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**16.1.9.**  
**Protocol-Specific Informed Consent Document**

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**Subject Information and Consent  
For Subject at West Pharmaceutical Services.**

**Effect of Multiple Intravenous Doses of LY333328 on the  
QTc Interval in Healthy Subjects**

## **Introduction**

You are invited to take part voluntarily in a research study of a study drug known as LY333328 or glycopeptide. LY333328 is an antibiotic that is being developed to treat bacterial infections. This study is being sponsored by Eli Lilly and Company.

Before agreeing to participate in this research study, it is important that you read and understand this form. It describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time. If you participate, you will receive a copy of this form to keep for your records.

## **Number of People Taking Part in The Study**

If you agree to participate, you would be one of up to 36 healthy men and women participating in this study. Your participation in this study is expected to last up to seven months. You will receive 10 single daily intravenous doses of LY333328 and two single daily intravenous doses of sugar water (placebo). You will not know when you are getting either the LY333328 or the placebo. The study medication will be injected into a vein. You will be admitted to the GFI Research Center (GFI) the night before the first dosing day. You will be required to stay at GFI for up to 15 nights and return to GFI for up to 6 outpatient visits.

## **Purpose of the Study**

The purposes of this study are to determine —

- The effect of LY333328 on ECG (heart tracing).
- The effect of different dose amounts of LY333328 (in different people) on the heart tracing.
- The safety of LY333328 at single daily doses that have not been given to healthy subjects before.

It is possible that information collected during this study will be analyzed by the sponsor in the future to evaluate LY333328 for other possible uses or for other medical or scientific purposes other than those currently proposed.

## **Qualifications to Participate**

The doctor in charge of this study or a member of the study staff has discussed with you the requirements for participation in this study. It is important that you are completely truthful with the doctor and staff about your health history. You should not participate in this study if you do not meet all qualifications.

A requirement to be in this study is --

- You must be between the ages of 18 and 65 years.

You cannot participate in this study if --

- You are allergic to LY333328, vancomycin (Vancocin®) or teicoplanin (Targocid® [not registered in the United States])
- You have taken certain prescription or “over-the-counter” medicines within the last 7 days
- You have donated blood in the last 60 days
- You have a current problem with alcohol or drug dependence or abuse
- You have participated in a clinical trial with an investigational drug within the past 30 days.

Since there is no information available on the effects of LY333328 on the developing fetus or unborn child, you cannot participate in this study if you are a woman and could possibly become pregnant.

You may smoke during the study, but only during smoking breaks in the designated smoking area.

You must agree to not consume alcohol-containing beverages for the entire duration of the study (approximately 4 ½ months).

## **Study Procedures**

If you participate, you have passed the blood and urine tests and the physical examination given to you by the study doctor. You also have had a chest x-ray and a heart tracing. If these tests show that you qualify for the study, you will receive 10 daily injection doses of LY333328 and 2 daily injection doses of sugar water (placebo) by vein over the span of 12 days. You will not know what medication you are receiving each day.

You will be admitted to the research unit the night before the first dosing day. You will be weighed and have your vital signs (heart rate, breathing rate, and blood pressure) recorded. You will have a pregnancy test (if you are female) as well as a heart tracing performed. On the first dosing day, you will have blood and urine tests performed and then you will be connected to a heart monitor which will show your heart rhythm and rate. The study drug will be administered by vein over 60 minutes while you lie resting in bed. You will not be allowed to get out of bed while the study drug is being administered. Blood will be collected by venipuncture (needle stick) to measure the amount of LY333328 in your blood and to measure your blood counts and liver and kidney functions. Heart tracings will be performed several times during the study. Your vital signs will be recorded multiple times as well. You will be required to stay on the

unit for up to 96 hours after your last dose of study medication and will continue to wear the heart monitoring equipment until the morning of the 8<sup>th</sup> study day.

You will be required to return to the unit over the next 4 months to have repeated blood and urine tests and have your heart tracings repeated. You will not be allowed to participate in another study or drink alcohol until you have completely finished and been released from this study.

The maximum number of blood samples that may be drawn from you is up to 50. The total amount of blood which may be drawn from you during the study is a less than 1 ½ cups. This is considered a safe amount of blood to donate over the time interval involved.

Physical examinations will be performed on various study days and at the conclusion of the study.

Your blood or urine sample will be tested for certain types of drugs (known as controlled substances in the United States) that may affect behavior and that may be regulated by law. If your test results show that you have taken these types of drugs, you will be notified of the test results and may be discontinued from the study based on the investigator's decision. The results of this test will be kept confidential and disclosed only as required by law.

## **Risks**

There may be risks to you if you participate in this study. LY333328 has been taken by about 166 people (healthy and disease patients). Possible side effects identified in animal studies include allergic-type reactions (such as rash, redness, flushing, shortness of breath, and low blood pressure), nausea, vomiting, diarrhea, lowered ability to fight infection, and abnormalities in red blood cell count, white blood cell count, liver tests, kidney tests, and some blood clotting tests.

In animal studies, these side effects completely or partially reversed following discontinuation of the drug. Animals receiving LY333328 at 200 times the rate planned for people have experienced possible convulsions.

Preliminary examination of test-tube data suggests but does not confirm the possibility that LY333328 could cause changes in heart rhythm (arrhythmia). The meaning of these test-tube findings is not known, but it suggests the study drug could cause an irregularity in your heart rhythm. There has been no evidence of life-threatening arrhythmias in animals or in subjects given to LY333328 to date.

Of 19 people given single doses of LY333328, one had low blood pressure and fast heart rate, another had a rash and itching, and one person experienced dizziness. Several people had temporary changes in liver tests. LY333328 may interfere with some blood clotting tests, but no bleeding problems have been noted. In two previous studies 27 of 39 people were given multiple doses of LY333328. Thirteen of these people had mild to

moderate irritation at the site of injection. One woman out of 10 had vaginal irritation. Some people also experienced mild abnormalities in liver tests but no symptoms.

In a blinded study (investigator and patient do not know which study medication the patient is receiving) where patients were given multiple doses of either LY333328 or other antibiotics (vancomycin/cephalexin) for skin infections, one patient experienced acute hepatitis that went away within a month. Another patient in this study had extra heartbeats while receiving study drug.

Because LY333328 is similar to the antibiotics vancomycin (Vancocin®) and teicoplanin (Targocid®), people who are known to be allergic to either of these two antibiotics should not receive LY333328. Antibiotics can cause diarrhea in some people, so this could also occur with LY333328. LY333328 may stay in the body for a longer period of time than most drugs. Therefore, side effects may take longer to go away.

For most people, needle punctures for blood draws do not cause any serious problems. However, they may cause bleeding, bruising, discomfort, infections and/or pain at the needle site or dizziness.

The risks associated with x-rays are low. The radiation resulting from x-rays is similar to the amount of natural radiation from living at a moderately high altitude for six months.

You may experience skin irritation or a rash from the patches that are applied to your skin to monitor your heart rhythm.

In addition to the risks named above, LY333328 or the study procedures may have other unknown risks.

There may be unknown risks of possible harmful interaction with other medication you may be taking.

If any important new information is found during this study that may affect your wanting to continue to be part of this study, you will be told about it right away.

## **Reporting Health Experiences**

If you have any injury, bad effect, or any other unusual health experience during this study, make sure that you immediately tell the nurses or contact Dr. Randall R. Stoltz, at (812) 474-6530. You can call at any time, day or night, to report such health experiences.

## **Participation in the Study**

Your taking part in this study is entirely voluntary. You may refuse to take part in the study or you may stop your participation in the study at any time, without a penalty or loss of benefits to which you are otherwise entitled.

Your participation also may be stopped by the study doctor or sponsor without your consent. If this happens, it might be due to a bad reaction you have to LY333328 safety or effectiveness.

If you stop being part of this study, the study doctor or one of the staff members will talk to you about any medical issues regarding the stopping of your participation.

### **Treatment and Compensation for Injury**

If you follow the directions of the study doctor and staff and you are physically injured due to any substance or procedure properly given under the plan for this study, the sponsor (Eli Lilly and Company) will pay the medical expenses for the treatment of that injury.

### **Possible Benefits**

Study drug and study procedures will be provided at no cost to you. You may receive information about your health from any physical examinations and laboratory tests to be done in this study.

Since you do not have any of the conditions for which LY333328 is being developed, you will not medically benefit from being a part of this study.

You will be paid \$\_\_\_\_\_ to reimburse you for [transportation, parking, meal, or others] expenses related to your participation in this study. If you withdraw from the study early, you will be paid for these expenses for the portion of the study that you did complete.

Information obtained from this study will benefit the sponsor of the study, Eli Lilly and Company, and may benefit patients in the future.

### **Investigator Payment**

The sponsor is paying the study doctor and/or West Pharmaceutical Services for their work in this study.

### **Questions**

If you have any questions about this study please contact Dr. Randall R. Stoltz, at (812) 474-6530.

If you have any questions about your rights as a participant in a research study, please contact the Ohio Valley Institutional Review Board at (812) 485-7562.

### **Confidentiality**

Your medical information will be kept confidential by the study doctor and staff and will not be made publicly available unless disclosure is required by law.

Data obtained from this study that does not identify you individually will be given to the sponsor and/or its representatives and may be published or given to regulatory authorities in the United States Food and Drug Administration and similar agencies in other countries, all of whom may look at your medical records or other countries in which regulatory approval of LY333328 may be sought.

Your original medical records may be reviewed by the sponsor and/or its representatives, the Ethical Review Board for this study, and regulatory authorities for the purpose of verifying clinical trial procedures and/or data. Your medical information may be held and processed on a computer.

By signing this consent form, you authorize the record review, information storage and data transfer described above.

## **Signatures**

To be entered into the study, you or a legal representative must sign and date the signature page (see Attachment 1).

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## Subject Information and Consent Form

### Attachment 1

### Signature Page

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To become a part of this study, you or your legal representative must sign this page.

By signing this page, you are confirming the following:

- You have read all of the information in this Subject Information and Consent Form, and you have had time to think about it.
- All of your questions have been answered to your satisfaction.
- You voluntarily agree to be part of this research study, to follow the study procedures, and to provide necessary information to the doctor, nurses, or other staff members, as requested.
- You may freely choose to stop being a part of this study at any time.
- You have received a copy of this Subject Information and Consent Form to keep for yourself.

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Subject Name (Print or Type)

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Subject Initials and  
Covance Number

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Signature of Subject

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Date (ddMMMyy) and  
Time

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Name of Individual Conducting Informed Consent  
Discussion (Print or Type)

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Signature of Individual Conducting Informed  
Consent Discussion

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Date (ddMMMyy)