Clinical Research Ethics Question of the Month: Car Accident

By Norman M. Goldfarb

You are on a jury in a courtroom trial. The plaintiff is suing “everyone” for serious injuries received when she was hit by a car driven by the subject. The subject was in a clinical study of a medication that might cause drowsiness. A witness has testified that the subject appeared to be asleep at the time of the crash. Who, if anyone, is most responsible for the plaintiff’s injuries?

**NOTE:** Respondents can hold more than one party most responsible.

**Question 1. If this were all you knew about the case, who, if anyone, is most responsible for the plaintiff’s injuries?**

Of the 175 respondents, 87% held the study subject most responsible for the subject’s injuries. Only 13% held the study sponsor most responsible, and only 9% held the investigator most responsible.

**Representative comments:**

Driving while drowsy, whether caused by a medication or not, the driver would be at fault.

If drowsiness was a known side effect, the subject should have read and understood the ICF and have been aware of the risks.

It is impossible to tell if the subject-defendant’s drowsiness was a direct result of the experimental drug.

Drowsiness is an effect that is detectable by the subject. Even if the subject was not warned about the possibility of experiencing drowsiness, the subject should have noticed being drowsy and either not started driving or pulled off the road. The exception would be if the subject was on the way back from the study location and the drowsiness came on suddenly while driving.
I would want to know how the site educated the subject on the side effect of drowsiness. Did they advise him not to drive?

Subject must be assessed prior to discharge and, if drowsiness was noted, either the subject remains in the center until the event passes OR the subject should have been driven to and from the visit.

Presumption of innocence means none other than subject is guilty.

**Question 2. If you learned only that the plaintiff was jaywalking at the time of the crash, who, if anyone, is most responsible for the plaintiff’s injuries?**

With this additional information, 55% of respondents held the study subject most responsible for the subject’s injuries and 44% held “none of the above,” i.e., the jaywalking plaintiff, most responsible. Only 7% held the study sponsor most responsible and 5% held the investigator most responsible.

**Representative comments:**

There should be a checkbox for the injured jaywalker. [author: yes]

The pedestrian has the right of way.

Drivers are legally responsible for being in control of their vehicle at all times.

It depends on local and state laws regarding pedestrian rights while jaywalking.

Even though the plaintiff was breaking the law, drivers have to be alert when driving so they can avoid pedestrians who may not be paying attention.

It is a shared responsibility of the plaintiff and the subject.

Jaywalking puts the onus on the plaintiff.

It depends on the distance from the driver when the plaintiff walked into roadway and whether the driver was speeding.

The driver is at fault unless, for example, the plaintiff darted out from between two parked cars.

**Question 3. If you learned only that the study subject had previously experienced drowsiness after taking the study medication, who, if anyone, is most responsible for the plaintiff’s injuries?**

With this additional information, 88% of respondents held the study subject most responsible for the subject’s injuries, 14% held the investigator most responsible, and 9% held the study sponsor most responsible.

**Representative comments:**

If the subject had previously experienced drowsiness as a result of taking the experimental drug, then he should have known not to drive after taking it.

Knowing how any medication affects one’s ability to drive is part of the responsibility of getting behind the wheel.

Did the subject tell the investigator? If so, and nothing was done, the investigator may be responsible.

I would need to know how many episodes had been experienced in order to establish whether the subject ought to have recognized the risk.

Causality of drowsiness needs to be assessed by an independent physician/scientist.
Question 4. If you learned only that the study subject’s wife, who has a driver’s license, was in the passenger seat at the time of the crash, who, if anyone, is most responsible for the plaintiff’s injuries?

With this additional information, 89% of respondents held the study subject most responsible for the subject’s injuries, 16% held the subject’s wife most responsible, 7% held the study sponsor most responsible, and 6% held the investigator most responsible.

Representative comments:

It’s possible the wife didn’t even know he was in the study or about the side effects of the medication. The driver is still responsible; he could have asked her to drive if he was feeling tired.

If the subject felt drowsy and unsafe to drive, he should have asked his wife to drive instead.

Subject might not have allowed his wife to drive. However, if the wife refused to drive, she is also responsible with the subject.

The passenger is irrelevant. The driver had the responsibility to recognize that, in his mental state, he was not safe to drive.

The wife would have no liability for the crash unless she was told that the subject should not operate a vehicle after study drug dosage. Even then, she did not contribute to the accident.

Unless the wife knew that the subject was experiencing drowsiness, it was not her responsibility.

The passenger may have also been unable to drive at the time because of drowsiness or a different reason.

The wife has a common sense and moral obligation to try to persuade her husband not to drive if he is visibly impaired, but I don’t think she has any legal or financial obligation.

If the wife knew the subject was feeling drowsy, both parties should have shared accountability.

Question 5. If you learned only that the study subject had initialed in the consent form that he should not drive a car during the study, who, if anyone, is most responsible for the plaintiff’s injuries?

With this additional information, 98% of respondents held the study subject most responsible for the subject’s injuries, 5% held the investigator most responsible, and 3% held the study sponsor most responsible.

Representative comments:

The subject was fully informed and made the decision to continue to drive while feeling drowsy.

If the subject definitely knew he shouldn’t be driving during the study, and there’s proof from his initials on the consent, he should be held responsible for plaintiff’s injuries.

Just recording in the consent form may not be sufficient documentation to confirm informed consent was given. If fully documented that participant was advised drug could cause drowsiness, to avoid driving, etc., then responsibility falls with participant.
**Question 6. If you learned only that study personnel did not discuss the drowsiness side effect with the subject during the consent process, who, if anyone, is most responsible for the plaintiff’s injuries?**

With this additional information, only 42% of respondents held the study subject most responsible for the subject’s injuries, 60% held the investigator most responsible, 41% held the study site most responsible, and 13% held the study sponsor most responsible.

**Representative comments:**

The study subject is still responsible for reading the informed consent document. The study site has some responsibility, since informed consent is not simply a form, it is a process.

Although informed consent is a combination of the discussion and the document itself, the subject did sign and should, at minimum, have read the informed consent document.

Even if it is included in the consent, most subjects do not read the consent.

If the subject is sleepy and still drives the car, he is still responsible for his actions.

It depends on whether the information was provided in the consent form. If it wasn’t (and was a known side effect), it would be the sponsor’s fault. It also depends on whether the site staff were adequately trained.

Even if this side effect was not in the consent form, if a person is feeling drowsy, they need to pull over, regardless of medication, amount of sleep, or anything else.

Investigator is responsible for confirming subject’s understanding of the ICF.

The investigator, the research staff, and the site bear most of the responsibility. You can never assume the subject has read every word of the consent form. It is the responsibility of the site and its research staff to ensure subjects understand the risks. We all know that most subjects will not read the entire consent form, which is why a member of the research team should go over every word of it with any subject during the consent process.

Whether sponsor is liable would depend on how the drug was provided, e.g., did it come in packaging from sponsor that could have had a warning on it.

It was everyone’s responsibility. The subject did sign the ICF. The site failed to discuss a risk. The IRB has the responsibility to ensure the study team is complying with their processes. Did the sponsor assess the practices of this site and confirm they understood the protocol?

The site (for failure to alert the subject), investigator, sponsor, and/or IRB (all for their failure to oversee) should be held to account/disciplined for inadequately educating the subject about this side effect. But the subject is still responsible for his/her own actions, unless the drowsiness came on suddenly while driving. Many everyday medications have drowsiness as a side effect, and experimental medications by the nature of their being experimental can have unexpected side effects.

**Question 7. If you learned only that an agreement to not drive was on page 18 of a 20-page consent form, who, if anyone, is most responsible for the plaintiff’s injuries?**

With this additional information, 84% of respondents held the study subject most responsible for the subject’s injuries, 22% held the investigator most responsible, 16% held the study sponsor most responsible, 15% held the study site most responsible, and 14% held the IRB most responsible.
Representative comments:
The subject has responsibility to read and understand what he signed.
The site is responsible for explaining all risks and must make sure the subject fully understands them prior to consenting.
Safety should not be buried.
The study sponsor writes the consent, but the IRB approves it.

**Question 8. If you learned only that an agreement to not drive was added to the consent form at the insistence of the study sponsor, who, if anyone, is most responsible for the plaintiff’s injuries?**

With this additional information, 84% of respondents held the study subject most responsible for the subject’s injuries, 18% held the investigator most responsible, 11% held the study site most responsible, 8% held the study sponsor most responsible, and 6% held the IRB most responsible.

Representative comments:
Well, obviously not the sponsor.
If the sponsor insisted that subjects had to agree not to drive, it becomes a condition of eligibility and enrollment. If the site and research team were very clear with the subject that he couldn’t drive, and he agreed to that stipulation and drove anyway, he bears responsibility for the accident. If the site did not inform the subject specifically or clearly that he could not drive while being treated in the study and document it in the record covering the consent process (and it’s hard to imagine any research team that would not do this very carefully because it is a huge concession by the subject), then and only then would the site and research staff have some liability.
Although the study team should, of course, emphasize the important points in the document during the consent process, an adult with both the ability to consent and a valid driver’s license is responsible to read and understand the study before consenting, and to evaluate their own ability to operate a vehicle under the influence of any medications.

**Question 9. If you learned only that the text of the consent form was changed from “causes drowsiness” to “might cause drowsiness” at the insistence of the study sponsor according to its best knowledge, who, if anyone, is most responsible for the plaintiff’s injuries?**

With this additional information, 72% of respondents held the study subject most responsible for the subject’s injuries, 37% held the study sponsor most responsible, 13% held the investigator most responsible, 11% held the study site most responsible, and 7% held the IRB most responsible.

Representative comments:
If drowsiness is known to be a common risk, the sponsor’s downgrading is a problem.
The subject is responsible for not driving while drowsy. He was made aware of the risk and was therefore responsible for taking it into account before driving.
Did the IRB question the change in the safety assessment?
Depending on the phase of the study, it is reasonable to say “might,” as it is still an investigational agent.
If the study drug does not always cause drowsiness, the sponsor was entitled to change the word “causes” to “might cause.”

The sponsor’s wording change might have been intended to minimize the reporting of drowsiness as a side effect by suggestible subjects.

Question 10. If you learned only that the study subject had accidentally taken two pills instead of one, who, if anyone, is most responsible for the plaintiff’s injuries?

With this additional information, 94% of respondents held the study subject most responsible for the subject’s injuries. Only 8% held the investigator most responsible, 6% held the study site most responsible, and 6% held the study sponsor most responsible.

Representative comments:

Did the site staff properly educate the subject?

If the subject was not instructed properly, the investigator shares responsibility. If the written information given to subject was not clear, the sponsor and IRB share responsibility.

If the subject’s understanding of dose has not been demonstrated and documented, it’s down to the investigator and the site.

Question 11. If you learned only that the study subject was in the placebo arm of the study, who, if anyone, is most responsible for the plaintiff’s injuries?

With this additional information, 87% of respondents held the study subject most responsible for the subject’s injuries. 2% to 4% held the investigator, study sponsor, study site, and subject’s wife most responsible.

Representative comments:

If the subject was on placebo, the ability to drive and not hit someone falls on the subject.

The placebo effect can be as strong as a drug.

The sponsor might still be responsible because of negative placebo effects.

It depends on what was in the placebo.

Discussion

“Ethics” is about the things a member of a society should or should not do based on what he, she or the society considers acceptable behavior. “Laws” are the rules that define a subset of those things as having legal consequences. In other words, while the plaintiff in this question is seeking recourse within the legal system, an ethical analysis can explore the issues more broadly. While legal standards will generally coincide with ethical standards, most people consider certain illegal acts acceptable and vice versa, depending on the circumstances.

When a legal proceeding begins, each party generally sees the facts, laws and ethics from their own perspective, while their lawyers often caution them that the other side is doing the same thing, and the decision in a courtroom trial might not be a foregone conclusion.

In this case, the laws, regulations, guidances and ethical standards of Good Clinical Practice, human subjects protection, and subject injury will enter a courtroom where the laws of personal injury govern. While this author has not had the privilege of experiencing a personal injury courtroom trial, it is probably fair to say that worlds will collide.
The primary question is this case whether the investigator, site, sponsor and IRB sufficiently fulfilled their “duty of care” to the study participant. Wikipedia says the following about “duty of care”:

In tort law, a duty of care is a legal obligation that is imposed on an individual requiring adherence to a standard of reasonable care while performing any acts that could foreseeably harm others. It is the first element that must be established to proceed with an action in negligence.

A tort is a civil wrong that causes a claimant to suffer loss or harm resulting in legal liability for the person who commits the tortious act.

Drivers have a duty of care to not crash their vehicles into pedestrians. Pedestrians have a duty of care to cross streets in crosswalks and keep an eye out for oncoming traffic. Clinical research investigators have a duty of care to caution study participants on the risks, e.g., possible drowsiness. Study sponsors have a duty of care to inform the investigator and IRB that a study drug might cause drowsiness, and so on. Determining responsibility in this case requires determining who did not meet their duty of care and to what extent that shortfall contributed to the injury. A courtroom trial might pin the responsibility on one party, all parties, or no party. An ethical analysis might do the same.

In this case, the study participant and/or the plaintiff directly caused the plaintiff’s injury. The secondary question in this case is whether any actions, or lack thereof, by the investigator, site, sponsor or IRB indirectly caused the injury and, if so, to what extent they should legally or ethically be liable for damages. The author is unfamiliar with the laws governing indirect damages, but the ethics of indirect harm seem to play down the distinction between direct vs. indirect causation. (The subject injury section of clinical trial agreements often limits the sponsor’s liability to direct injuries, i.e., to the study participant, but study subjects (and pedestrians) are not parties to clinical trial agreements.)

Most respondents agreed that the subject driving the car was fully or partially responsible for the accident. Signing a consent form and joining a study does not make an adult a passive ward of the study without personal responsibility for their actions.

Most respondent comments about the investigator, site, sponsor and IRB focused on whether those parties fulfilled their duty of care to the study participant. If not, respondents assigned some measure of responsibility accordingly. For example, if the informed consent process was inadequate, the investigator, site, sponsor and IRB might all, in their respective roles, have failed the study participant. At least some comments seemed to look beyond a strict reading of the applicable clinical research laws and regulations. That is a reasonable perspective when entering a jury trial, which is one reason attorneys can seem so paranoid. This paranoia about legal proceedings, however, can lead to an overabundance of caution within the workaday world of clinical research.

Many of the respondents noted that more must be known about the specific circumstances of the case, something every lawyer points out when asked for a legal opinion.

At least one respondent said that the investigator must ensure that study participants understand the material in the consent form. This requirement does not, in fact, exist in the laws and regulations, for two reasons. First, mind reading is a rare talent. Second, informed consent researchers are impressed when test subjects comprehend even 80% of the basics. The actual requirement is that the language in an informed consent form must be “understandable” to the subject (21 CFR 50.20). In any case, study participants are unlikely to remember much of what they understood for very long, e.g., three months later when they need to drive to town.
Given this perspective, if drowsiness while driving was a serious risk in this study, the investigator’s duty of care to the study participant should have continued with periodic reminders beyond the initial consent process. In addition, the study sponsor could have included something about driving in the protocol eligibility criteria, and the IRB should have reviewed that provision with care.

As a side note, two respondents noted that telling study participants about the drowsiness effect might create a placebo (actually, “nocebo”) effect, thereby adding a risk factor to participants in both arms of the study. It would be interesting to know if this nocebo effect has been observed with marketed drugs.

**Next Month’s Question**

You are a member of an IRB reviewing a study of a marketed drug for treating depression. Previous studies of this drug have shown minimal side effects. They have also shown a very high, enduring placebo effect. In fact, the symptoms of most study participants improved, regardless of whether they received the study drug or the placebo. This study has a twist: The goal is not to assess the efficacy of the drug, but to assess the efficacy of participating in a study of the drug. In other words, the study itself is the treatment under investigation. Would you vote to approve this study? Read the full question and give us your answer at https://www.surveymonkey.com/r/WG2RPRX.

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