MERCK
Be well

Merck & Co., Inc.
Division of Clinical Development

Congratulations on becoming selected for the second round of interviews for Director of Clinical Trials on an exciting new project at Merck & Company.

We appreciate your continued interest in a position in the Division of Clinical Development at Merck Pharmaceuticals. As a member of this team, you will be part of an exciting effort to determine the effectiveness of a new antidepressant medication. At Merck, we are fully committed to improving health through the ethical and safe development of new medications. As covered in your initial interview, the answers you give in this process are confidential. You are also bound by the non-disclosure agreement you signed during the initial interview process. Please answer all of the questions to your best ability. We look forward to seeing you during the final interview process.

Michael Turner
Vice-President for Operations
Division of Clinical Development

Applicant name:

Application date: 29 July 2010

Position: Director of Clinical Trials

Salary range: $1,000,000-$2,000,000 (plus benefits)

Please check if you would not wish your answers to be used to assess learning outcomes

Ethics

At Merck, ethics are our first priority. We are looking for scientists, managers, administrators, and workers who share this priority.

Give your thoughts, in a paragraph, on the important factors to consider when designing an *ethical* study in order to test a new drug.

There are several considerations that must be attended to in order to design an ethically sound drug study. Participants must be provided with an informed consent form so that they know their rights about participating. This would include information about the possible use of placebo. Because administering a drug may result in physical harm, it must also be considered so that the benefits of the study outweigh the risks. Researchers must also protect the privacy of the participants because they may not want others to know about the study. Withholding information is another factor that must be addressed. Since the participants would not know if they are receiving the active drug or not, after the study the participants should be debriefed. Another ethical factor to be considered is the withdrawal of treatment. The study should not conclude with the withdrawal of a drug that may help them. All of these ethical issues should be addressed in order to design an ethical study.

Ethics

Think of a situation in which you have had to think about ethics in research design. What did you learn from the experience?

For an assignment in a research methodology class, the famous obedience study by Stanley Milgram was examined. This study had several ethical problems including psychological harm, deception, and lack of informed consent. Although the study is unethical, it provided valuable information about authority and obedience. This experience taught me both about the challenges and the importance of creating an ethical study. I learned that some studies may require the use of deception in order to keep the results of the study valid. Milgram's study also shows the importance of debriefing. If he had not debriefed the participants, they probably would have continued to think that they killed the confederate which would impose greater psychological stress. I also learned that informed consent is necessary, but it may bias the study. This assignment also opened my eyes to more ethical research designs such as role-playing, simulation studies, and honest experiments. Overall, the ethics assignment taught me that ethics must be a first priority in research design.

Study Design

We are currently about to start a Phase 3 human clinical trial in order to test the effectiveness of our newly developed antidepressant, *Serenique* (elevexor).

As Director of Clinical trials, you will work with your team to design and oversee the research studies for this exciting new depression treatment. Describe, in general, how you will go about this. Please give specific information on important research methodology considerations for this study.

This new drug, Serenique, will be studied under typical Phase 3 standards. Serenique will be compared to an older antidepressant to measure the drug's effectiveness in treating depression. An informed consent form would be given to make them aware of their right when participating. Participants would be selected if they are depressed based on a self-report measure for depression. The exclusion of participants would be on the basis of confounding the study or the safety of the participant. The study would employ random assignment of the participants to each group to prevent systematic biases. This would be necessary to make in internally valid study. Before the drug is given, participants would rate their depression symptoms as a pretest. This will allow us to see if there are any changes in individual scores, as well as to assess the equivalence of the two groups. The drug would be administered using the double-blind technique so that expectancy effects can be eliminated. After a few months of treatment, the posttest would be given. This would allow evaluation of the effectiveness of the treatment with the new drug. If the scores on the posttest are similar, then Serenique is an effective way to treat depression. If the score are significantly different, then the drug may not be effective.

Study Design

You are in the second round of interviews because of your research methodology experience.

Describe a time in the past when you have conducted your own research. What problems did you encounter and what did you learn?

For an assignment, I studied territoriality in a grocery store parking lot. This was measure by timing how long it takes for a car to back out when another car is present versus when no car is waiting. I was looking at a difference in gender and territorial behavior. Because this was an observational study, it was unpredictable when a person would return to their car from the store. Even though I observed the store on a crowded day, there could be significant time in between recordings. There were also times when several cars would leave at the same time, which made it impossible to record. I also found a problem with cars pulling through so that there is no need to back up. The large size of the parking lot also made it difficult to observe the intended behavior because most cars did not wanted to park away from other cars rather than taking a previously occupied space. Another problem I encountered was people seeing me observe them. Although I don't know for sure if it affected their behavior, I'm sure that it freaked them out. From this experience I learned how to conduct non-experimental research. I also learned that some research requires creative ways to observe behavior. I think that the use of a partner would have made me look less suspicious.

Study Design

Explain in what ways science may be limited for studies testing the effectiveness of antidepressant medications.

Science is limited when studying antidepressants because it is also limited when diagnosing depression. Because there are no physiological measures that have been accepted, researchers must rely on self-report measures. Antidepressants are usually studied along with a placebo or another antidepressant for comparison in order to determine efficacy. Self-report measures are then used to determine the effectiveness. This limits the experimenters to the most unreliable measure which may result in participants being deceptive. If the experiment uses a pre-test and post-test, there may a difference but it could not be related to the actual drug. Science may also be limited because of the placebo effect. If there is a difference between the two groups, then it is said that the drug is effective. Because of the placebo effect, it is difficult to determine how much of the effect of the drug is due to the actual drug mechanism rather than just the placebo effect.

The Merck Team

Though you are applying to be a member of the Division of Clinical Development, members of this division often work with members of the Division of Marketing and Advertising. Merck & Co., Inc. expects *Serenique* (elevexor) will compete with the antidepressant *Pristiq* (desvenlafaxine) made by Wyeth Pharmaceuticals. We would like you to review their television and internet advertisements for this product prior to answering the following questions. (Trademark requirements prohibit us from providing links to their advertisements.)

Please identify any claims of fact made for *Pristiq and* the basis AND the validity of those claims.

ALSO please provide additional explanations for why their claims of effectiveness might not be true or why the claims may be questionable. Your answer may continue on the next page.

Both the television and internet advertisements made the claim of fact that Pristiq is "proven to treat depression." The basis for this claim is said to be from the results of the drug studies which showed that there was improvement compared to placebo. The statement may not be valid because of the small difference between the groups. Wyeth Pharmaceutics claims that it will effectively treat depression but the research study may not support that claim. The statement is questionable because the research only showed a small difference between the placebo and drug groups. Although it does show statistical significance, it may not be significant enough to treat depression. Pristiq was also not studied with another antidepressant to compare the efficacy. The drug's effectiveness was also not studied beyond 8 weeks. The basis for effectiveness in based on improvement in functional outcomes which showed an average improvement of less than 1 on the 10 point scale compared to placebo. The claim may be questionable because the research showed that increased dose did not result in expected decrease in depression based on self-report measures.

The Merck Team (continued)

Other information

In this section please supply us with any information you feel may help us with your application. For example, you may describe what you feel you have learned about research methodology in your course work or in other activities. You may also tell us how understanding research is important for everyday life. We would also like to know how you feel our consumers may or may not understand research and how that affects how we develop and market our life improving pharmaceuticals.

In research methodology, I learned about topics that will help me in both my future studies and other areas. In regards to education, I will be able to use what I have learned in other classes especially when completing research projects. One of the most important lessons I learned was about evaluating research which is useful in academics and everyday life. When looking at a newspaper article or advertisement, it is important to be able to understand the research that was conducted. I think that many consumers do not understand research so when they see an article claiming a fact, it is likely that they believe it is the truth. This allows pharmaceutical companies to say that a drug is “proven” to be effective and not be challenged because consumers do not understand the research behind the drug. It seems to be an effective way of marketing because billions of dollars is spent on pharmaceuticals each year. If consumers were to understand research, I think that it would be detrimental to the sales of drugs because they would realize that not all claims are based on fact.