

APPENDIX 12.1.2 – SAMPLE INFORMED CONSENT FORM

Phase I, Open Label Study to Evaluate Skin Tissue Penetration and Total Renal Clearance of Dalbavancin (VER001) Following Administration of a Single 1000 mg Intravenous Dose to Healthy Volunteers
Principal Investigator: Alice B. Gottlieb, M.D., Ph.D.

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Name of Study: Phase I, Open Label Study to Evaluate Skin Tissue Penetration and Total Renal Clearance of Dalbavancin (VER001) Following Administration of a Single 1000 mg Intravenous Dose to Healthy Volunteers

Protocol No.: VER001-10

Sponsor: Versicor

Principal Investigator Name:

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RESEARCH STUDY:

You have been invited to participate in a clinical research study that is designed to help treat infections requiring antibiotic therapy. In order to make an informed decision regarding your participation in this research study, it is important that you understand all the risks and benefits associated with the study. This process is known as informed consent.

This consent form gives you detailed information about the research study. A member of the research team will discuss all aspects of the research study and consent form with you. This discussion should explain and clarify all aspects of this research: its purposes, the procedures that will be performed, any risks of the procedures, and possible benefits. Once you understand the study and all your questions have been answered, if you still wish to participate, you, along with the investigator as a witness, will be asked to sign this informed consent document. You will receive a copy of it to keep as a record.

I _____ have been invited to take part in this research study under the direction and medical supervision of Dr. Alice B. Gottlieb, M.D. I understand that while the study will be under the supervision of this study doctor, other professionals who work with him/her may be designated to assist or act for him/her.

SUBJECTS:

You will be one of approximately 12 subjects, male or female, 18 to 65 years old, who will participate in this trial. Six subjects in Part A and six subjects in Part B. Each subject who participates in both part A and B reduces the required total maximum number by one volunteer.

PURPOSE:

Presently, the number of bacterial infections that are resistant to currently available antibiotics is increasing. These types of infections can be especially dangerous to individuals who have weakened immune systems or are hospitalized. In order to more effectively treat these bacterial infections, Versicor, Inc. is developing a new antibiotic, known as Dalbavancin (study drug). It may be effective against a variety of bacterial infections that are currently difficult to treat.

The purpose of this research study is to measure the skin and blood levels of Dalbavancin (study drug), and calculate how much is passed in the urine when it is given to healthy human volunteers.

INCLUSION CRITERIA:

You must meet the following criteria to be eligible for participation in the study:

- You must be 18 to 65 years old
- You must use effective birth control, be post menopausal or surgically sterile
- Women of child-bearing potential must have a negative pregnancy test
- You must agree to follow all steps of study
- You must have a normal hearing test
- You must fully understand the informed consent and sign the informed consent before any procedures are done
- You must not require medical treatment that in the opinion of the investigator may effect the study

EXCLUSION CRITERIA:

If you meet any of the following criteria, you are NOT eligible for participation in the study:

- If you have abnormal findings on examination of the ears
- If you have an abnormal hearing test

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- If you have a history of persistent ringing in ears, off-balance, ear surgery, tumors in the head, neck
- If you have been in a study within 4 weeks of entry to this study
- If you have an allergy to Gentamycin, Amakacin, Tobramycin or Vancomycin
- If you have a history of alcohol or drug abuse
- If you are pregnant or breast feeding
- If you have an abnormal blood test on the screen that the study director feels would effect the study
- If you are unwilling to use birth control during the study and or at least 6 months after
- If you are taking Coumadin
- If you refuse to stay away from excessive noise during the course of the study
- If you have an infection
- If you have had to start new medication within the past 6 weeks of study start

DURATION:

The study will consist of 42 days of follow-up after receiving a single dose of 1000mg of Dalbavancin, no matter which study part you participate in.

If you chose to volunteer to participate in this study, you will have the choice of participating in one or both of the following study parts:

Study Part A will require that you have 5 skin tissue samples 1/5 inch in depth and 1/5 inch in width removed from me and a total of 22 teaspoons of blood taken at different time intervals during the study. You will be admitted to the Clinical Research Center the afternoon prior to being given the study drug and will be discharged the morning after receiving the study drug. Subsequent visits will be on an out patient basis Day 3-7, 14, 21, 28 and 42.

Study Part B will require that you be admitted to the Clinical Research Center the evening prior to being given the study drug and remain for 7 days after receiving the study drug. Subsequent visits will require me to remain in the Clinical Research Center for 24 hours on days 14, 21, 28 and 42. During these time periods all my urine will be collected and a total of 22 teaspoons of blood will be collected at different time intervals.

Study Part A and Part B If you agree to participate in both studies, you will be admitted the afternoon prior to receiving the study drug and remain for 7 days after being given study drug. Subsequent visits will require me to remain in the Clinical Research Center for 24 hours on days 14, 21, 28 and 42. During these time periods, all my urine will be collected, a total of 22 teaspoons of blood will be obtained and 5 skin tissue samples 1/5 inch in depth and 1/5 inch in width will be removed at different time intervals during the study.

PROCEDURES:

You have been told that during the course of this study, the following will occur:

Screening

Before entering this study or undergoing any tests for the study, you will be asked to sign this consent form, indicating my willingness to participate. You also understand that to be eligible to participate in this study, you must meet certain criteria that will be evaluated and determined by the study physician (Principal Investigator). You agree to attend all scheduled visits and follow instructions given to me by the study staff. If you agree to participate in this study, the following events will occur:

You will choose which study part(s) (Part A and/or Part B) that you wish to participate in. After you make my choice, and during the seven days before the start of the study, a study doctor or staff will ask me about

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my medical history and will give me a complete medical exam including a history of any medication you are taking or have taken in the past 4 weeks. You will also be given a drug screen to test for drug of abuse and alcohol. Urine will be collected and blood will be drawn for laboratory tests. The blood and urine collected will be used to measure blood counts and blood chemistries and routine urine analysis. If you are a female of childbearing potential, the blood or urine tests will include pregnancy testing. In addition, you will have two standard hearing tests known as audiology testing and have a 12-lead ECG (test to evaluate my heart rhythm). If the procedures and test results from my screening indicate that you are eligible for this study, you will be notified and admitted to the Clinical Research Center the evening prior to being given the study drug. The total blood obtained for screen will be 3 teaspoons. The total urine obtained will be 6 teaspoons.

Study Part A - If you chose to participate in Part A only, a single skin sample will be obtained the day before you receive the study drug. You will be admitted the afternoon prior to being given the study drug. The study doctor who will take the skin sample is a board-certified dermatologist and is very experienced in taking these type of tissue samples. The study doctor will discuss with you the biopsy site which will be on your arms or legs either above the knees or elbows. If possible, the same general area will be used for the 5 skin samples obtained throughout the study. The skin site selected for biopsy will be cleansed and numbed. After the sample is obtained, the wound will be sutured and a sterile dressing applied.

On the morning of Day 1 two catheters (small plastic flexible tubes) will be inserted into my vein one in each arm. The catheters will allow the study personnel to administer the study drug through one tube and obtain blood samples from the other tube. You will give a urine sample to test for drug abuse, alcohol and pregnancy, if you are a female of child bearing potential. A blood sample will be taken to measure the levels of the study drug in my blood before the study drug is given. You will then receive a single dose of 1000mg of Dalbavancin (study drug) through one of the catheters in my vein over 30 minutes. Blood samples will be drawn at the end of infusion 1, 2, 4, 6, 12 and 18 hours after infusion. You will have a 12-lead ECG (test to evaluate my heart rhythm) done shortly after the completion of the infusion. My blood pressure, pulse, respiration and temperature will be taken before study drug infusion and at the end of infusion 1, 2, 3, 4, and 12 hours after infusion. Six to eight hours after the infusion has ended, a skin sample will be taken as described above. You will be required to stay in the Clinical Research Center for observation for at least 24 hours after the study drug infusion has been completed.

On the morning of Day 2 blood pressure, pulse, respiration, temperature, blood and skin sample will be obtained at approximately the same time the study drug was started.

You will be able to go home after the observation period and return to the Clinical Research Center for additional visits. Blood will be taken to measure blood levels of the study drug on days 3 – 7, 14, 21, 28 and 42. You will return at approximately the same time that the study drug was started on Day 1. Blood chemistries, complete blood count and urinalysis will also be done on Days 4, 6, and 7. Blood pressure, pulse, respiration and temperature will be done on day 7. I will have skin samples taken on Days 7 and 28 as described above. You will have hearing tests performed on Days 14 and 42. Upon completion of the study (Day 42), you will have a physical examination 12-lead ECG (test to evaluate my heart rhythm) and a pregnancy test if you are of child bearing potential. The total blood obtained will be 22 teaspoons. The total urine obtained will be 12 teaspoons.

Study Part B If you chose to participate in Part B only, you will be admitted to the Clinical Research Center the evening prior to dosing. On the morning of Day 1 two catheters (small plastic flexible tubes) will be inserted into your vein, one in each arm. The catheter will allow the study personnel to administer the study drug through one tube and obtain blood samples from the other. You will give a urine sample to test for drug abuse, alcohol and pregnancy if you are a female of child bearing potential prior to me receiving the study medication. You will receive a single dose of 1000mg of Dalbavancin (study drug) through one of the catheters in my arm over 30 minutes. A blood sample will be taken to measure the levels of the study drug in my blood before infusion, at the end of infusion 1, 2, 4, 6, 12 and 18 hours after the start of infusion. You will empty your bladder before the study drug is given. All of your urine will be collected for the first week after the study drug infusion. On Day 1 urine samples will be collected over the 0-2, 2-4, 4-6, 6-12,

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12-18 and 18-24 hour time intervals. Your blood pressure, pulse, respiration, temperature will be taken before, at the end of the infusion and 1, 2, 3, 4, and 12 hours after the start of the infusion. An 12-lead ECG (test to evaluate your heart rhythm) will be taken shortly after the completion of the study drug infusion. Day 2-7, you will remain in the Clinical Research Center to collect all of my urine. The urine collected will be used to measure levels of the study drug over the course of the study. Blood will be taken to measure blood levels of the study drug on Days 2-7, 14, 21, 28 and 42 at approximately the same time that the study drug was started on Day 1. Blood chemistries, complete blood count and urinalysis will be done on day 4, 6, and 7. You will go home on Day 7 after all procedures have been completed.

You will return to the Clinical Research Center on days 14, 21, 28 and 42 all of your urine will be collected over a 24 hour period starting at about the same time that the study drug was started on Day 1. You will be discharged following the 24 hour urine collection. A hearing test will be done on days 14 and 42. Upon completion of the study (day 42) you will have a complete physical examination and a 12-lead ECG (test to evaluate your heart rhythm) and pregnancy test if you are of child bearing potential. The total blood obtained will be 22 teaspoons. All urine will be collected.

Study Part A and B – If you chose to participate in both Study Part A and B, you will be admitted the afternoon before being given the study drug. A skin sample will be obtained before being given the study drug (Day -1). On the morning of Day 1 two catheters will be inserted into my vein, one in both arms. You will give a urine sample to be tested for drug abuse, alcohol and pregnancy if you are a female of childbearing potential. You will empty my bladder and blood samples for study drug levels will be obtained prior to being given the study drug. All of your urine will be collected for the first week after the study drug infusion on Day 1.

You will received a single dose of 1000mg Dalbavancin through one of the catheters in my arm over 30 minutes. Blood samples will be drawn at the end of infusion 1, 2, 4, 6, 12 and 18 hours after infusion. Urine will be collected over 0-2, 2-4, 4-6, 6-8, 8-12, 12-18 and 18-24 hour time intervals. You will have an 12-lead ECG (test to evaluate your heart rhythm) shortly after the completion of the infusion. Your blood pressure, pulse, respiration and temperature will be taken before, at the end of infusion 1, 2, 3, 4 and 12 hours after infusion. You will have a skin sample taken as described above 6-8 hours after receiving the study drug.

You will be required to stay in the Clinical Research Center for 7 days after the infusion of the study drug. Blood for study drug level will be done on days 2-7 approximately the same time the study drug was started on Day 1. Urine collection will continue over 24-48, 48-72, 72-96, 96-120, 120-144 and 144-168 hour intervals. On day 4, 6, and 7 a complete blood count, blood chemistry and urinalysis will be done. You will have your blood pressure, respiration, pulse and temperature checked as well as a skin sample done on day 7 before discharge.

You will return to the Clinical Research Center on days 14, 21, 28 and 42, all of my urine will be collected over a 24 hour period starting at about the same time that the study drug was started on Day 1. You will go home following the 24 hour urine collection. Blood for study drug level will be done on day 14, 21, 28 and 42. Skin sample will be taken on day 28.

You will have hearing tests done on days 14 and 42. Upon completion of the study (day 42) you will have a complete physical examination, a 12-lead ECG (test to evaluate your heart rhythm) and urine pregnancy test if you are of child bearing potential. Total blood obtained will be 22 teaspoons. All urine will be collected.

RISKS/DISCOMFORTS:

You have been told that the study described above may involve the following risks and/or discomforts:

Risks associated with drawing blood from my arm include pain, bruising, swelling, lightheadedness, and on rare occasion, infection and nerve damage (numbness, tingling). The electrocardiogram (ECG, electrical tracing of heart activity) procedure may cause minimal discomforts during the attachment and removal of the

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ECG leads to and from the skin of your chest area. Skin biopsies may produce a small, permanent scar in the skin. In rare instances, a superficial, temporary wound infection at the site of biopsy has been observed. Possible side effects associated with administration of the Dalbavancin study drug may include liver damage, kidney damage, diarrhea, abdominal pain, heartburn, and damage to hearing.

In a previous similar study none of the 36 treated subjects demonstrated any (hearing damage) after receiving Dalbavancin. No signs of hearing damage or hearing loss were observed for any dose in the previous study, even at the very sensitive high frequency range. Volunteers in the previous study received single doses of up to and including 1120 mg and multiple doses of up to 1000 mg dalbavancin on Day 1 followed by daily doses of 100 mg for 6 days (total cumulative dose of 1600mg over 7 days). Although there is little indication that antibiotics similar to Dalbavancin cause hearing loss when given alone without additional drugs, the possibility of hearing loss cannot be excluded.

There is a possibility that you could develop an allergic reaction to the study drug. This could result in temporary symptoms such as hives, swelling, shortness of breath, chest tightness or decrease of blood pressure. These symptoms can be usually relieved by Tylenol and/or Benadryl. These medications will be available if you need them.

If you become pregnant during the course of this study, you should notify the Principal Investigator of this fact as soon as possible since the risks to the fetus or me are unknown. You will be referred to an obstetrician.

There also may be risks and discomforts that are not yet known.

BENEFITS:

No direct benefit can be guaranteed to me by participating in this clinical study. Even if no personal benefit is realized, you may be helping future patients by providing important information about this potentially useful antibiotic drug.

ALTERNATIVES:

This study is not designed to provide treatment. The only alternative to participation is to not participate in this study.

NEW FINDINGS:

During the course of the study, you will be told about any new information that may affect my willingness to remain in the study.

CONFIDENTIALITY:

Every effort will be made to maintain the confidentiality of my study records. The Institutional Review Board and the sponsoring company (*Versicor, Inc.*), and the U. S. Food and Drug Administration (if applicable), will be allowed to inspect sections of my medical and research records related to this study. If the findings from the study are published, you will not be identified by name. Your identity will remain confidential unless law requires disclosure. Documentation, data, and all other information generated will be held in strict confidence.

UMDNJ DISCLAIMER:

If you participate in this study, you may be exposed to certain risks of physical injury in addition to those connected with standard forms of therapy. In addition, it is possible that in the course of these studies, new adverse effects of the study drug that result in physical injury may be discovered. Medical therapy will be arranged by the investigator for any physical injury to you which occurs as a direct result of your

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participation in this research. Your health insurance carrier or other third party payor will be billed for the cost of this medical therapy. No other compensation is available.

FINANCIAL COSTS TO THE SUBJECT:

Your participation in this study will involve no cost to you. You will not be responsible for the cost of the study drug or laboratory tests and assessments as required by this clinical study. Versicor, Inc. will pay for medical care to treat any physical injury incurred by you as a direct result of the study drug or study procedures. No financial payments or other forms of compensation (such as lost wages or discomfort) or medical treatment beyond that which is offered above will be offered to me by Versicor, Inc.; however, you should realize that you do not waive your legal rights by signing this form.

PAYMENT FOR PARTICIPATION:

You have been told that you will receive \$2,000.00 for Part A, \$3,000.00 for part B, \$4,000.00 for Part A and B for your participation in this study according to the following schedule:

If you leave the study for any reason before you complete all the required visits, you will be paid according to the following fee schedule:

<u>Study Part A Only</u>	<u>Study Part B Only</u>	<u>Study Part A & B Only</u>
\$200.00 per in patient visit \$50.00 per out patient visit	\$200.00 per in patient visit	\$200.00 per in patient visit \$200.00 per biopsy

RIGHT TO REFUSE OR WITHDRAW:

Your participation is voluntary and you may refuse to participate, or may stop my participation at any time, without penalty or loss of benefits to which you are otherwise entitled. The investigator has the right to withdraw you from the study at any time.

In the event that you stop participating in the study for any reason, you will be asked to return to the research center to undergo the final evaluations (hearing assessment, 12-Lead ECG, and lab work (blood and urine). It is important for you health and safety to have these final procedures completed.

INDIVIDUAL(S) TO CONTACT:

If you have any questions about my treatment in this study or you think you have experienced a research-related illness or injury you can contact: Alice Gottlieb, MD or the research staff at (732) 418-8484.

If you have any questions about my rights as a research subject, you can contact: Ann Vaughan, IRB Director, at (732) 235-6357

You will receive a copy of this consent form if you agree to participate in this research study.

_____ Subject's initials (*bottom of each page*)

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SIGNATURE OF SUBJECT

I have read this entire form, or it has been read to me, and I understand it completely. All of my questions regarding this form or this study have been answered to my complete satisfaction. I agree to participate in this research study.

Check one of the following:

Part A _____ Part B _____ Part A and Part B _____

Subject: Name: _____ Signature: _____

Witness: Name: _____ Signature: _____

Date: _____

SIGNATURE OF READER/TRANSLATOR IF THE SUBJECT DOES NOT READ ENGLISH WELL

The person who has signed above, _____, does not read English well. I read English well and am fluent in (name of the language) _____, a language the subject (his/her parent/legal guardian) understands well. I have translated for the subject (his/her parent/legal guardian) the entire content of this form. To the best of my knowledge, the subject (his/her parent/legal guardian) understands the content of this form and has had an opportunity to ask questions regarding the consent form and the study, and these questions have been answered to the complete satisfaction of the subject (his/her parent/legal guardian).

Reader/ Name: _____ Signature: _____
Translator: _____

Witness: Name: _____ Signature: _____

Date: _____

SIGNATURE OF INVESTIGATOR OR RESPONSIBLE INDIVIDUAL

To the best of my knowledge the subject, _____, has assimilated the entire content of the above consent form, and understands the study and its risks well. The subject's questions have been accurately answered to his/her/their complete satisfaction.

Investigator: Name: _____ Signature: _____

Witness: Name: _____ Signature: _____

Date: _____