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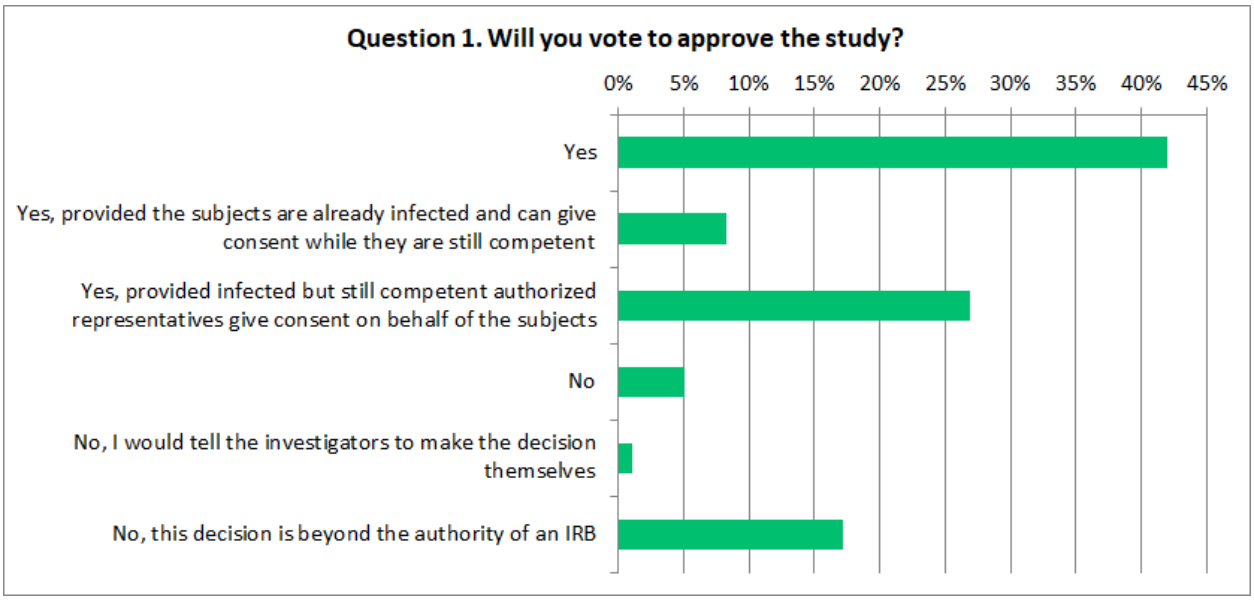
Clinical Research Ethics Question of the Month: Zombie Apocalypse

By Norman M. Goldfarb

The zombie apocalypse has arrived and is threatening the survival of the human race. Researchers have developed a treatment that might restore zombies to normal health and non-infectivity. There is a reasonable probability that the treatment will work as a cure but not as a protective measure. Failure of the treatment would be fatal for the subject. Potential study participants will not have the capacity to give consent. To the contrary, they will vigorously resist participation. No other possible treatments are known. There are no functioning governmental authorities, so the fate of humanity rests on your IRB. Time is of the essence. As a member of the IRB, will you vote to approve the study?

Results



Of the 279 respondents, 42% would vote to approve the study, and 29% would vote to approve the study, provided infected but still competent authorized representatives give consent on behalf of the subjects. Six percent would vote against approving the study. Seventeen percent would consider this decision beyond the authority of an IRB.

Several respondents stated that the benefit to the study participants outweighed the risks.

Numerous respondents took the position that survival of the species is more important than regulatory compliance. They placed the rights of the living above the rights of the undead.

Several respondents noted that, since killing zombies is generally encouraged, enrolling them in a clinical study does not seem unreasonable.

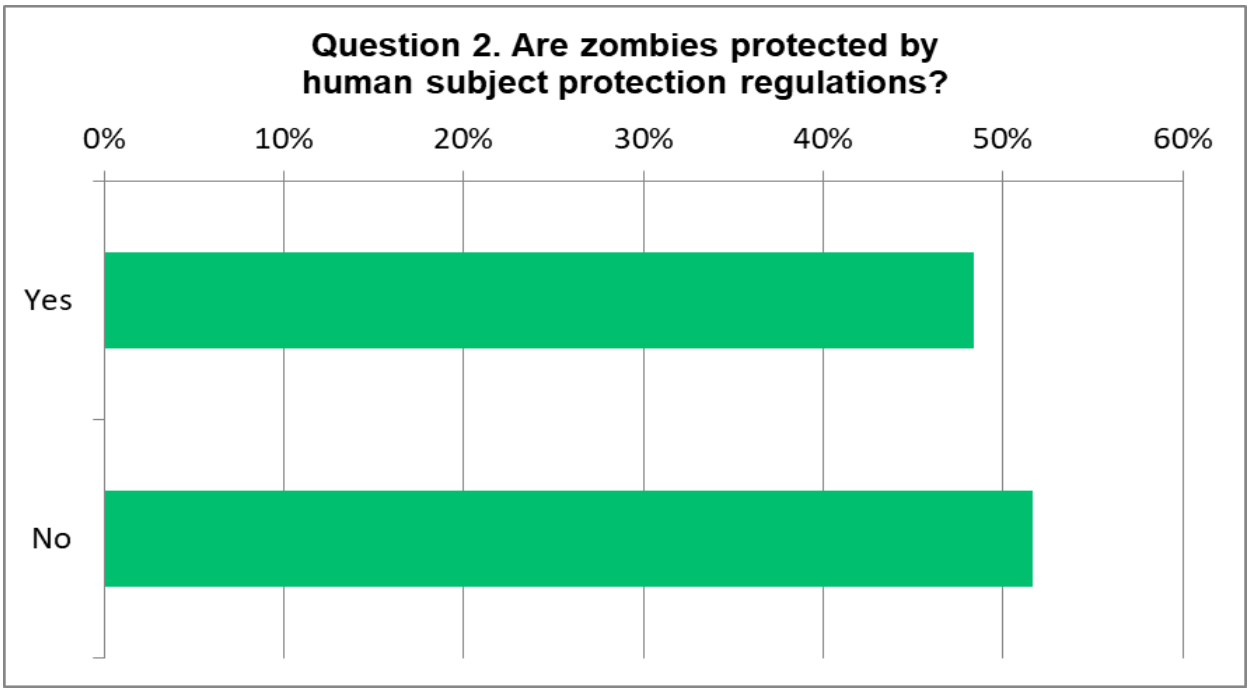
Several respondents stated that study participants will die anyway, so they have nothing to lose.

One respondent questioned whether "living" as a rotting corpse might be worse than death.

Several respondents commented that, since there is no government to enforce the regulations, the IRB can follow its ethical dictates without worrying about the regulations. Other respondents took this reasoning to the next level: Without a government to enforce the regulations, there is no need for IRB approval. One respondent also noted that, when a healthcare institution ceases to exist, so does its local IRB. [Is this an argument for central IRBs?] However, one respondent said IRB approval would still be a vote of moral confidence in the investigators.

One respondent suggested that the IRB should require two independent clinicians to screen prospective study participants to confirm the diagnosis.

One respondent stated, "My IRB has discussed this situation in the past. Although participants in the study are dead, they are the living dead. The living dead and reanimated tissue would potentially meet the definition of a 'human subject.' The research should go forward, due to the public health crisis, as a very large emergency use trial."



Forty-eight percent of respondents believe zombies are protected by human subjects protection regulations and 52% believe they are not covered.

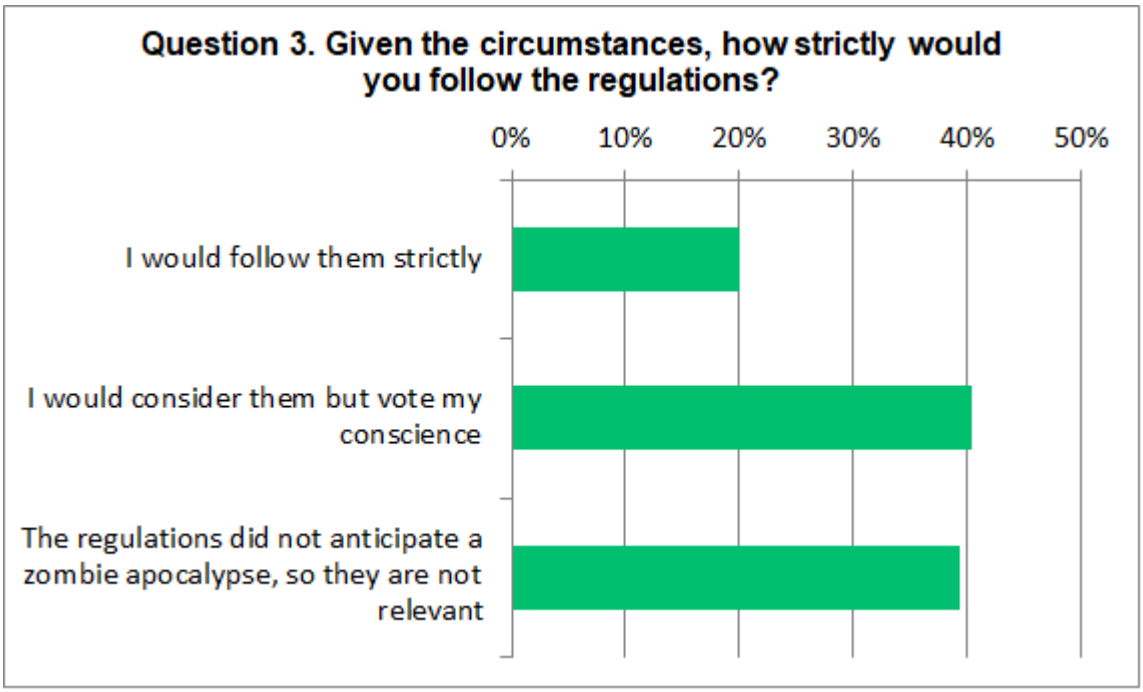
One respondent stated: "Zombies would fall under the same guidelines that regulate those subjects with dementia or other mental illness." Another respondent stated: "They should be considered to be mentally incapacitated human subjects, since this treatment proposes to turn them back into fully functioning humans." Another respondent stated: "Since researchers have developed a potential treatment, you would need to classify [zombification] as a disease, so a zombie would be a protected as if they have an infective disease."

One respondent stated: "If the IRB were functioning as a privacy board, a Waiver of Authorization would be required."

One respondent pointed out that having a soul is a fundamental characteristic of being human and "we do not know if they have a soul."

One respondent stated: "We would probably need a definitive clinical endpoint to establish who was still 'human' and who was 'zombie.' I'm guessing we could base that on whether the desire to eat human brains and flesh were present."

One respondent stated, "I would look at the individual as two parts: a living human and a dead zombie. The zombie might resist the study intervention, but I would no more take this into consideration than a tumor's objection to chemotherapy. The human subject, i.e., the part that might be restored to a normal human state, should be given the maximum human subject protections possible."



Twenty percent of respondents would strictly follow the regulations. Forty-one percent would consider the regulations but vote their conscience. Thirty-nine percent would consider the regulations irrelevant under the circumstances.

One respondent stated: "Without order, we would devolve into chaos. Or more chaos, since the zombie apocalypse is already upon us." Another respondent stated: "When or if something like this happened, there would be mass hysteria and there would be need for some sort of order to fall back on."

One respondent stated: "As the severity increases and humans head towards extinction, the regulations matter less because without a human population, regulations cease to exist."

One respondent stated: "The regulations were written loosely so that every circumstance did not have to be anticipated."

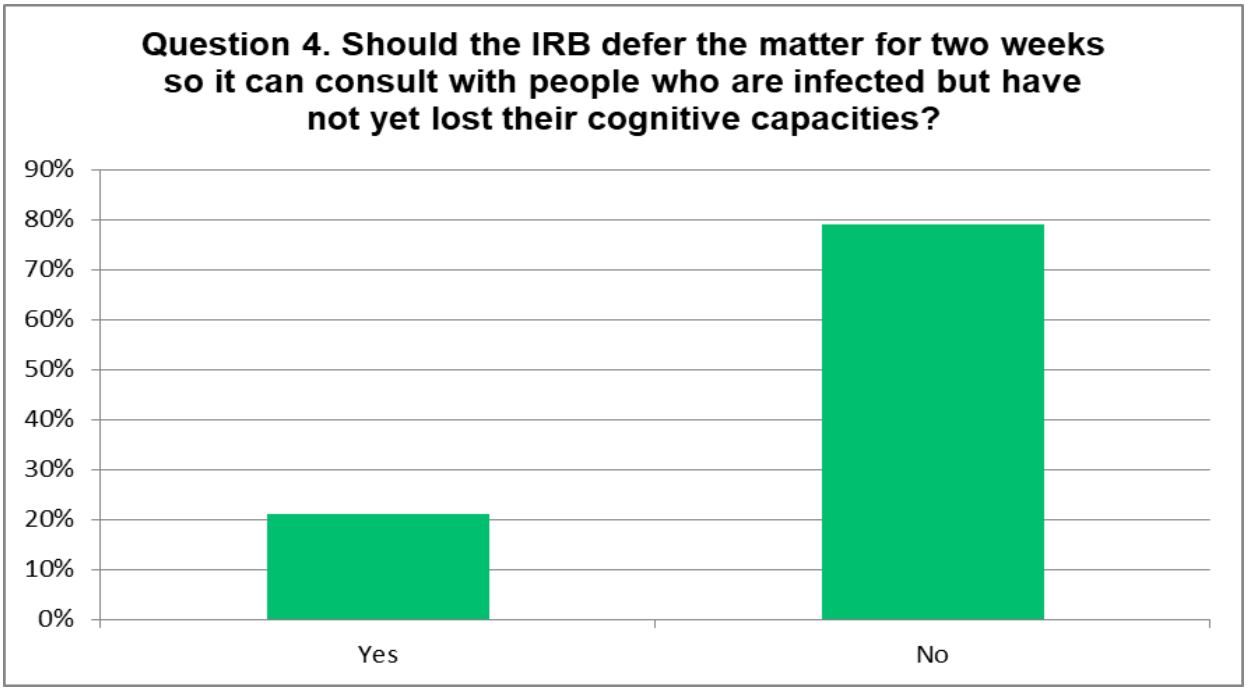
One respondent stated: "I wouldn't go so far as to say the regulations are not relevant, but there will certainly be aspects that are not applicable. As an IRB, it is our job to thoughtfully and carefully apply research ethics principles to the studies we encounter. In an ideal world, these will correspond 1:1 with the regulations, but I'm sure all of us have encountered studies where ethics and regulations do not completely align — we may apply more protections, or determine that some are not relevant/applicable."

One respondent commented: "I would be concerned that some doctor would use this opportunity to perform cruel acts 'in the name of research' that have no scientific basis."

One respondent would follow the spirit of the regulations.

One respondent said: "'Consider the regulations but vote my conscience' is always how I vote."

One respondent observed: "The fate of humanity versus a slap on the wrist...hmmm, let me think."



Twenty-one percent of respondents would defer the matter for two weeks so the IRB can consult with people who are infected but have not yet lost their cognitive capacities. Seventy-nine percent would not wait.

One respondent stated: "Good idea to consider, depending on the rate of transmission." Another respondent stated: "Input from the 'patient' population is important and might lead to better ways of recruiting and implementing the study." Another respondent stated: "People who are infected but not yet zombies could provide valuable moral fiber to the decision, as well as provide data on the zombification process, potentially improving the study design."

One respondent expressed caution, since even pre-zombies "might like to pick your brains about the study."

Several respondents questioned whether useful knowledge could be gained by such consultation.

Several respondents suggested a 24-hour consultation period.

One respondent suggested that the IRB approve the study now and then revisit the decision in two weeks.

One respondent recommended first conducting a Phase 1 study with healthy volunteers and then a Phase 2 study with infected but still competent patients, before conducting the proposed study.

A number of respondents expressed urgency in getting the study underway, for example:

- "The zombie apocalypse is upon us and you want to wait two more weeks?"
- "Time is wasting people!"
- "Might as well plan on a panel of full-on zombies for the next IRB meeting."

Discussion

Governing Authorities

As a number of respondents commented that, in the absence of a government, an IRB would have no authority to act. In addition, there would be no government to enforce the regulations. However, in the absence of government, an IRB can still fulfill its ethical responsibilities as if the government still existed, but with more flexibility. The IRB's work could help lead to the reconstitution of government.

Emergency Use

Federal regulations permit limited emergency use of a test article:

> Emergency use means the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval. (21 CFR 56.102(d))
>
> Emergency use of a test article [is permitted], provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review" (21 CFR 56.104)

FDA's "Emergency Use of an Investigational Drug or Biologic – Information Sheet" states:

> FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

The reporting and subsequent use requirements in the regulations are ambiguous, but it appears to permit giving multiple patients simultaneous single doses without prior IRB approval.

Risk vs. Benefit

Federal regulations allow IRBs to approve studies that expose study participants to risk:

> Risks to subjects [must be] reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies that subjects would receive, even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility. (21 CFR 56.111(2))

This regulation allows considering "the importance of the knowledge that may be expected to result." In the case of a zombie apocalypse, a study that indicates that a treatment would be effective would have great importance and would, therefore, make great risk acceptable.

It would be reasonable for an IRB to conclude that reversing zombification would be a great benefit to a study participant. Provided the probability of success was reasonable under the circumstances, this potential benefit would justify placing study participants at great risk.

The life expectancy of living zombies appears to be subject to adequate nutrition, normal wear and tear, and avoiding decapitation and other severe injuries. The fact that participants in a study will die anyway does not remove the IRB's obligation to protect their current life expectancy, although their life expectancy can be considered in the risk vs. benefit calculation. Another factor to consider is that dezombification might be fatal to a zombie. One respondent noted that dezombified study participants might be at risk of rezombification.

A zombie's quality of life should also be considered. It would appear that, untreated, they can expect a very poor quality of life. However, inpatient care might protect them from injury. (One has to wonder why pharmaceutical companies have not recognized zombies as a promising market for OCD, hydration and topical antibiotic medications…or have they?)

The study treatment would be unlikely to reverse all the infirmities that a zombie can acquire over time. The IRB should, therefore, require the study to enroll only those zombies that are in good condition. The IRB, assuming a quorum remains available, should review the results of the initial treatments in a timely manner.

Are Zombies Living Individuals?

For purposes of this discussion, zombies can be categorized into three basic types:

- The original *Voodoo* zombies have been mentally incapacitated by exposure to a toxin, but can function adequately as servants. They are not dangerous.
- *Reanimated* zombies had been dead and inanimate, but can now move about. They are dangerous and contagious through biting.
- *Living* zombies have been infected with a virus. They are not yet dead, they are very dangerous, and they are very infectious.

Given that the scenario in question envisions a zombie apocalypse, we can assume that the study would be with the *living zombie* type (hereinafter referred to as just "zombies").

The Terri Schiavo case highlighted the ambiguity in our definition of "death." The criteria in her case were whether she was in an "irreversible, persistent vegetative state." The court found that she was and allowed removal of life support.

Zombies are not in a persistent, vegetative state. According to the study's principal investigator, zombification might not be irreversible. Therefore, zombies do not meet any of the Schiavo criteria for death. Nevertheless, there is no statutory definition of "'living" vs. "dead," and the IRB does not have to accept the Schiavo case as precedent.

The Common Rule definition (45 CFR 46.102(f)) of a living person — "Human subject means a living individual" — does not exclude living people who are *also* dead. If "undead" is a synonym for "living dead," zombies meet this definition. However, if zombies are *undead* but not *living dead*, they are not living individuals covered by the regulations. Regulatory clarification would be helpful here.

Thus, according to the Common Rule, if zombies are the living dead, human subjects protections apply.

FDA regulations state: "Human subject means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient." (21 CFR 50.3(f)) While zombies cannot be considered healthy, they could be patients under the care of a physician, e.g., the investigator. Agency intent might have been to limit "individuals" to living persons, but federal agencies often write regulations broadly so they can be applied to unforeseen circumstances. However, this regulation applies only to drugs accepted by the FDA for human subjects testing, which does not appear to be the case in this scenario, since there is no FDA.

Capacity to Consent

Several respondents noted that zombies deserve the protections that any population lacking capacity to consent would receive, for example those with dementia. While zombies would strongly object to participation in this study, an IRB could consider that a feature of incapacity to consent due to dementia. The IRB might require the study to enroll only those patients for whom a competent legally authorized representative is available. One respondent noted, however, that LARs might not be able to understand the zombie's perspective well enough to speak for them.

Public Health

One respondent raised the issue of contagion, which is a public health question related to quarantines. If there were a Secretary of the DHHS, he or she would have statutory authority for administering interstate and foreign quarantine regulations, but not waiving IRB regulations without the statutory public comment period.

Other Scenarios

While a zombie apocalypse does not appear imminent, the chance of a deadly pandemic is not zero. There is also an above-zero possibility that the remains of certain people who would be considered dead by today's standards might someday be treated, transplanted or preserved in some manner that allows restoration to life. The ethical deliberations in this article might become relevant in these scenarios.

Next Month's Question

You are a member of the board at Florida Central IRB. You are reviewing a Phase 2 vaccine study for Zika2, a deadly infectious disease that has recently emerged in Florida and is spreading fast. The only clinical studies discussed in the Investigator's Brochure were conducted in Brazil, where Zika2 originated. They provide scientifically sound evidence that supports the proposed study. However, you have just learned that, because of the emergency situation in Brazil, the investigators made the decision to conduct their studies without regulatory or ethics committee approval, in a vulnerable population, and without proper informed consent. The Brazilian manufacturer and investigators will not be involved in the proposed study. Time is of the essence. Will you vote to approve the study?

Read the full question and give us *your* answer at:
https://www.surveymonkey.com/r/DJZP585

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.