

**SUBJECT INFORMATION SHEET****Study: TMC207-TiDP13-C208**

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**PROTOCOL TITLE**

A Phase II, placebo-controlled, double-blind, randomized trial to evaluate the anti-bacterial activity, safety, and tolerability of TMC207 in subjects with sputum smear-positive pulmonary infection with multi-drug resistant Mycobacterium tuberculosis (MDR-TB)

**CONTACT DETAILS INVESTIGATOR**

Name: .....

Address: .....

Telephone number: .....

**ADDITIONAL CONTACT DETAILS (IF APPLICABLE)**

Name: .....

Address: .....

Telephone number: .....

**SPONSOR: TIBOTEC BVBA, GENERAAL DE WITTELAAN L11 B3, 2800  
MECHELEN, BELGIUM**

**TABLE OF CONTENTS**

Protocol Title .....	1
Contact Details Investigator.....	1
Additional Contact Details (if applicable) .....	1
Introduction.....	3
Part I: Study Specific Information.....	3
Description and Purpose of the Study .....	3
Study Procedures .....	5
Risks and Benefits .....	8
Your Role in the Study .....	10
Study-Related Injury.....	10
Costs .....	10
Remuneration.....	10
Part II: General Information.....	11
Sample Handling and Retention .....	11
Insurance.....	11
Participation and Termination .....	11
Confidentiality .....	12

## INTRODUCTION

You have been asked to participate in a research project with a new investigational medication called TMC207-TiDP13 (called 'TMC207' further in the text) being developed by Tibotec BVBA, Generaal De Wittelaan L11 B3, 2800 Mechelen, Belgium (also called 'sponsor' further in this text). TMC207 is being studied to help treat patients that are infected with the bacterium *Mycobacterium tuberculosis*. This bacterium usually affects the lungs in humans, causing the serious illness called tuberculosis (TB). TMC207 is the first in a new class of anti-TB medications; it has a unique structure and a new way of working. It might have potential value in combination with other anti-TB medications in the treatment of TB.

Before you agree to take part in this study, please read this consent form carefully. It contains important information to help you decide whether or not it is in your best interest to participate in this study. If you have questions that are not properly explained or answered in this consent form, someone of the research staff will be available to give you more information. You will have time to ask as many questions as you need in order to be sure you understand the study procedures, including possible risks and benefits.

Once you understand the study and if you decide to take part in it, you will be asked to sign the attached consent form and you will be given your own copy. No procedures related to the study will be started before you have given your consent to participate in the study. You may be removed from the study without your consent if your study doctor decides that continuing in the study would harm you or because of other protocol-specific reasons.

Your participation in the study is entirely voluntary. You may decide not to take part or to withdraw from the study at any time without losing the benefits of any routine medical care.

## PART I: STUDY SPECIFIC INFORMATION

### DESCRIPTION AND PURPOSE OF THE STUDY

This new investigational medication called TMC207-TiDP13 is being developed for the treatment of tuberculosis. TMC207-TiDP13 is not approved for use by the US Food and Drug Administration (FDA), nor by Regulatory Authorities in the European Economic Area (EEA), the Medicines Control Council of the Republic of South Africa, or any other regulatory authority. Therefore, it can only be used in this research study.

#### What is the purpose of the study?

The main purpose of this study is to investigate whether treatment of TB with TMC207 is safe and effective. This study investigates how soon the bacteria that cause TB die with or without TMC207 added to standard of care treatment (the treatment of TB always consists of giving more than one TB medication at the same time).

Other aims of the study are to determine the amount of TMC207, and of the product TMC207 breaks down into in your body, in your blood after repeated doses of TMC207 and to explore effects that may be caused by combining TMC207 with the other TB medications. This information will help determine an effective and safe combination of TMC207 with other TB medications in clinical studies that will investigate a better cure for TB.

### Who will participate in the study?

To participate in the study, you must be between 18 and 65 years old, have the disease TB affecting the lungs, more specifically so-called multi-drug resistant (MDR)-TB. MDR-TB means that you are infected with bacteria on which the TB medications rifampin and isoniazid have no effect. You must not have been treated before for MDR-TB, but you may have been treated with so-called first-line TB medications. Additionally, you must have enough sputum as well as enough TB bacteria in your sputum, for the laboratory to be able to evaluate your treatment.

There are certain other requirements for entering this study and if you meet these requirements (as will be explained by your study doctor), you may be included in the study. The process of evaluation in the study begins with a so-called screening period of 7 days. During this screening period a physical examination and certain laboratory and medical tests will be performed. You will have to stop taking any TB medication that you might be taking and you will have to agree on being hospitalized (as part of standard health care) during the screening period and during the first part of your TB treatment. All tests that will be done during the study are explained below in this informed consent document.

Including you, about 200 patients will take part in this study. The study will be conducted in 2 parts and patients in both parts will be equally divided into 2 treatment groups. Initially, in the first part of the study, about 50 patients will participate and will be treated for 2 months. After these patients have finished treatment and results of this part of the study have been evaluated, another 150 patients will be included in the study and will be treated in 2 treatment groups for 6 months.

### What treatment will be given to you?

If you choose to enter the study, you will start treatment after the screening period. You will be randomly allocated to one of 2 treatment options: medications that are already on the market to help cure MDR-TB combined with TMC207 or combined with inactive substance that looks like the investigational product (placebo). Random allocation means that you are assigned to a treatment group by chance, similar to toss of a coin. This is the most exact and fair way of assigning a treatment, as the choice of who gets what treatment is not made by a person but by a computer. It is important to realize that you cannot choose which treatment you will receive. This study is blinded, which means that neither you nor your study doctor will know which treatment group you have been assigned to. However, this information will be immediately available to your study doctor if it is needed for any medical reason.

If you are participating in the first part of the study this treatment will last for 2 months. However, after the treatment period you will be asked to come back to the clinic regularly for another 2 years. During this time you will be treated with TB medications according to national guidelines for the treatment of MDR-TB but you will no longer take any investigational medication. If you are participating in the second part of the study you will be treated with TMC207 or placebo for 6 months, after which you will also be asked to come back to the clinic regularly for another 2 years and be treated with TB medications according to national guidelines for the treatment of MDR-TB but during which you will no longer take any investigational medications.

The dose of TMC207 that will initially be used in this study will be 400 mg per day (i.e., 4 tablets of TMC207 or placebo) for the first 2 weeks. After these first 2 weeks you will be asked

to take 200 mg three times a week (i.e., 2 tablets of TMC207 or placebo) during the rest of the treatment period. Three times weekly intake will mean that you need to take the study medication on days that are separated by at least one day.

Intake of TMC207 or placebo will be oral within 10 minutes after a standard breakfast. Most of the time you will be asked to take the other TB medications before breakfast, except on days of specific assessments when the other TB medications will also be taken after breakfast. All intakes will be supervised.

Please do not eat grapefruit or drink grapefruit juice from 7 days before the first time that you are asked to take study medication until the last time that you need to take study medication. This may decrease the activity of the investigational medication.

## STUDY PROCEDURES

If you participate in this study, you will be asked to go see your study doctor at regular intervals for a medical check-up and assessments. Visits for assessments will be weekly for the first 2 months, followed by every two weeks for the next 4 months, monthly for the following 3 months, and every three months until the end of the study, afterwards.

You will be asked to take the study medication and the other TB medication at these visits. The study consists of three phases during which you are subjected to several tests, as outlined below.

Throughout the entire study, blood samples will be taken. The volume of blood that will be taken at each visit is distributed as follows:

- Screening visit: about 2 tablespoons;
- Treatment period:
  - If you are participating in the 2-month treatment period of the first part of the study, between 1/3<sup>rd</sup> and 2 tablespoons at each visit;
  - If you are participating in the 6-month treatment period of the second part of the study, either no or between 1/3<sup>rd</sup> and 2 tablespoons at each visit.
- 2-year Follow-up period: between 1½ and 2 tablespoons at each visit;
- In case of dropout: about 1½ tablespoons at the time of dropout or the following morning, and another 1½ tablespoons 5 to 7 days later;
- In case of a retest for safety reasons: about 1½ tablespoons;
- In addition, for a subset of subjects, there will be 3 (if you participate in the first part of the study) or 2 (if you participate in the second part of the study) visits during the treatment period at which additional blood samples will be taken: in total 4 to 5 tablespoons over several timepoints after intake of study medication.

### Screening visit (7 days before start of study medication)

During the first visit to the study doctor you will be asked a number of questions about your medical past, menstrual cycle (for women only), recent or previous medication related allergies, current medical condition, and any medications you might be taking, to determine if you can participate in the study. Before any procedure will be started, you will have the chance to review this information sheet and discuss any questions you might have. You will be hospitalized and will need to stop taking all TB medications that you might be taking.

Other assessments that will be made or samples that will be taken are:

- a complete physical and eye examination;

- heart rate, blood pressure, and breathing rate measurement;
- a test called ECG (electrocardiogram) to record the activity of your heart;
- a chest X-ray to determine the location of the TB infection in your lungs;
- blood samples for routine safety testing. Please make sure that you have not eaten for at least 10 hours prior to blood sample collection.
- for all women, a pregnancy test on the collected blood sample;
- a urine sample for routine analysis. An additional urine sample must be provided in order to identify if you used any drugs that would disqualify you from the study (amphetamine, sleeping tablets, cocaine, cannabis, opium, and isoniazid).
- 3 spot sputum samples to check the presence of TB bacteria and their resistance to the TB medications Rifampicin and Isoniazid. This information will be made available to your study doctor in order to help treat your TB disease.
- An AIDS/HIV test will be done and the number of your CD4+ cells (blood cells that affect your ability to fight infections) will be counted. You will have the choice to know the results of your HIV test. Test results will not be made available to any third parties in such a way that your identity will be known.

### Treatment period

On the day before you are to receive your first dose of study medication, the study doctor will check if you still meet the requirements to participate in this study. Assessments will be made and samples will be taken as described below.

The following day you will be allocated to one of the 2 treatment groups and you will start intake of TMC207 or placebo within 10 minutes after breakfast. This breakfast will be a standardized breakfast and you will be asked to finish it within 30 minutes. The intake of study medication will always be supervised. You will also start taking the other TB medications on this day, before breakfast. TMC207 or placebo will be given to you for 2 or 6 months, depending on the part of the study you are taking part in. During the first two weeks, TMC207 or placebo will be given to you every day. The rest of the treatment period, TMC207 or placebo will be given three times per week.

During the treatment period, the following assessments will be made on a regular basis:

- spot sputum samples to check the presence or absence of TB bacteria. The TB bacteria from your sputum sample will be preserved and tested for the development of resistance to the study medication and to other TB medications.
- overnight sputum collection to count the number of TB bacteria in sputum in some patients. The sample will also be used to determine the amount of TMC207 and its breakdown product in your sputum;
- blood samples to determine the level of TMC207 and its breakdown product in your blood. These samples will be taken within 10 minutes before intake of study medication. On a regular basis, for a subset of subjects, additional blood samples will be taken 5 hours after intake of study medication or at several timepoints during the first 24 or 48 hours after intake of study medication. It is on these days of 24- or 48-hour samplings

that you will be asked to take the other TB medications after breakfast instead of before. On all days of blood sampling to determine the level of study medication in your blood, you will be asked to have a lunch 5 hours after intake of the study medication and to go back to your usual diet after 8 hours. Please do not drink caffeinated coffee or tea on these days (decaffeinated coffee is allowed), as caffeine may influence the concentrations of certain medications in the blood;

- a complete physical, eye and sometimes also ear examination;
- heart rate, blood pressure, and breathing rate;
- an ECG recording to monitor the activity of your heart. This will be done before breakfast, but on some days an additional reading will be done 5 hours after intake of study medication;
- a blood sample and urine sample for routine safety testing, before breakfast. Please make sure that you have not eaten for at least 10 hours prior to collection of these samples;
- a chest X-ray to locate the place of your infection in your lungs;
- for females, a urine pregnancy test;
- for HIV-infected patients, the number of your CD4+ cells.

#### Follow-up period – 2 years

When you complete the treatment period, you will enter a follow-up period of 2 years. You will no longer be treated with TMC207 or placebo but you will continue to receive medication for the treatment of MDR-TB as per national treatment guidelines. Follow-up visits are scheduled at regular intervals during these 2 years after the last intake of study medication.

The following assessments will be made at regular timepoints during the follow-up period:

- spot sputum samples;
- overnight sputum samples for patients who had overnight sputum collection during the treatment period;
- blood samples to determine the level of TMC207 and its breakdown product in your blood;
- a complete physical, eye and sometimes ear examination;
- heart rate, blood pressure, and breathing rate;
- a urine sample and blood sample for routine safety testing. Again, please make sure that you have not eaten for at least 10 hours prior to blood sample collections;
- an ECG recording before breakfast, but on some days an additional reading will be done 5 hours after intake of study medication,
- a chest X-ray;
- for females, a urine pregnancy test;
- for HIV-infected patients, the number of your CD4+ counts.

In case you drop out of the study before it is completed, 2 more visits must be performed: one at the time of dropout or the following morning, and one 5 to 7 days later. At these visits, the following assessments will be made:

- a complete physical and eye examination;
- heart rate, blood pressure, and breathing rate;
- a spot sputum sample;
- a urine sample and blood sample for routine safety testing. Please make sure that you have not eaten for at least 10 hours prior to blood sample collections.
- an ECG recording;
- a chest X-ray;
- a urine pregnancy testing for females;
- CD4+ counts for HIV-infected patients.

If you discontinue the study your study doctor will be asked to follow up on your health status until the last patient in the study has completed his/her last visit. Contact will be made between the site where you participated in this study and any clinics where you might receive further TB treatment, approximately every 6 months. However, you may ask your study doctor not to follow up for the study any longer. This decision will have no effect on the future care you may receive.

## **RISKS AND BENEFITS**

By participating in this study, your condition will be closely monitored. It is possible that by participating in this study your condition may improve and that this study may be helpful in developing a new therapy for others with similar disease. However, it may also be that you do not benefit from participation in this study.

The efficacy of 7 days treatment with 400 mg TMC207 was demonstrated in a study that included 75 TB-infected patients who had not previously (or not within the last 3 years) been treated for TB. However, 7 days treatment with TMC207 is not enough to provide information on its activity over a long period of time, which is usually required to treat TB. There is thus a need to explore the activity of TMC207 for a timeperiod longer than 7 days of treatment (this will be investigated in this study which you are invited to participate in).

All therapies have the potential to cause some side effects. Therefore, by participating in this study, the evolution of your condition will be closely monitored.

From 6 previous studies of TMC207 with a total of 173 healthy volunteers treated, we learned that TMC207 is generally safe and well tolerated. The most common side effects in these studies were headache, nasopharyngitis (common cold), hyperuricemia (an amount of uric acid in the blood that is higher than normal), and postural dizziness (dizziness while sitting down).

Also from a study in 75 TB-infected patients, we learned that TMC207 is generally safe and well tolerated. The most commonly reported side effect in this study was hemoptysis (coughing up blood; this is a common event in patients with TB). No serious side effects, no significant changes, and no treatment-related effects on clinical laboratory tests, vital signs, or ECG parameters, related to TMC207, were observed.

Because of the side effects of TMC207 described in animals and humans in whom TMC207 was studied, you will be monitored specifically for the development of injuries to muscles, pancreas, and liver, and for changes in safety parameters to be determined in blood samples.

It is important that you follow your study doctor's and/or study nurses' instructions exactly and that you inform your study doctor as soon as any changes in your medical condition occur.

You have the right to ask any questions concerning the potential and/or known hazards of this study at any time. Should you as a result of the participation in this study, be harmed in any way, you will receive appropriate medical treatment.

If additional information on any risks becomes available during the study that might affect your willingness to continue in this study, you or your legally acceptable representative will be informed in a timely manner.

### **Blood Draw Risks**

Blood drawing may cause some discomfort, bleeding or bruising where the needle enters the body (1%). A small blood clot may form at this site or there may be swelling in the area. Rarely, fainting or local infection may occur. Care will be taken to prevent these complications.

Due to the high number of blood samples required in this study, a cannula (small plastic tube) may be inserted in one of the veins in your arm. A local sedative may be used at the discretion of your study doctor.

### **Unknown Risks**

You might experience side effects or discomforts that are not listed in this form. Some side effects may not be known yet. It is possible that you will be the first patient to experience a particular effect. Tell the study doctor or study staff right away if you have any problems.

### **Reproductive Risks**

If you are a woman, you may not take part in this study if you are breastfeeding, are pregnant, think that you may be pregnant, or are trying to get pregnant. If you are pregnant or breastfeeding, there may be risks to you and the baby that are not known at this time. Women will be tested for pregnancy during the study.

If you are a woman able to get pregnant, you must avoid getting pregnant in order to take part in this study. Unless you have a vasectomized partner or are not sexually active, you should use a method of birth control that is acceptable to you, the study doctor, and the sponsor throughout the entire period of treatment with TB medications. You should be aware of the fact that hormone-based methods of birth control may not be reliable when taking TMC207. Women of childbearing potential who are having heterosexual intercourse should use two methods of birth control (an oral and mechanical method (e.g. condom) or 2 mechanical methods).

It is important for you to tell the study doctor at once if you get pregnant or think that you might be pregnant while you are in the study. If this happens, the study doctor will discuss with you what you should do. Since there might be risks for an unborn child, which are currently unknown, you will be asked to stop taking part in the study if you get pregnant. You may also be asked questions about your pregnancy and the baby.

If you are a man, it is important that you use a condom or other appropriate contraceptive measures to prevent pregnancy when having heterosexual intercourse, since the effects of a new

medication on conception are unknown. These precautions apply throughout the entire period of treatment with TB medications.

## **YOUR ROLE IN THE STUDY**

For this study to be successful, it is important that you fully cooperate with your study doctor and that you follow his/her instructions precisely.

Your responsibilities as a study subject include the following:

- cooperate with your study doctor;
- provide correct and accurate information about your medical history and current conditions;
- tell the study doctor about any problems you have during the study or if you suffer any unexpected or unusual symptom;
- do not take any other medications or remedies (either prescription, over the counter, or herbal remedies) unless the study doctor has approved them. You should tell the study doctor of any new medicine or medication you take during the study;
- do not consume grapefruit or grapefruit juice from 7 days before first study medication intake until last intake of first study medication;
- Use acceptable methods of birth control as described above.

## **STUDY-RELATED INJURY**

In compliance with the applicable laws, the sponsor has provided for medical treatment and/or compensation in the event of damage and/or a lesion resulting from participation in the study.

In case of study-related injury or in case you need additional information concerning the study and your rights and obligations as a clinical study subject, you should contact *specify name, address and telephone of the investigator and/or contact person according local regulations*, at any time.

If you have any questions about your rights as a research patient, you should contact the Independent Ethics Committee (IEC) /Institutional Review Board (IRB) at *insert number*.

After you have consulted your study doctor or ethics committee and if they have not provided you with answers to your satisfaction, you should contact *specify name and address*.

## **COSTS**

The sponsor will provide all consultations, hospitalizations, etc. related to the study. The sponsor will provide you with the investigational medication or placebo, free of charge during the treatment period. The other TB medications will be provided locally.

Additional costs you may have as a result of your participation in this study (such as travel costs or childcare) will be reimbursed based upon evidence (e.g., receipt or ticket).

## **REMUNERATION**

You will not be compensated for participation in this study.

The study doctor/ institution will receive a reasonable financial compensation for conducting this study.

## **PART II: GENERAL INFORMATION**

### **SAMPLE HANDLING AND RETENTION**

After the study tests are completed, any of your blood plasma that is left over may be stored (with usual protection of your identity) and may be used by the sponsor for research in the future. Remaining plasma samples may be used for additional exploratory studies on study medication and breakdown product levels in the blood, as well as the effects on other drugs taken during the study. In addition, samples of TB bacteria from your sputum that have been cultured will be stored to determine the genetic constitution of TB bacteria that are resistant to TB medications. No characterization of human genetic material will be done.

The sponsor may retain such blood and sputum samples for long-term storage until filing of the study data for marketing authorization in a controlled environment.

### **INSURANCE**

In compliance with the applicable laws, the sponsor has provided for medical treatment and insurance coverage in the event of damage and/or a lesion resulting from participation in this clinical study. The corresponding compensation in event of such damage is consistent with compensation provided for by law applicable in your country.

### **PARTICIPATION AND TERMINATION**

Your participation in this study is voluntary. You may refuse to participate or you can withdraw from the study at any time. Your refusal to participate or wish to withdraw before completion of the study will not influence in any way current or potential future medical care. In the event of the withdrawal of consent to participate in the study, no new information will be added to the database, except for follow-up information on your health status until the last patient in the study has completed his/her last visit, in case you have agreed on being contacted for the collection of such follow-up data through this informed consent form. According to national provisions, you may want all previous retained identifiable samples to be destroyed to prevent further analysis.

Your participation in this study may be terminated if your study doctor decides that it is in your best interest to stop or if the sponsor decides to stop the conduct of the study. Early withdrawal can also occur in case the procedures described in this document are not properly followed or in case forbidden medication was taken.

If you leave the study prematurely, you are asked to come in for two final evaluations for your own safety, i.e., one at the time of dropout and one 5 to 7 days after dropout. During these visits you will be asked about any undesirable effects you may have encountered during the study.

Additionally, your study doctor will be asked to follow up on your health status until the last patient in the study has completed his/her last visit. Contact will be made between the site where you participated in this study and any clinics where you might receive further TB treatment, approximately every 6 months.

## CONFIDENTIALITY

Representatives of the sponsor (monitors and auditors), the IEC/IRB and/or Regulatory Authorities will be granted direct access to your original medical records for verification of clinical study procedures and/or data, without violating your confidentiality according to the laws and regulations applicable in your country. By signing this informed consent form you are authorizing such access.

All records that identify you will be kept confidential and will not be made publicly available. If the results of the study are published, your identity will remain confidential. If reference to you is made, this will only be done using code numbers. The study doctor will ensure that the link between your name and these code numbers will never be released outside the study site.

The information collected during this study will be processed electronically by the sponsor. This information shall be used within the context of this study and to conduct additional reviews of the data in order to study the safety and effectiveness of the study medication and other products and treatments, to develop a better understanding of the disease or to improve the efficiency of future clinical studies. By signing the attached informed consent form, you are authorizing such processing of data.

You have the right to request reasonable access to your personal data, via your study doctor, and to request correction of any inaccuracies regarding your personal data. However, your access to your personal data may be postponed until the end of the study if such access would interfere with the conduct of the study. Even if you withdraw your consent, certain personal data obtained within the scope of this study may still be processed by the sponsor if permitted by the applicable legislation.

Your personal data generated during this study may be passed on to the appropriate authorities, to the sponsor / manufacturer of the medicinal product under investigation and to people or companies working on behalf of the sponsor / manufacturer. The information may also be communicated to other countries of the European Economic Area (EEA) and to the USA. Some of the non-EEA countries to which the data may be transferred may offer varying levels of personal data protection. However, information that directly identifies you, such as your name and address, will not be transmitted. The sponsor may use the collected information to determine if the study medication is safe and effective, to compare the study medication to other medications, for regulatory activities and for future research activities that are unanticipated at this time. All personal data will be entered anonymously and your identity will not be revealed.

This permission to share your personal health information for this study does not have an expiration date. If you no longer want to share your personal health information, you may cancel your permission at any time by writing to the study staff and/or the study doctor at the address below:

*Insert address*

If you cancel your permission after you have started in the study, the study staff and the study doctor will stop collecting your personal health information needed for study purposes. Although they will stop collecting new information about you, they will need to use the information they have already collected to evaluate the study results. If you start the study and then cancel your permission, you will not be able to continue to participate in the study. This is because the study staff and/or the study doctor would not be able to collect the information needed to evaluate the

study medication. By signing the attached informed consent form, you are authorizing follow-up data on your health status to be collected, even after you cancel your permission to participate in this study. Such data will be asked from any clinics where you might receive further TB treatment, approximately every 6 months.

With your permission, the study doctor will inform your primary doctor about your participation in this study.

**SUBJECT'S INFORMED CONSENT****TMC207-TIDP13-C208**

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I, \_\_\_\_\_ (name in printing) have read and understood the attached Subject Information Sheet (07-Jan-2008) and I agree to take part in this study of TMC207-TiDP13 under protocol TMC207-TiDP13-C208.

I was given a copy of this signed and dated Informed Consent Form and the corresponding Subject Information Sheet. I have received an explanation of the nature, purpose, duration, and foreseeable effects of this study and of what I will be expected to do. The possible risks and benefits of this study and the alternative treatments available for my illness have been explained to me. I was given enough time and opportunity to inquire about the study and all my questions were answered to my satisfaction.

I agree to fully co-operate with the study doctor and will tell him if I suffer from any unexpected or unusual symptoms. I confirm that I have informed the study doctor of any medication/drug, of whatever nature, I have taken in the month preceding the start of the study, or I am taking or plan to take, whether prescribed or not.

I have been informed that the sponsor may use left over samples for further exploratory work.

I agree that further exploratory work will be done as specified in part II.

Yes	No *
<input type="checkbox"/>	<input type="checkbox"/>

(\* Please initial the 'yes' or 'no' box)

I have been informed that TB bacteria collected from my sputum samples will be stored and studied for the development of resistance to the medications used in this study and to other TB medications, and for the determination of the genetic constitution of resistant TB bacteria.

I agree that these specimens may be preserved for these tests.

Yes	No *
<input type="checkbox"/>	<input type="checkbox"/>

(\* Please initial the 'yes' or 'no' box)

I have been informed that a blood sample will be collected to determine HIV infection.

I agree that this analysis will be performed on my blood sample.

Yes	No *
<input type="checkbox"/>	<input type="checkbox"/>

(\* Please initial the 'yes' or 'no' box)

I have been informed that the sponsor will follow-up on my health status in case I drop out of the study prematurely.

I agree that follow-up on my health status will be done.

Yes	No *
<input type="checkbox"/>	<input type="checkbox"/>

(\* Please initial the 'yes' or 'no' box)

I have been informed that, in compliance with the applicable laws, the sponsor has provided for medical treatment and/or compensation in the event of damage and/or lesion resulting from participation in the clinical study.

I am aware that this study has been reviewed and approved by an IEC/IRB.

I am free to withdraw from the study at any time, without the need to justify my decision and without any disadvantage to my potential medical treatment.

I agree that results of this study may be passed on to the appropriate authorities and to the sponsor of the medication under investigation. My name and address will be kept secret.

I understand that representatives of the sponsor, the IEC/IRB or Regulatory Authorities may wish to inspect my medical records to verify the information collected. By signing this document I give permission for this review of my records.

I understand that no new data will be added to the database in the event of withdrawal of consent and that I may require destruction of all previously retained identifiable samples.

I am aware that the study doctor may ask to renew my consent in case of additional analyses (other than specified in part II of the subject information sheet) on retained identified samples and that I have the right to refuse.

I understand that I will be entitled to request confirmation of the existence of personal data held by the sponsor and will have the right to rectify false or inaccurate data.

I understand why electronic processing and transfer of the data obtained during this clinical study are needed, and I agree with it.

I voluntarily consent to participate in this study.

\_\_\_\_\_  
*Subject's Signature*

\_\_\_\_/\_\_\_\_/\_\_\_\_\_  
*Date (DD/MMM/YYYY)*

I confirm that I have explained the nature, purpose and foreseeable effects of the study to the subject whose name is printed above. The subject consented to participate by his/her personally dated signature.

\_\_\_\_\_  
*Informed Consent Provider's Signature*

\_\_\_\_/\_\_\_\_/\_\_\_\_\_  
*Date (DD/MMM/YYYY)*

\_\_\_\_\_  
*Informed Consent Provider's Name in printing*

**SUBJECT'S INFORMED CONSENT  
(BY LEGALLY ACCEPTABLE REPRESENTATIVE)****TMC207-TiDP13-C208**

I, \_\_\_\_\_ (name of the legally acceptable representative in printing) have read and understood the attached Subject Information Sheet (07-Jan-2008) and I agree to the participation of the following subject: \_\_\_\_\_ (name of the subject in printing) in this study of TMC207-TiDP13 under protocol TMC207-TiDP13-C208.

I was given a copy of this signed and dated Informed Consent Form and the corresponding Subject Information Sheet. The subject and myself received an explanation of the nature, purpose, duration and foreseeable effects of this study and of what the subject will be expected to do. The possible risks and benefits of this study and the alternative treatments available for the subject's illness have been explained. The subject and myself were given enough time and opportunity to inquire about this study and all questions were answered to our satisfaction.

I agree to fully cooperate with the study doctor and will tell him if the subject suffers from any unexpected or unusual symptoms. I confirm that I have informed the study doctor of any medication/drug, of whatever nature, the subject has taken in the month preceding the start of the study, or is taking or plans to take, whether prescribed or not.

We have been informed that the sponsor may use left over samples for further exploratory work.

I agree that further exploratory work will be done as specified in part II

Yes

☐

No \*

☐*(\* Please initial the 'yes' or 'no' box)*

We have been informed that TB bacteria collected from the subject's sputum samples will be stored and studied for development of resistance to medications used in this study and to other TB medications, and for the determination of the genetic constitution of resistant TB bacteria.

Yes

☐

No \*

☐

I agree that these specimens may be preserved for these tests.

*(\* Please initial the 'yes' or 'no' box)*

We have been informed that a blood sample will be collected to determine HIV infection.

Yes

☐

No \*

☐

I agree that this analysis will be performed on the subject's blood sample

*(\* Please initial the 'yes' or 'no' box)*

We have been informed that the sponsor will follow-up on the subject's health status in case he/she drops out of the study prematurely.

Yes

☐

No \*

☐

I agree that follow-up on the subject's health status will be done.

*(\* Please initial the 'yes' or 'no' box)*

We have been informed that, in compliance with the applicable laws, the sponsor has provided for medical treatment and/or compensation in the event of damage and/or lesion resulting from participation in the clinical study.

I am aware that this study has been reviewed and approved by an IEC/IRB.

I understand that the subject is free to withdraw from the study at any time, without the need to justify this decision and without any disadvantage to the potential medical treatment.

I agree that results of the study may be passed on to the appropriate authorities and to the sponsor of the medication under investigation. The subject's name and address will be kept secret.

I understand that representatives of the sponsor, IEC/IRB or Regulatory Authorities may wish to inspect the subject's medical records to verify the information collected. By signing this document I give permission for this review of the subject's medical records.

I understand that no new data will be added to the database in the event of withdrawal of consent and that the subject may require the destruction of all previously retained identifiable samples.

I am aware that the study doctor may ask to renew the consent in case of additional analyses (other than specified in part II of the subject information sheet) on retained identified samples and that the subject has the right to refuse.

I understand why electronic processing and transfer of the data obtained during this clinical study are needed, and I agree with it.

I agree to the subject's participation in this study.

\_\_\_\_\_  
*Legally Acceptable Representative's Signature*

\_\_\_\_/\_\_\_\_/\_\_\_\_\_  
*Date (DD/MMM/YYYY)*

\_\_\_\_\_  
*Legally Acceptable Representative's name in printing*

\_\_\_\_\_  
*Legally Acceptable Representative's relation to the subject*

I confirm that I have explained the nature, purpose and foreseeable effects of the study to the subject's Legally Acceptable Representative whose name is printed above, and that he/she agreed on the subject's participation in this study. The Legally Acceptable Representative confirmed the subject's participation in this study by the above dated signature.

\_\_\_\_\_  
*Informed Consent Provider's Signature*

\_\_\_\_/\_\_\_\_/\_\_\_\_\_  
*Date (DD/MMM/YYYY)*

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*Informed Consent Provider's Name in printing*