.com.