RCR Casebook: First-in-Human Research: Selecting Appropriate Subjects

This is a 4 person role play involving 3 scientists who are planning to translate pharma research on animals to Phase I clinical trials on humans, specifically to test the safety a new anti-psychotic drug for schizophrenia. The director of the overall program has asked them to work out the details of the volunteers they plan to recruit for the study. Since all 3 research scientists are very mindful of the uncertainty concerning the toxicity and danger of the test substance in humans, they each take a strong position about the kind of subjects who should be recruited. However, they each take different positions. **Roles** • An advocate for enrolling healthy volunteers • An advocate for enrolling stable patients with schizophrenia • An advocate for enrolling unstable patients with schizophrenia • The director of the overall research program **Scenarios** • Scenario One: 3 Researchers meet with Director of Research	**Role Play Tips** • Detailed role descriptions and prompts are provided to guide the role play. This is not a strict script. Encourage role players to familiarize themselves with their characters and get creative! • Encourage role players to use their actual names in place of character names. • Experiment with changing the prompts to inject some variability in role play dynamics (e.g., have a character offer a conciliatory opening line or a belligerent opening line to see how that changes the course of the role play). • Run a role play more than once, changing role players.

Role Play: Advocate for Enrolling Healthy Volunteers Role Guide

Character Description: An Advocate for Enrolling Healthy Volunteers

You are thrilled to be moving from animal studies to clinical trials, testing an anti-psychotic drug that may better control the symptoms of schizophrenia with reduced side effects. Your long-term professional goal is to make a positive difference in the lives of those afflicted with schizophrenia. This line of research could also be pivotal to your scientific career.

It is clear to you that there are powerful scientific and ethical justifications for enrolling healthy volunteers into the Phase 1 studies. Since there is much uncertainty about the efficacy of the drug for treating schizophrenia as well as its toxicity in humans, it would be cruel and dangerous to recruit patients with schizophrenia who are currently being treated and are stable, or worse, patients who are not stable.

First, healthy volunteers will not fall victim to the therapeutic misconception that their participation in Phase 1 will cure them. They don't have schizophrenia, hence don't need a cure.

Second, the IRB is less likely to worry about the decisional capacity of participants who consent to be in the study.

Third, healthy volunteers are not already being treated with other anti-psychotic drugs, and while all patients would go through a "wash-out" period, healthy volunteers are in some sense "cleaner" models for testing toxicity of the new drug.

Role Play: Advocate for Enrolling Stable Schizophrenics Role Guide

Character Description: An Advocate for Enrolling Stable Schizophrenics

You are thrilled to be moving from animal studies to clinical trials, testing an anti-psychotic drug that may better control the symptoms of schizophrenia with reduced side effects. Your long-term professional goal is to make a positive difference in the lives of those afflicted with schizophrenia. This line of research could also be pivotal to your scientific career.

It is clear to you that there are powerful scientific and ethical justifications for enrolling stable, reasonable patients with schizophrenia as volunteers into the Phase 1 studies. First, the principle of justice generally requires that the population most likely to benefit from the results of research also shoulder the burdens of research. Patients with schizophrenia are most likely to benefit from the study of an antipsychotic medication.

Second, patients with schizophrenia who are stable typically retain decisional capacity. The study would include a brief assessment of decisional capacity, which should satisfy the IRB.

Finally, any body chemistry that distinguishes patients with schizophrenia from others may have important implications for the results of the Phase 1 trials. These effects would be lost if healthy volunteers were enrolled.

Role Play: Advocate for Enrolling Unstable Schizophrenics Role Guide

Character Description: An Advocate for Enrolling Unstable Schizophrenics

You are thrilled to be moving from animal studies to clinical trials, testing an anti-psychotic drug that may better control the symptoms of schizophrenia with reduced side effects. Your long-term professional goal is to make a positive difference in the lives of those afflicted with schizophrenia. This line of research could also be pivotal to your scientific career.

It is clear to you that there are powerful scientific and ethical justifications for enrolling schizophrenics who have little hope in life. These are patients with schizophrenia who are not benefitting from existing therapies. They stand to gain the most if this drug proves to be safe and effective.

You are worried about involving patients with schizophrenia who are doing well on their current medications. This study would require wash out—or temporary discontinuation of current medications—and restabilizing patients following washout can be difficult.

Regarding informed consent, consistent with state law, your IRB will allow surrogate consent if the patient assents and the research might offer some therapeutic benefit. Although you know it's a safety trial, you're convinced you've seen patients benefit from phase I trials.

Finally, any body chemistry that distinguishes patients with schizophrenia from others may have important implications for the results of the Phase 1 trials. These effects would be lost if healthy volunteers were enrolled.

Scenario One

Three scientists have convened with the director of their research program to work on the design of their research study. They plan to recruit human subjects.

Prompt

The director of the research program opens the meeting, saying "Have you considered how you will recruit people for this study? You know it will have major implications for the way we work out the budget and administration of the study, not to mention for your IRB application. What population are you going to recruit from?"

The three scientists: *How do you respond?*

Take Away Points:

- There are many considerations that need to be taken into account when determining which human subjects populations to sample from and enroll in a research study. Considerations include whether there are scientific and ethical justifications for enrolling certain subjects, fair selection of subjects, whether subjects are likely to be vulnerable, and whether subjects possess adequate capacity to make decisions.