endTB Clinical Trial
Research Assent Form

Version 3.5 Version Date: 15 December 2020

Subject Identification

Protocol Title: endTB (Evaluating Newly approved Drugs for multidrug-resistant TB)

Sponsor: Médecins Sans Frontières (Doctors Without Borders) -France

Principal Investigators: Carole Mitnick, Sc.D. and Lorenzo Guglielmetti, M.D.

Site Principal Investigator: [Insert PI Name]

Research Center: [Insert Research Center Name]

Participant Name (please print): _____

Study Subject ID: _____

About this assent form

Please read this form, called research assent form, carefully. It tells you important information about this study, called endTB. A member of our research team will also talk to you about taking part in this study. People who agree to be in the study are called "participants" in this consent form. Recruitment of participants for this study has been approved by the [Research Center Ethics Committee] [and the applicable national regulatory authority].

If you have any questions about the study or about this form, please ask us. Taking part in this study is up to you. You do not have to be in the study if you do not want to. Because you are a minor (between 15 and [17] years old), we will also ask your parent(s) or someone else who takes care of you (legal guardian) to give permission for you to take part in the study, by signing a parental consent. We will need permission from both you and your parent(s) or legal guardian before you take part in this study. If you decide not to participate, nobody else can force you to participate. Your decision not to take part cannot be over-ridden by your parent(s) or legal guardian. Your parents or legal guardian may be informed of results of trial procedures [*to be adapted locally*].

If you decide to take part in this study, we will ask that you sign this form to confirm that you want to take part. We will give you a signed copy of this research assent form to keep. You can decide not to take part in this study at any time if you do not want to, even after signing this form.

If you are not able to sign the consent form, but you would like to participate, you can ask someone you know to sign for you and you can make a thumbprint to show that you understand the study and would like to take part.

Introduction

You have been asked to join a study called endTB clinical trial. Researchers want to know what combinations of drugs work better for people who have multi-drug resistant tuberculosis (MDR-TB). Drugs work differently in different people, and it is not clear what combination of drugs is best for any one person. The new combinations of drugs used in this study are called "experimental": they have been used before but we do not know how well they work together.

We are asking you to take part in this study because you are at least 15 years old and have tuberculosis that is affecting your lungs. You completed the screening process of this study and are eligible to take part. During the study, we will do some more tests to make sure that you may safely take part. 750 participants in 8 countries will participate in this study. About [number to be locally adapted] participants will take part at [Research Center Name].

Médecins Sans Frontières (Doctors Without Borders) –France is the sponsor of this study.

Why is this study being done?

Current treatment for MDR-TB has 5-9 drugs taken daily for 18 to 24 months. Treatment may be oral or include a daily shot. In some cases, depending on the characteristics of your MDR-TB, a shorter treatment duration (9 to 12 months) with an all-oral standardized treatment regimen including 7 drugs may be a possible option. This treatment may cause many mild and some serious side effects, for example: feeling sick to the stomach, throwing up, hearing loss, numbness/tingling in fingers and toes, kidney damage, mental illness/feeling sad, etc. Two new drugs (delamanid and bedaquiline) have recently become available. New treatments containing at least one of these drugs may be shorter for example, 9 months and/or simpler (without injection). Such treatments must be tested to see if they are safe and work well for people with MDR-TB. We are asking you to take part in this study to compare new experimental treatment regimens to the current treatment for MDR-TB.

How long will I take part in this study?

It will take you between 1.5 to 2 years (73 to 104 weeks) to complete this research study. During this time, we will ask you to make 26 to 30 study visits to [Research Center Name]. All study visits will take place at [Research Center Name].

What will happen in this study?

If you choose to take part in this study, we will ask you to sign this consent form before we start the study with you. If you are currently taking any medications that can't be taken with your study drugs, you may need to stop these medications before you can start taking the study drugs. Your doctor may give you new drugs instead of your current medications. This could make you feel bad. If this happens, please tell the study doctor. If your medication cannot be replaced by other treatment, or needs to be stopped for more than 2 weeks before taking study drugs, you may not be able to take part in this study.

At the beginning of the study, you will be assigned by chance (like rolling a dice) to one of 6 treatment groups described below. Most patients will get one of the experimental treatments. A smaller number will get the regular treatment for MDR-TB. We don't know exactly how many patients will get each treatment because, as we learn how the different treatments are performing, more patients will be assigned to the treatments that are helping more patients. You, your parents/legal guardian, and the study doctor cannot choose your study treatment group.

If you are assigned to an experimental treatment, you will get 4 or 5 study drugs that will be taken by mouth. You will take the study drugs for 39 weeks (9 months).

If you are assigned to the control treatment, you will get the treatment used for MDR-TB according to current practice in your country and to international guidelines from World Health Organization. You will receive medications by mouth and, if needed, by needle shots. The treatment will last for 18 to 24 months, or in some cases from 9 to 12 months.

If you are receiving an experimental regimen with linezolid, one of the drugs used for MDR-TB, we will change your linezolid dose after about 4 months of treatment or earlier if you are having important side effects that might be caused by linezolid. We are looking at two ways to lower the total dose of linezolid: in one, we reduce the daily dosage (dose still daily but lower - for example, 1 pill instead of 2 pills every day) or by giving it less often (same dose but not every day; for example, 2 pills every 2 days instead of 2 pills every day). We do not know if one way is better than the other.

If you are receiving an experimental regimen with linezolid, one of the ways of lowering the linezolid dose will be assigned to you by chance. You, your parents/legal guardian, and the study doctor cannot choose how your linezolid dose will be reduced.

For all your study drugs at all times during treatment, your study doctor will tell you how many pills of each drug you will take. Study staff will teach you how, how often and where you should take your medications and for how long. You must follow these instructions carefully and should not stop taking the study drugs without telling the study workers. A study worker *[to be adapted locally based on the setting for DOT/treatment support]* will be with you every time you take your study drugs and bring all the unused study drugs back to the [Research Center].

If you miss doses or a study visit, a study worker may call you or go to your home to check if you are well and discuss with you ways to help you keep taking your study drugs and go to your study visits. *[to be adapted locally based on the site set-up]*

With your agreement, the study doctor will inform your regular doctor or other doctors who may be treating you, of your participation in the study.

You will go to the [Research site name] for study visits until at least 73 weeks (17 months) and possibly as late as 104 weeks (24 months) after you start your study treatment. The exact time you spend in the study will depend on the overall progress of the study. You might still be on treatment at the end of the study; if so, we will help you talk to the regular TB doctors to make sure you can finish your treatment.

Visit procedures

All participants have the same visits. What happens at each visit is explained here:

Visit before starting treatment

At this visit, we will:

- Answer all your questions and get your consent to take part in the study.
- Ask about your job and schooling.
- Ask about any changes in your medical history or medicines being taken since the screening visit. The study doctor might change some of your medications and will discuss and recommend birth control methods so you can avoid pregnancy (yourself or your partner) while taking study medications.
- Ask about smoking or alcohol use.
- Perform a brief exam and ask you about TB symptoms.
- Check your vision, hearing, movement, mental health status, and ask about your daily activities.
- Collect ½ tablespoon of blood samples for laboratory testing (we might not do some of these tests if you have had these tests recently); and for a pregnancy test if you are a woman who can get pregnant. The pregnancy test might be repeated if the study medications are started a few days after the first test.
- Do an electrocardiogram to check if your heart is working normally.
- Depending on what tests you have had recently, we might:
    - Collect ½ tablespoon of blood sample for CD4 and HIV load testing if you are HIV-infected.
    - Ask you to cough up two sputum specimens if you do not already have one test result from the study laboratory to show the TB germ is resistant to rifampin and susceptible to fluoroquinolone.
    - Perform a chest X-ray.

Follow-up Visits (Week 1 to Week 73-104)

After you start taking the study drugs, you will return to [Research site name] for your follow-up visits every week during the first 3 months, then approximately every month until the end. At each visit, our study worker will schedule the next visit and write the date on your study

identification card. If you need to change a visit date, please let the study worker know as early as possible. Each visit will take about 1 ½ hours including waiting time.

If needed, your study doctor might call you/your parents for additional examinations.

Doctor's exams:

At each visit, we will:

- Ask about any changes in your medical history and any change in medicines you are taking since the last visit. The study doctor may change some of your prescriptions if you are taking medicines that can have interactions with drugs in your TB regimen.
- Perform a brief exam and ask you about TB symptoms and how you are feeling.
- Check if you are taking your study medications correctly and answer all your questions.
- If you are a woman who can get pregnant, we will ask you about your last menstrual period and use of birth control methods. The study doctor might do a pregnancy test.
- The study doctor will discuss and recommend birth control methods so you can avoid pregnancy (yourself or your partner) while taking study medications.
- If you are affected by other diseases, for example hepatitis C, we might collect the exam results that your doctor will prescribe according to clinical routine practice.

Other special exams

- An electrocardiogram will be done to check your heart at every visit until Month 12, then once again at Month 17 (25 times).
- Your vision, hearing, and movement status will be checked every 4 weeks until Month 8, then at Months 9, 10, 11, 17, and 24[1] (up to 15 times).
- Your ability to carry out your daily activities will be reviewed at Months 9, 17, and 24[1].
- Your mental health status will be checked at Months 17 and 24[1].
- A chest X-ray will be done at Months 2, 9, 17 and 24[1].

Collecting your sputum samples

- You will provide 2 sputum samples to our study workers every 2 weeks for the first month for the study, then at Month 2, and then at every visit after Month 3 until study completion.

[1] Exams after Month 17 will be conducted only if your study follow-up is still ongoing.

- You must follow our study workers' instructions on how to collect and pack your samples properly.

Collecting your blood samples

- One tablespoon of blood will be collected at the clinic to check for possible side effects approximately every 4 weeks until Month 11.
- 1/2 tablespoon of blood will be collected for CD4 and HIV viral load at Months 6, 11 and 17 if you are HIV-infected.
- 1/2 tablespoon of blood will be collected to check blood sugar at Months 6, 11, and 17 if you have abnormal blood sugar level at screening/baseline visit.

Stopping or withdrawing from the study early

If you start the study and decide you want to stop, you should tell us. We will make sure that you stop the study safely. We will ask you to make a termination visit. At this visit, we will:

- Ask about changes in your medical history and in medicines you are taking since the last visit.
- Perform a brief body exam and ask about TB-related symptoms and how you are feeling.
- Check your vision, hearing, movement, functional and mental health status.
- Obtain 2 tablespoons of blood for laboratory testing.
- If you are a woman who can get pregnant, we will ask you about your last menstrual period and use of birth control methods. The study doctor might prescribe you a pregnancy test.
- Collect 2 sputum specimens.
- Do an electrocardiogram to check your heart.
- Do a chest X-ray (unless recent results are available).

We will talk to you about follow-up care, if needed.

Also, the study doctor might decide to take you out of the study before you finish it. This might happen because:

- You are a female participant and become pregnant.
- The study doctor thinks it is best for you to stop taking the study drug.
- You can't make the required study visits.

- We stop doing the study for any reason.

If this happens, the study doctor will explain why you need to stop taking part in the study. We will invite you to come in for the termination visit as described above. We will also help arrange other care for you, if needed.

If your study termination occurs before Week 39 (Month 9) or before Week 73 (Month 17), we will ask to come back for follow-up visits at the time of Week 39 and Week 73.

At this/these visit(s), we will:

- Ask about changes in your medical history and in medicines you are taking since the last visit.
- Perform a brief body exam and ask about TB-related symptoms and how you are feeling.
- Collect 2 sputum specimens.
- Unless recent results are available, we will:
    - Do a chest X-ray,
    - Collect up to 1/2 tablespoon of blood sample to measure your sugar level if it was abnormal when you started the study,
    - Collect up to 1/2 tablespoon of blood sample for CD4 and HIV viral load testing if you are HIV-infected.

The termination visit or the Week 73 follow-up visit will be your last visit for the study.

What will happen to me after the end of the study?

Once you complete your participation in the study, any follow-up of your disease will be done by your regular doctor.

If you complete the study with side effect(s) that are not yet resolved, your study doctor may contact you until the side effect goes away or is stable.

If you decide to leave or are taken out of the study early, and you still have ongoing side effect(s) at this time, your study doctor may contact you until the side effect goes away or is stable. You might also be contacted by your study doctor if you experience a new side effect.

Please let your study doctor know if you do not want to be contacted even for updates on the ongoing side effects. You do not have to give any information that you don't want to.

Managing your Samples and Health Information in the Study

We will label all your samples and health information with a code instead of your name to keep all your information private. The key to the code connects your name to your samples and health information. The study doctor will keep the key to the code in a password-protected computer and/or locked file.

The samples and bacteria isolates obtained from your sputum samples might be tested for drug resistance confirmation and further analyses on the bacteria in a specialized laboratory in Belgium.

Storing Isolates (strains) and Health Information for Future Research

We would like to store some of the bacteria isolates (TB bug) and health information for future research related to TB, which will be collected during this study. All your health information and bacteria isolates will be handled in a way to keep all your information private. Any use of stored bacteria isolates and your health information for other research inside your country or in other countries will be approved by the ethics committee of your country.

This future research is independent from your participation in the endTB study and your decision to participate in the future research will not affect your participation in the study.The bacteria isolates found in your sputum samples and your health information may be stored for up to 20 years in a special place (bank or repository) created to safely store them. The stored isolates and your health information will be used only to help future research in TB and to improve diagnosis (including resistance testing) and treatment of TB. During your participation in the endTB study, and the following storage period of 20 years after completion of the study, you can contact your study doctor or the email address endTB.clinicaltrial@paris.msf.org to request any information regarding the use, storage and location of your health information and bacteria isolates.

Do you agree that your health information and bacteria isolates found in your sputum samples may be stored for 20 years and used only for future TB research? You are free to refuse such storage and further use for TB research of your health information and bacteria isolates and you will still be able to take part in the study.

☐ Yes ☐ No [Initials or signature, to be adapted locally]_____

You have the right to change your mind, and to later want your health information and/or bacteria isolates destroyed. In that case, during your participation in the endTB study, and the following storage period of 20 years after completion of the study, you can contact your study doctor or the email address endTB.clinicaltrial@paris.msf.org to request any information regarding the use, storage and location of your health information and bacteria isolates and/or their destruction.

Will anything bad happen to me from being in this study?

Risks of Taking Study Drugs:

You will take a combination of MDR-TB drugs when you are on this study, whether you get an experimental treatment or the control treatment. The drugs used in the control are the nation's standard MDR-TB medications, according to international guidelines from World Health Organization. Experimental treatments will use together 4 or 5 of the following drugs: bedaquiline, delamanid, clofazimine, linezolid, moxifloxacin, levofloxacin, and pyrazinamide.

Medications for MDR-TB have different side effects. We do not know which of the combinations is the easiest to take. Your doctor will tell you the most common side effects that you may have while taking study treatment and you will be given a document entitled "participant information leaflet " that summarizes the main side effects. There may be other risks of the study drugs that are not known yet. You will be closely followed through clinical, laboratory and other examinations (hearing test, heart test) in order to detect and treat promptly possible side effects. And, your doctor will explain more in detail when you should get in touch with him/her.

As with any drug, an **allergic reaction** can happen. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing.

Some of the drugs may have an effect on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant. It is possible that this effect is unknown and may be harmful. Because of these unknown risks, women cannot start this study if they are:

- known to be pregnant;
- trying to become pregnant;
- unwilling or unable to stop breastfeeding an infant.

If you are female and have had any well-documented method of surgical sterilization, you will not need to have a pregnancy test and are not considered able to become pregnant. Methods of surgical sterilization include having had a hysterectomy (removal of the uterus), bilateral oophorectomy (removal of both ovaries), a tubal ligation (having your tubes tied), and transvaginal occlusion (plugging the opening of the tubes with a coil). All other women must have a negative pregnancy test before starting the study drugs.

Regardless of your sex, if you are sexually active and able to become pregnant or father a child, you must agree to abstain from sex (have no sex) or use acceptable birth control (methods listed below) while taking study drugs. Your doctor may also discuss with you the use of birth control after you finish taking your study drugs. Acceptable birth control may be achieved by using a single "highly effective" method or by using a combination of other methods.

Acceptable "highly effective" single birth control methods for use in this study are:

- Hormonal method: birth control pills, patches, injections, vaginal rings, or implants.
- Intrauterine device (IUD).

An acceptable combination birth control method for use in this study is:

Condom (male or female)[2] used with or without a spermicide[3] AND one of the following used with a spermicide[3]: diaphragm, cap, or sponge;

These options are also summarized in the table below:

Method	**Use alone or in combination.**[2,4]
Hormonal method: birth control pills, patches, injections, vaginal rings, or implants.	Highly effective alone; needs no combination.
Intrauterine device (IUD).	Highly effective alone; needs no combination.
Condom (male) used with or without a spermicide.[3,2]	To be used in combination with one of the following: diaphragm, cap, or sponge AND spermicide.[3]
Condom (female) used with or without a spermicide.[2,3]	To be used in combination with one of the following: diaphragm, cap, or sponge AND spermicide.[3]
Diaphragm, cap, or sponge used with a spermicide.[3]	To be used in combination with male or female condom[2], with or without spermicide.

For female participants, if you miss a period, or think you might be pregnant during the study, you must tell the study doctor immediately. *[to be adapted locally]* If you become pregnant, your treatment might be changed and you might stop taking part in the study. The study doctor will ask for permission to collect information about the outcome of your pregnancy and the condition of your newborn.

For male participants, if your female partner becomes pregnant, we would like to follow the outcome of the pregnancy. You should let us know immediately if your partner becomes pregnant. You will not have to stop taking the study drugs or stop taking part in the study if your partner becomes pregnant.

[2] Male and female condom should not be used together.
[3] Spermicide: a foam cream or gel that kills sperm.
[4] Withdrawal (coitus interruptus) and/or periodic abstinence during fertile times are unacceptable on their own but may be used in combination with any highly effective method or acceptable combination.

Risks of Taking the Study Drugs with Other Medications

Some drugs are not safe to be taken together with the study medications, or may not work when taken with the study medications. Please inform and consult your study doctor if, at any time of the study, you are prescribed or begin using any other medications.

For your safety during this study, call your study doctor BEFORE you take any:

- new medications prescribed by another doctor;
- other medications sold over-the-counter without a prescription;
- dietary or herbal supplements.

Risks of Blood Draws

You may have a bruise (a black and blue mark) or pain where we take the blood samples. There is also a small risk of infection, light-headedness, and/or fainting.

What are the possible benefits from being in this study?

By participating in the study, you may receive a shorter all-oral treatment compared to the current treatment recommended for MDR TB. There is no guarantee that any of these shorter treatments will work better than the current [18 to 24 – *to be adapted if short regimen available*] months standard treatment. During this study, we will learn more about the treatments and use the information to assign more patients to treatments that are helping other patients. When you receive the study drugs, we expect your medical condition/symptoms to improve. It is also possible that the TB bacteria are or become too strong to be killed by the study drugs you receive. If that happens, your study doctor will change your treatment. You will have more tests that allow the doctors to know what kind of anti-TB drugs they should use. The study doctors can also take care of your side effects sooner and better by having those extra tests. However, it may be harder for you to be cured if very few drugs work against your TB bacteria.

You will receive greater treatment support from the study team throughout the study than during regular MDR-TB treatment. Others with MDR-TB may benefit in the future from what we learn in this study**.**

What other treatments or procedures are available for my condition?

You do not have to take part in this study to be treated for MDR-TB. Other treatment is available to treat MDR-TB in your country through [local TB care provider/entity]. This treatment is similar to that in the control arm in the study. It is a combination treatment with several drugs. Your doctor will recommend treatment for either 18-24 months or for 9-12 months. In some cases, it will include a daily shot of about 6 months. Talk with the study doctor if you have questions about the other treatment.

Can I still receive TB treatment if I do not take part in this study?

Yes. Taking part in this study is up to you. You can decide not to take part. You will receive treatment through [local TB care provider/entity] if you do not take part in this study. There will be no penalty, and you will not lose any benefits you receive now or have a right to receive. The treatment outside the study is also free of charge.

What should I do if I want to stop taking part in the study?

If you take part in this study and decide you want to stop, you should tell us. We will make sure that you stop the study safely.

Also, it is possible that we will have to ask you to leave the study before you finish it. If this happens, we will tell you why.

We will tell you if we learn any new information that could make you change your mind and choose to leave the study.

If any of these happens, we will talk to you about follow-up care, if needed, and you will be encouraged to come back at least for one additional visit ("termination visit").

Information collected during your participation may be used to help answer study questions. When you leave the study, your health information, and information obtained from sputum samples and bacteria isolates previously collected will still be used and stored for 20 years for the study and future TB research. However, if you prefer this information is not used and that it is destroyed, you can contact your study doctor or the email address endTB.clinicaltrial@paris.msf.org.

Will I be paid to take part in this study?

You will not be paid to take part in this study. We will pay the transportation costs for study visits. You will also receive [local arrangement for monthly food supplements] when you take part in the study. In sum, you will be reimbursed [local currency]_____ for transportation for the baseline visit, [local currency]_____ for each follow-up visit, for any unscheduled visits, and [local currency]_____ for your final visit.

What will I have to pay for if I take part in this study?

You will not have to pay in order to take part in this study. You also will not have to pay for the study drugs, or for any study-related procedures and visits.

What happens if I am injured as a result of taking part in this study?

The sponsor has made insurance arrangements to pay for an injury you suffer due to your participation in the study.

If you suffer physical injury from this study please inform your doctor and seek medical attention right away, _____ will ensure that you receive appropriate medical treatment.

[Research site name] will not pay to treat a medical condition or disease you had before joining this study or expenses for injury, treatment, or hospitalization you may require that are not the result of your participation in the study.

In an emergency, the study sponsor has made plans to pay for your visit to see a specialist, the related treatment, and/or your stay in the hospital. For non-urgent situations, the sponsor may pay for your visit to see a specialist. The study team will review your situation and decide whether the sponsor will pay for the resulting treatment if your condition is not the result of your participation in the study.

Who can I speak to if I have questions, concerns or complaints?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

[PI Name and title] is the person in charge of this study. You can call him/her at [PI telephone number]. You can also call [Clinical Investigator] at [CI number] with questions about this study. If you have questions about the scheduling of appointments or study visits, call [Study Coordinator] at [SC number].

For medical emergencies outside business hours, please contact **[Must include 24/7 phone number of licensed site physician investigator here].**

If you want to speak with someone not directly involved in this study, please contact the [Research Center IRB] office. You can call them at [Research Center IRB number].

If I take part in this study, how will you protect my privacy?

We are careful to protect the identity of the people in this study to the extent permitted by law. We also keep your information secure and confidential. Electronic study information will be password-protected, and paper files will be stored in a locked office at [Research site]. Your study records will be kept at the clinic/hospital for XX years [*to be adapted locally*] following the completion of the study. If needed to monitor the study quality, your study information and other information about you may be looked at by institutions responsible for quality and privacy such as the sponsor, Ethics Committee and Competent Authorities.

For the study, we will store some non-medical information about you, such as your date of birth and city of residence. You can ask us to access, modify, complete, update, or delete this information. If you have any complaints about the protection of your data, you could contact your local/national Data Protection Authority [*Name and contact to be adapted locally*].

The information collected for this study will be used for the following purposes:

- For the purpose of this study. The sponsor, the study doctor, or other doctors involved in the study may publish reports or articles on the study or present the study findings to scientific groups. After the study is completed you may see your records, and you may be told the results of the study.

- Secondary use for TB research; your coded information may be used and shared with other institutions only for the purpose of further TB research during and after completion of the study and notably with the World Health Organization.

In all cases your identity will never be disclosed.

Your coded information may be sent electronically to other researchers or institutions, If sent, it will be encrypted (scrambled so it cannot be read by people who should not see it).

We guarantee that, when we send your coded information, it will be protected according to European Economic Area standards.

Subject Identification

Informed Assent and Authorization

You completed the screening process for this study and are eligible to take part, or you completed the screening process for another study (endTB-Q) and were found to be eligible for this study (endTB). In the second case, you agree that your data and personal information collected during endTB-Q screening will be used for the endTB study.

Your signature on this document means the following:

I have read this assent form. This study has been explained to me, including risks and possible benefits, other possible treatments or procedures, and other important things about the study. I have had the opportunity to ask questions. I understand the information given to me. I recognize that my participation is voluntary and that I can refuse or end my participation at any time, without any loss of benefits that I would otherwise have. I recognize that by signing this document, I do not lose any of my legal rights as a participant. I will receive a complete, signed, dated copy of this research assent form.

By signing below, I agree to take part in this study.

Signature of Participant

_____ _____

Signature or thumbprint of participant | Date (DD/MMM/YYYY) and Time

_____

Name of participant, printed in capital letters

Witness (if applicable):

_____ _____

Signature of witness | Date (DD/MMM/YYYY) and Time

_____

Name of witness, printed in capital letters

Subject Identification

Study representative who obtained informed assent:

I have explained this study to the participant and have answered all of his/her questions. He/she understands the information described in this document and accepts voluntary participation in the study.

_____ _____

Signature of study representative Date (DD/MMM/YYYY) and Time

_____

Name of study representative, printed in capital letters

Schedule of Visits

Visit	Consent	Doctors' Exam	Nurses' Interview	Blood Collection	Sputum Collection	ECG	Chest X-ray
Baseline	✓	✓	✓	(✓)	(✓)	✓	(✓)
Week 1		✓	✓			✓	
Week 2		✓	✓		✓	✓	
Week 3		✓	✓			✓	
Month 1		✓	✓	✓	✓	✓	
Week 5, 6, 7		✓	✓			✓	
Month 2		✓	✓	✓	✓	✓	✓
Week 9, 10, 11		✓	✓			✓	
Month 3, 4, 5, 6, 6.5, 7, 8		✓	✓	✓	✓	✓	
Month 9		✓	✓	✓	✓	✓	✓
Month 10, 11		✓	✓	✓	✓	✓	
Month 12		✓	✓		✓	✓	
Month 13.5, 15		✓	✓		✓		
Month 17		✓	✓	(✓)	✓	✓	✓
Month 19, 20, 22[1]		✓	✓		✓		
Month 24[1]		✓	✓	✓	✓		✓

endTB Clinical Trial
Research Parental Consent Form

Version 3.5 Version Date: 15 December 2020

Subject Identification

Protocol Title: endTB (Evaluating Newly approved Drugs for multidrug-resistant TB)

Sponsor: Médecins Sans Frontières (Doctors Without Borders) - France

Principal Investigators: Carole Mitnick, Sc.D. and Lorenzo Guglielmetti, M.D.

Site Principal Investigator: [Insert PI Name]

Research Center: [Insert Research Center Name]

Participant Name (please print): _____

Study Subject ID: _____

About this consent form

Please read this form, called research parental consent form, carefully. It tells you important information about this study, called endTB. A member of our research team will also talk to you and your child about taking part in this study. People who agree to be in the study are called "participants" in this consent form. Recruitment of participants for this study has been approved by the [Research Center Ethics Committee] [and the applicable national regulatory authority].

You have the option of having your child join a study. Because your child is a minor (between 15 and [17] years old), we will need both permissions from you and your child before having your child taking part of this study. If you have any questions about the research or about this form, please ask us. Taking part in this study is up to you and your child. Your child does not have to be in the study if you or your child does not want to.

If you decide to let your child take part in this study, we will ask that you sign this form to confirm that you want him/her to take part. We will give you a signed copy of this research parental consent form to keep. We will also give your child the same information and ask for his/her permission to take part in the study, by signing an assent form. Your child will be free to refuse to take part in the study even after you give permission for him/her to participate. His/her decision not to take part cannot be over-ridden by your decision. Your child can also decide to stop taking part in this study at any time if you or your child does not want to, even after signing this form.

If you are not able to sign the consent form, but you would like your child to participate, you can ask someone you know to sign for you and you can make a thumbprint to show that you understand the study and would like your child to take part.

Introduction

Your child has been asked to join a study called endTB clinical trial. Researchers want to know what combinations of drugs work better for people who have multi-drug resistant tuberculosis (MDR-TB). Drugs work differently in different people, and it is not clear what combination of drugs is best for any one person. The new combinations of drugs used in this study are called "experimental"; they have been used before but we do not know how well they work together.

We are asking your child to take part in this study because he/she is at least 15 years old and has tuberculosis that is affecting his/her lungs. Your child completed the screening process of this study and is eligible to take part. During the study, we will do some more tests to make sure that your child may safely take part. 750 participants in 8 countries will participate in this study. About [number to be locally adapted] participants will take part at [Research Center Name].

Médecins Sans Frontières (Doctors Without Borders) –France is the sponsor of this study.

Why is this study being done?

Current treatment for MDR-TB has 5-9 drugs taken daily for 18 to 24 months. Treatment may be oral or include a daily shot. In some cases, depending on the characteristics of your MDR-TB, a shorter treatment duration (9 to 12 months) with an all-oral standardized treatment regimen including 7 drugs may be a possible option. This treatment may cause many mild and some serious side effects, for example: feeling sick to the stomach, throwing up, hearing loss, numbness/tingling in fingers and toes, kidney damage, mental illness/feeling sad, etc. Two new drugs (delamanid and bedaquiline) have recently become available. New treatments containing at least one of these drugs may be shorter for example, 9 months and/or simpler (without injection). Such treatments must be tested to see if they are safe and work well for people with MDR-TB. We are asking you to take part in this study to compare new experimental treatment regimens to the current treatment for MDR-TB.

How long will my child take part in this study?

It will take your child between 1.5 to 2 years (73 to 104 weeks) to complete this study. During this time, we will ask you and your child to make 26 to 30 study visits to [Research Center Name]. All study visits will take place at [Research Center Name].

What will happen in this study?

If your child chooses to take part in this study, we will ask your child to sign the assent form and you to sign this parental consent form before we start the study with you. If your child is currently taking any medications that can't be taken with your study drugs, s/he may need to stop these medications before starting the study drugs. Your child's doctor may prescribe new drugs instead of your child's current medications. This could make your child feel bad. If this happens,

please tell the study doctor. If your child's medications cannot be replaced by other treatment or need to be stopped for more than 2 weeks before taking study drugs your child may not be able to take part in this study.

At the beginning of the study, patients will be assigned by chance (like rolling a dice) to one of 6 treatment groups described below. Most patients will get one of the experimental treatments. A smaller number will get the regular treatment for MDR-TB. We don't know exactly how many patients will get each treatment because, as we learn how the different treatments are performing, more patients will be assigned to the treatments that are helping more patients. You, your child and the study doctor cannot choose your child's study treatment group.

If your child is assigned to an experimental treatment, he/she will get 4 or 5 study drugs that will be taken by mouth. Your child will take the study drugs for 39 weeks (9 months).

If your child is assigned to the control treatment, he/she will get the treatment used for MDR-TB according to current practice in your country and to international guidelines from World Health Organization. Your child will receive medications by mouth and, if needed, by needle shots. The treatment will last for 18 to 24 months, or in some cases from 9 to 12 months.

If your child is receiving an experimental regimen with linezolid, one of the drugs used for MDR-TB, we will change his/her linezolid dose after about 4 months of treatment or earlier if s/he is having important side effects that might be caused by linezolid. We are looking at two ways to lower the total dose of linezolid: in one, we reduce the daily dosage (dose still daily but lower - for example, 1 pill instead of 2 pills every day) or by giving it less often (same dose but not every day; for example, 2 pills every 2 days instead of 2 pills every day). We do not know if one way is better than the other.

If your child is receiving an experimental regimen with linezolid, one of the ways of lowering the linezolid dose will be assigned to him/her by chance. You, your child and the study doctor cannot choose how linezolid dose will be reduced.

For all your child's study drugs at all times during treatment, your child's study doctor will tell you how many pills of each drug he/she will take. Study staff will teach you and your child how, how often and where your child should take his/her medications and for how long. Your child must follow these instructions carefully and should not stop taking the study drugs without telling the study workers. A study worker *[to be adapted locally based on the setting for DOT/treatment support]* will be with your child every time he/she takes his/her study drugs and bring all the unused study drugs back to the [Research Center].

If your child misses doses or a study visit, a study worker may call you or go to your home to check if your child is well and, if needed, discuss ways to help your child keep taking his/her study drugs and go to his/her study visits.*[to be adapted locally based on the site set-up]*

With your agreement, the study doctor will inform your child's regular doctor or other doctors who may be treating him/her, of his/her participation in the study.

You and your child will go to the [Research site name] for study visits until at least 73 weeks (17 months) and possibly as late as 104 weeks (24 months) after your child start his/her study treatment. The exact time your child will spend in the study will depend on the overall progress of the study. Your child might still be on treatment at the end of the study; if so, we will help you and your child talk to the regular TB doctors to make sure your child can finish his/her treatment.

Visit procedures

All participants have the same visits. What happens at each **visit** is explained here:

Visit before starting treatment

At this visit, we will:

- Answer all your and your child's questions and get your consent and your child's assent to take part in the study.
- Ask about your child's job and schooling.
- Ask about any changes in your child's medical history or medicines being taken since the screening visit. The study doctor might change some of your child's medications and will discuss and recommend birth control methods so your child can avoid pregnancy (himself/herself or his/her partner) while taking study medications.
- Ask about your child's smoking or alcohol use.
- Perform a brief exam and ask about TB symptoms.
- Check your child's vision, hearing, movement, mental health status, and ask about his/her daily activities.
- Collect ½ tablespoon of blood for laboratory testing (we might not do some of these s/he has had these tests recently); and for a pregnancy test if your child is a woman who can get pregnant. The pregnancy test might be repeated if the study medications are started a few days after the first test.
- Do an electrocardiogram to check if his/her heart is working normally;
- Depending on what tests your child has had recently, we might:
    - Collect ½ tablespoon of blood for CD4 and HIV viral load testing if your child is HIV-infected.
    - Ask your child to cough up two sputum specimens if he/she does not already have one test result from the study laboratory to show the TB germ is resistant to rifampin and susceptible to fluoroquinolone.
    - Perform a chest X-ray.

Follow-up Visits (Week 1 to Week 73-104)

After your child starts taking the study drugs, he/she will return to [Research site name] for the follow-up visits every week during the first 3 months, then approximately every month until the end. At each visit, our study worker will schedule the next visit and write the date on your child's study identification card. If your child needs to change a visit date, please let the study worker know as early as possible. Each visit will take about 1 ½ hours including waiting time.

If needed, your child's study doctor might call you/your child for additional examinations.

Doctor's exams:

At each visit, we will:

- Ask about any changes in your child's medical history and any change in medicines he/she is taking since the last visit. The study doctor may change some of your child's prescriptions if s/he is taking medicines that can have interactions with drugs in his/her TB regimen.
- Perform a brief exam and ask your child about TB symptoms and how he/she is feeling.
- Check if your child is taking his/her study medications correctly and answer all your questions.
- If your child is a woman who can get pregnant, we will ask her about her last menstrual period and use of birth control methods. The study doctor might do a pregnancy test.
- The study doctor will discuss and recommend birth control methods so she can avoid pregnancy (herself or her partner) while taking study medications.
- If s/he is affected by other diseases, for example hepatitis C, we might collect the exam results that his/her doctor will prescribe according to clinical routine practice.

Other special exams

- Electrocardiograms will be done to check your child's heart at every visit until Month 12, then once again at Month 17 (25 times).
- Your child's vision, hearing, and movement status will be checked every 4 weeks until Month 8, then at Months 9, 10, 11, 17, and 24[1] (up to 15 times).
- Your child's ability to carry out his/her daily activities will be reviewed at Months 9, 17, and 24[1].

[1] Exams after Month 17 will be conducted only if your child study follow-up is still ongoing.

- Your child's mental health status will be checked at Months 17 and 24[1].
- A chest X-ray will be done at Months 2, 9, 17 and 24[1].

Collecting your child's sputum samples

- Your child will provide 2 sputum samples to our study workers every 2 weeks for the first month for the study, then at Month 2, and then at every visit after Month 3 until study completion.
- Your child must follow our study workers' instructions on how to collect and pack his/her samples properly.

Collecting your child's blood samples

- One tablespoon of blood will be collected at the clinic to check for possible side effects approximately every 4 weeks until Month 11.
- 1/2 tablespoon of blood will be collected for CD4 and HIV viral load at Months 6, 11 and 17 if your child is HIV-infected.
- 1/2 tablespoon of blood will be collected to check blood sugar at Months 6, 11, and 17 if your child has abnormal blood sugar level at screening/baseline visit.

Stopping or withdrawing from the study early

If your child starts the study and decides he/she wants to stop, you should tell us. We will make sure that your child stops the study safely. We will ask your child to make a termination visit. At this visit, we will:

- Ask your child about changes in his/her medical history and in medicines he/she is taking since the last visit.
- Perform a brief body exam and ask your child about TB-related symptoms and how he/she is feeling.
- Check your child's vision, hearing, movement, functional and mental health status.
- Obtain 2 tablespoons of blood for laboratory testing.
- If your child is a woman who can get pregnant we will ask her about her last menstrual period and use of birth control methods. The study doctor might prescribe her a pregnancy test.
- Collect 2 sputum specimens.
- Do an electrocardiogram to check your child's heart.
- Do a chest X-ray (unless recent results are available).

We will talk to you and your child about follow-up care, if needed.

Also, the study doctor might decide to take your child out of the study before he/she finishes it. This might happen because:

- Your child is a female participant and become pregnant.
- The study doctor thinks it is best for your child to stop taking the study drug.
- Your child can't make the required study visits.
- We stop doing the study for any reason.

If this happens, the study doctor will explain why your child needs to stop taking part in the study. We will invite you and your child to come in for the termination visit as described above. We will also help arrange other care for your child, if needed.

If your child's study termination occurs before Week 39 (Month 9) or before Week 73 (Month 17), we will ask you and your child to come back for follow-up visits at the time of Week 39 and Week 73.

At this/these visit(s), we will:

- Ask about changes in your child's medical history and in medicines s/he is taking since the last visit.
- Perform a brief body exam and ask about TB-related symptoms and how you s/he is feeling.
- Collect 2 sputum specimens.
- Unless recent results are available, we will:
    - Do a chest X-ray,
    - Collect up to 1/2 tablespoon of blood sample to measure his/her sugar level if it was abnormal when your child started the study,
    - Collect up to 1/2 tablespoon of blood sample for CD4 and HIV viral load testing if your child is HIV-infected.

The termination visit or the Week 73 follow-up visit will be his/her last visit for the study.

What will happen to your child after the end of the study?

Once your child completes his/her participation in the study, any follow-up of his/her disease will be done by his/her regular doctor.

If your child completes the study with side effect(s) that are not yet resolved, the study doctor may contact you and your child until the side effect goes away or is stable.

If you or your child decide to leave the study or if your child is taken out of the study early, and s/he still has ongoing side effect(s) at this time, your study doctor may contact you and your child until the side effect goes away or is stable. You might also be contacted by your study doctor if your child experiences a new side effect.

Please let your study doctor know if you do not want you and your child to be contacted even for updates on the ongoing side effects. You and your child do not have to give any information that you don't want to.

Managing Samples and Health Information in the Study

We will label all your child's samples and health information with a code instead of his/her name to keep all your child's information private. The key to the code connects your child's name to his/her samples and health information.

The bacteria isolates from your sputum samples might be tested for drug resistance confirmation and further analyses on the bacteria in a specialized laboratory in Belgium.

Storing Isolates (strains) and Health Information for Future Research

We would like to store some of the bacteria isolates (TB bug) and your child's health information for future research related to TB, which will be collected during this study. All your child's health information and bacteria isolates will be handled in a way to keep all his/her information private. Any use of stored bacteria isolates and your child's health information for other research inside your country or in other countries will be approved by the ethics committee of your country.

This future research is independent from your child's participation in the endTB- study and your decision to let your child participate in the future research will not affect your child's participation in the study.

The bacteria isolates found in his/her sputum samples and his/her health information may be stored for up to 20 years in a special place (bank or repository) created to safely store them. The stored isolates and your child's health information will be used only to help future research in TB and to improve diagnosis (including resistance testing) and treatment of TB. During your child's participation in the endTB study, and the following storage period of 20 years after completion of the study, you can contact the study doctor or the email address endTB.clinicaltrial@paris.msf.org to request any information regarding the use, storage and location of your child's health information and bacteria isolates.

Do you agree that your child's health information and the bacteria isolates collected from his/her sputum samples may be stored for 20 years and used only for future TB research? You are free to

refuse such storage and further use for TB research of your child's health information and bacteria isolates and still have your child taking part in the study.

☐ Yes ☐ No [Initials or signature, to be adapted locally]_____

You and your child have the right to change your mind and to later want your child's health information and/or bacteria isolates destroyed. In that case, during your child participation in the endTB study, and the following storage period of 20 years after completion of the study, you can contact your child's study doctor or the email address endTB.clinicaltrial@paris.msf.org to request any information regarding the use, storage and location of your child's health information and bacteria isolates and/or their destruction.

Will anything bad happen to my child from being in this study?

Risks of Taking Study Drugs:

Your child will take a combination of MDR-TB drugs when he/she is on this study, whether your child gets an experimental treatment or the control treatment. The drugs used in the control are the nation's standard MDR-TB medications, according to international guidelines from World Health Organization. Experimental treatments will use together 4 or 5 of the following drugs: bedaquiline, delamanid, clofazimine, linezolid, moxifloxacin, levofloxacin, and pyrazinamide.

Medications for MDR-TB have different side effects. We do not know which of the combinations is the easiest to take. Your child's doctor will tell you and your child the most common side effects that he/she may have while taking study treatment and you will be given a document entitled "participant information leaflet" that summarizes the main side effects. There may be other risks of the study drugs that are not known yet. Your child will be closely followed through clinical, laboratory and other examinations (hearing test, heart test) in order to detect and treat promptly possible side effects. Your child's doctor will explain more in detail when you or your child should get in touch with him/her.

As with any drug, an **allergic reaction** can happen. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing.

Some of the drugs may have an effect on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant. It is possible that this effect is unknown and may be harmful. Because of these unknown risks, women cannot start this study if they are:

- known to be pregnant;
- trying to become pregnant;
- unwilling or unable to stop breastfeeding an infant.

If your child is female and has had any well-documented method of surgical sterilization, she will not need to have a pregnancy test and is not considered able to become pregnant. Methods of surgical sterilization include having had a hysterectomy (removal of the uterus), bilateral oophorectomy (removal of both ovaries), a tubal ligation (having your tubes tied), and transvaginal occlusion (plugging the opening of the tubes with a coil). All other women must have a negative pregnancy test before starting the study drugs.

Regardless of your child's sex, if he/she is sexually active and able to become pregnant or father a child, your child must agree to abstain from sex (have no sex) or use acceptable birth control (methods listed below) while taking study drugs. Your doctor may also discuss with you and your child the use of birth control after your child finishes taking his/her study drugs. Acceptable birth control may be achieved by using a single "highly effective" method or by using a combination of other methods.

Acceptable "highly effective" single birth control methods for use in this study are:

- Hormonal methods: birth control pills, patches, injections, vaginal rings, or implants.
- Intrauterine device (IUD).

An acceptable combination birth control method for use in this study is:

Condom (male or female)[2] used with or without a spermicide[3] AND one of the following used with a spermicide[3]: diaphragm, cap, or sponge;

These options are also summarized in the table below:

Method	**Use alone or in combination.[2,4]**
Hormonal method: birth control pills, patches, injections, vaginal rings, or implants.	Highly effective alone; needs no combination.
Intrauterine device (IUD).	Highly effective alone; needs no combination.
Condom (male) used with or without a spermicide.[3,2]	To be used in combination with one of the following: diaphragm, cap, or sponge AND spermicide.[3]
Condom (female) used with or without a spermicide.[2,3]	To be used in combination with one of the following: diaphragm, cap, or sponge AND spermicide.[3]

[2] Male and female condom should not be used together.
[3] Spermicide: a foam cream or gel that kills sperm.
[4] Withdrawal (coitus interruptus) and/or periodic abstinence during fertile times are unacceptable on their own but may be used in combination with any highly effective method or acceptable combination.

Diaphragm, cap, or sponge used with a spermicide.3	To be used in combination with male or female condom[2], with or without spermicide.

For female participants, if your child misses a period or thinks she might be pregnant during the study, you must tell the study doctor immediately. *[to be adapted locally]* If your child becomes pregnant, her treatment might be changed and she might stop taking part in the study. The study doctor will ask for permission to collect information about the outcome of her pregnancy and the condition of her newborn.

For male participants, if a female partner becomes pregnant, we would like to follow the outcome of the pregnancy. You or your child should let us know immediately if your child's partner becomes pregnant. Your child will not have to stop taking the study drugs or stop taking part in the study if his partner becomes pregnant.

In both cases, the study doctor will ask for permission to collect information about the outcome of the pregnancy and the condition of the newborn.

Risks of Taking the Study Drugs with Other Medications

Some drugs are not safe to be taken together with the study medications, or may not work when taken with the study medications. Please inform and consult your study doctor if, at any time of the study, your child is prescribed or begin using any other medications.

For your child's safety during this study, call your study doctor BEFORE your child takes any:

- new medications prescribed by another doctor;
- other medications sold over-the-counter without a prescription;
- dietary or herbal supplements.

Risks of Blood Draws

Your child may have a bruise (a black and blue mark) or pain where we take the blood samples. There is also a small risk of infection, light-headedness, and/or fainting.

What are the possible benefits from being in this study?

By participating in the study, your child may receive a shorter all-oral treatment compared to the current treatment recommended for MDR-TB. There is no guarantee that any of these shorter treatments will work better than the current [18 to 24 – *to be adapted if short regimen available*] months standard treatment. During this study, we will learn more about the treatments and use the information to assign more patients to treatments that are helping other patients. When your child receives the study drugs, we expect his/her medical condition/symptoms to improve. It is also possible that the TB bacteria are or become too strong to be killed by the study drugs he/she receives. If that happens, the study doctor will change your child's treatment. Your child will

have more tests that allow the doctors to know what kind of anti-TB drugs cannot fight the TB bacteria in his/her body, so the doctors will know if your child need any special treatment. The study doctors can also take care of your child's side effects sooner and better by having those extra tests. However, it may be harder for your child to be cured if very few drugs work against his/her TB bacteria.

Your child will receive greater treatment support from the study team throughout the study than during regular MDR-TB treatment. Others with MDR-TB may benefit in the future from what we learn in this study**.**

What other treatments or procedures are available for my child's condition?

Your child does not have to take part in this research study to be treated for MDR-TB. Other treatment is available to treat MDR-TB in your country through [local TB care provider/entity]. This treatment is similar to that in the control arm in the study. It is a combination treatment with several drugs. Your doctor will recommend treatment for either 18-24 months or for 9-12 months. In some cases, it will include a daily shot of about 6 months. Talk with the study doctor if you or your child have questions about the other treatment.

Can my child still receive TB treatment if he/she does not take part in this study?

Yes. Taking part in this study is up to you and your child. Your child can decide not to take part. Your child will receive treatment through [local TB care provider/entity] if your child does not take part in this study. There will be no penalty, and you will not lose any benefits you receive now or have a right to receive. The treatment outside the study is also free of charge.

What should we do if we want to stop taking part in the study?

If your child takes part in this study and decides that he/she wants to stop, you or your child should tell us. We will make sure that your child stops the study safely.

Also, it is possible that we will have to ask your child to leave the study before he/she finishes it. If this happens, we will tell you and your child why.

We will tell you and your child if we learn any new information that could make you or your child decide that your child will leave the study.

If any of these happens, we will talk to you about follow-up care, if needed, and you will be encouraged to come back at least for one additional visit ("termination visit").

Information collected during your child's participation will be used to help answer study questions. When your child leaves the study, his/her health information, and information obtained from sputum samples and bacteria isolates previously collected may still be used and stored for 20 years for the study and future TB research. However, if you and your child prefer

this information is not used and that it is destroyed, you can contact your child's study doctor or the email address endTB.clinicaltrial@paris.msf.org.

Will we be paid to take part in this study?

You and your child will not be paid to take part in this study. We will pay the transportation costs for study visits. You or your child will also receive [local arrangement for monthly food supplements] when your child takes part in the study. In sum, you or your child will be reimbursed [local currency]_____ for transportation for the baseline visit, [local currency]_____ for each follow-up visit, [local currency] _____for any unscheduled visits and [local currency]_____ for your child's final visit.

What will we have to pay for if my child takes part in this study?

You and your child will not have to pay in order to take part in this study. You and your child will also will not have to pay for the study drugs, any study-related procedures, and visits.

What happens if my child is injured as a result of taking part in this study?

The sponsor has made insurance arrangements to pay for an injury your child suffers due to his/her participation in the study.

If your child suffers physical injury from this study please inform your doctor and seek medical attention right away, _____ will ensure that your child receives appropriate medical treatment.

[Research site name] will not pay to treat a medical condition or disease your child had before joining this study or expenses for injury, treatment, or hospitalization your child may require that are not the result of your child's participation in the study.

In an emergency, the study sponsor has made plans to pay for your child's visit to a specialist, the related treatment, and/or your child's stay in the hospital. For non-urgent situations, the sponsor may pay for your child's visit to see a specialist. The study team will review you and your child's situation and decide whether the sponsor will pay for the resulting treatment if your condition is not the result of your participation in the study.

Who can we speak to if we have questions, concerns or complaints?

You or your child can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you or your child want.

[PI Name and title] is the person in charge of this study. You or your child can call him/her at [PI telephone number]. You or your child can also call [Clinical Investigator] at [CI number] with questions about this study. If you or your child have questions about the scheduling of appointments or study visits, call [Study Coordinator] at [SC number].

For medical emergencies outside business hours, please contact **[Must include 24/7 phone number of site licensed physician investigator here].**

If you or your child want to speak with someone not directly involved in this study, please contact the [Research Center IRB] office. You or your child can call them at [Research Center IRB number].

If my child takes part in this study, how will you protect our privacy?

We are careful to protect the identity of the people in this study to the extent permitted by law. We also keep your child's information secure and confidential. Electronic study information will be password-protected, and paper files will be stored in a locked office at [Research site]. Your child's study records will be kept at the clinic/hospital for XX years [*to be adapted locally*] following the completion of the study. If needed to monitor the study quality, your child's study information may be looked at by institutions responsible for quality and privacy such as the sponsor, Ethics Committee and Competent Authorities.

For the study, we will store some non-medical information about your child, such as his/her date of birth and city of residence. You can ask us to access, modify, complete, update, or delete this information. If you have any complaints about the protection of your data, you could contact your local/national Data Protection Authority [*Name and contact to be adapted locally*].

The information collected for the study will be used for the following purposes:

- For the purposes of this study. The sponsor, the study doctor, or other doctors involved in the study may publish reports or articles on the study or present screening findings to scientific groups. After the study is completed, you may see your child's records, and you may be told the results of the study.
- Secondary use for TB research; your child's coded information may be used and shared with other institutions only for the purpose of further TB research during and after completion of the study and notably with the World Health Organization.

In all cases your child's identity will never be disclosed.

Your child's coded information may be sent electronically to other researchers or institutions. If sent, it will be encrypted (scrambled so it can't be read by people who shouldn't see it).
We guarantee that, when we send your coded information, it will be protected according to European Economic Area standards.

Subject Identification

Informed Consent and Authorization

Your child completed the screening process of this study and is eligible to take part, or he/she completed the screening process for another study (endTB-Q) and was found to be eligible for this study (endTB). In the second case, you agree that your child's data and personal information collected during endTB-Q screening will be used for the endTB study.

Your signature on this document means the following:

I have read this consent form. This study has been explained to me, including risks and possible benefits, other possible treatments or procedures, and other important things about the study. I have had the opportunity to ask questions. I understand the information given to me. I recognize that my child's participation is voluntary and that I can refuse or end my child's participation at any time, without any loss of benefits that I would otherwise have. I recognize that by signing this document, I do not lose any of my legal rights as a parent/guardian of the participant. I will receive a complete, signed, dated copy of this research parental consent form.

By signing below, I give my permission to let my child take part in this study.

Signature of Parent/Guardian of the Participant

_____ _____

Signature or thumbprint of parent/guardian of the participant Date (DD/MMM/YYYY) and Time

_____

Name of parent/guardian of the participant, printed in capital letters

Witness (if applicable):

_____ _____

Signature of witness Date (DD/MMM/YYYY) and Time

_____

Subject Identification

Name of witness, printed in capital letters

Study representative who obtained informed consent:

I have explained this study to the parent/guardian of the participant and have answered all of his/her questions. He/she understands the information described in this document and accepts voluntary participation of his/her child in the study.

_____ _____

Signature of study representative Date (DD/MMM/YYYY) and Time

_____

Name of study representative, printed in capital letters

Schedule of Visits

Visit	Consent	Doctors' Exam	Nurses' Interview	Blood Collection	Sputum Collection	ECG	Chest X-ray
Baseline	✓	✓	✓	(✓)	(✓)	✓	(✓)
Week 1		✓	✓			✓	
Week 2		✓	✓		✓	✓	
Week 3		✓	✓			✓	
Month 1		✓	✓	✓	✓	✓	
Week 5, 6, 7		✓	✓			✓	
Month 2		✓	✓	✓	✓	✓	✓
Week 9, 10, 11		✓	✓			✓	
Month 3, 4, 5, 6, 6.5, 7, 8		✓	✓	✓	✓	✓	
Month 9		✓	✓	✓	✓	✓	✓
Month 10, 11		✓	✓	✓	✓	✓	
Month 12		✓	✓		✓	✓	
Month 13.5, 15		✓	✓		✓		
Month 17		✓	✓	(✓)	✓	✓	✓
Month 19, 20, 22[1]		✓	✓		✓		
Month 24[1]		✓	✓	✓	✓		✓

endTB Clinical Trial
Pregnant Partner Consent Form

Version 3.5 Version Date: 15 December 2020

Subject Identification

Protocol Title: endTB (Evaluating Newly approved Drugs for multidrug-resistant TB)

Sponsor: Médecins Sans Frontières (Doctors Without Borders) - France

Principal Investigators: Carole Mitnick, Sc.D. and Lorenzo Guglielmetti, M.D.

Site Principal Investigator: [Insert PI Name]

Research Center: [Insert Research Center Name]

Participant Name (please print): _____

Partner Study Subject ID: _____

About this consent form

Please read this form, called pregnant partner consent form, carefully. It tells you important information about a research study. The purpose of this form is to request your consent to follow the progress of your pregnancy and the birth and health of your baby. A member of our research team will also talk to you about this research study.

If you have any questions about the research or about this form, please ask us. Signing this form is voluntary; it is up to you to decide whether to agree to the collection of this information or not. If you agree to the collection of this information, we will ask that you sign this form to confirm that you want to take part. We will give you a signed copy of this form to keep. You can decide not to share any information with this research study at any time if you do not want to, even after signing this form.

If you are not able to sign the consent form, but you would like to provide information, you can choose someone you know to sign for you and you can make a thumbprint to show that you understand the study and would like to take part.

Introduction

Your partner is or has been taking part in the research study called the endTB clinical trial. Some of the drugs that your partner is taking for this research may move into the semen. This is why when he started in the study, your partner was asked to use birth control while taking the study drugs. The effects of your partner's study medications on pregnancy and the developing fetus (baby still in the womb) are currently not known or not fully understood. For this reason, we would like to collect medical information about your pregnancy and the birth and health of your baby. We want to follow your pregnancy and try to find out if the study medications have any effect on your pregnancy and the health of your baby.

What will happen if I agree to provide information about my pregnancy?

If you agree to sign this consent form, we will review and collect medical information relating to your pregnancy, the delivery of your baby and the health of your baby at least at 6 and 12 months of age for any important medical issues.

Will anything bad happen to me?

Risks of Providing Information about Your Pregnancy:

We are careful to protect the identity of the people to the extent permitted by law. We also keep your and your baby's information secure and confidential. Electronic study information will be password-protected, and paper files will be stored in a locked office at [Research site]. Your and your baby's records will be kept at the clinic/hospital for XX years [*to be adapted locally*] following the completion of the study. If needed to monitor the trial quality, your and your baby's information and other information about you may be looked at by institutions responsible for quality and privacy such as the sponsor, Ethics Committee and Competent Authorities.

For the study, we will store some non-medical information about you and your baby, such as date of birth and city of residence. You can ask us to access, modify, complete, update, or delete this information. If you have any complaints about the protection of your data, you could contact your local/national Data Protection Authority [*Name and contact to be adapted locally*].

The information collected for this study will be used for the following purposes:

- For the purpose of this research. The sponsor, the study doctor, or other doctors involved in the study may publish reports or articles on the study or present the study findings to scientific groups. After the study is completed you may see your and your baby's records, and you may be told the results of the study.
- Secondary use for TB research; yours and your baby coded information may be used and shared with other institutions only for the purpose of further TB research during and after completion of the study and notably with the World Health Organization.

In all cases your identity will never be disclosed.

Your and your baby's coded information may be sent electronically to other researchers or institutions, If sent, it will be encrypted (scrambled so it cannot be read by people who should not see it).

We guarantee that, when we send your coded information, it will be protected according to European Economic Area standards.

What are the possible benefits?

There are no direct benefits to you or your baby for providing information relating to your pregnancy. However, we hope that the information we gather about your pregnancy will help future patients and their children by helping us understand the potential effects of the study medications on pregnancy women and developing babies.

What should I do if I want to stop providing information about my pregnancy?

If you decide you want to stop providing information to this study or if you change your mind later, you should tell us.

Information collected from you will be used to help answer study questions. When you leave, your information previously collected will still be used and stored for 20 years for the study and future TB research. However, if you prefer this information not to be used and destroyed, you can contact your study doctor or the email address endTB.clinicaltrial@paris.msf.org.

Will I be paid to provide information about my pregnancy?

This study will not cover any costs related to your pregnancy, delivery or care of your baby.

What will I have to pay for if I provide information about my pregnancy?

The sponsor will cover the costs of collecting your or your baby's medical information. There will be no cost or payment to you.

Who can I speak to if I have questions, concerns or complaints?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

[PI Name and title] is the person in charge of this research study. You can call him/her at [PI telephone number]. You can also call [Clinical Investigator] at [CI number] with questions about this research study. If you have questions about the scheduling of appointments, call [Study Coordinator] at [SC number].

If you want to speak with someone not directly involved in this research study, please contact the [Research Center IRB] office. You can call them at [Research Center IRB number].

endTB Clinical Trial
Pregnant Partner Consent Form

Version 3.5 Version Date: 15 December 2020

Subject Identification

Informed Consent and Authorization

Your signature on this document means the following:

I have read this consent form. I have had the reasons explained to me as to why data with regard to the pregnancy, the delivery and the health of the baby are required. I have had the opportunity to ask questions. I understand the information given to me. I will receive a complete, signed, dated copy of this informed consent form.

By signing below, I freely agree to allow the data concerning the pregnancy and the outcome of this pregnancy to be held on the Doctors Without Borders Drug Safety Database and being forwarded to regulatory agencies as necessary.

Signature of Pregnant Partner

_____ _____ _____

Signature or thumbprint of pregnant partner Date (DD/MMM/YYYY) Time

_____

Name of pregnant partner, printed in capital letters

Witness (if applicable):

_____ _____ _____

Signature of witness Date (DD/MMM/YYYY) Time

_____

Name of witness, printed in capital letters

Subject Identification

Study representative who obtained informed consent:

A verbal explanation of the research project, including drugs involved, risks and reasons why Doctors Without Borders is seeking data with regard to the outcome of the pregnancy, has been given to the person named above and I believe they understood that explanation. A copy of this signed and dated Pregnancy Data Release Form will be provided to the above named for their record.

_____ _____ _____

Signature of representative Date (DD/MMM/YYYY) Time

_____

Name of study representative, printed in capital letters

endTB Clinical Trial
Treatment during pregnancy Consent Form

Subject Identification

Version 3.5 Version Date: 15 December 2020

Protocol Title: endTB (Evaluating Newly approved Drugs for multidrug-resistant TB)

Sponsor: Médecins Sans Frontières (Doctors Without Borders) - France

Principal Investigators: Carole Mitnick, Sc.D. and Lorenzo Guglielmetti, M.D.

Site Principal Investigator: [Insert PI Name]

Research Center: [Insert Research Center Name]

Participant Name (please print): _____

Study Subject ID: _____

About this consent form

We are asking you to read this form because you are currently receiving study drugs to treat your tuberculosis ("TB") as part of the research study endTB clinical trial, you are at least 18 years of age, and because you are now pregnant. Please read this form carefully. The purpose of this form is to request your consent to continue participating in the study. A member of the research team will also explain to you verbally the information provided in this form.

When you initially consented to participate into the study, we explained that we don't know if some of the medications given in the study are safe if taken during pregnancy. We explained that pregnant women cannot enter the study and we asked you to use birth control while taking the study drugs.

After the _____ dose of the study treatment _____, but before treatment was complete, we learned that you are pregnant. Your study doctor believes that there are more benefits than risks for you to be in the study. Since your condition has changed, we are asking again if you are still willing to participate in the study.

If you have any questions about the information provided, the reason we are asking for your consent or about this form, please ask us. Signing this form is voluntary; it is up to you to decide whether you will stay in the study and keep receiving the study drugs without terminating the pregnancy. If you agree, we will ask you to sign this form to confirm that you want to continue. We will give you a signed copy of this form to keep. You can decide to stop taking part in this study at any time if you do not want to, even after signing this form.

If you are not able to sign the consent form, but you would like to participate, you can ask someone you know to sign for you and you can make a thumbprint to show that you understand and would like to continue taking part.

Why is it proposed that I stay in the study even though I'm pregnant?

The effects of your study medications on pregnancy and on the developing fetus (baby still in the womb) are currently not known or not fully understood.

However, based on the information now available about your clinical condition, the drugs you are taking, and your treatment options if you elect another option, your study doctor believes that the expected benefits of continuing to receive the study medications are bigger than the risks for you and your baby.

Will I be told why the doctor thinks I should stay in the study?

Based on the TB study medications you are currently taking and your clinical condition, your study doctor will explain you why s/he has proposed that you stay in the study.
In detail s/he will explain all the options available to you, and:

- the available information about the safety of taking these drugs during pregnancy;
- the possible risks and benefits to you and your baby if you stay in the study;
- the possible risks and benefits to you and your baby if you leave the study;
- the possible (treatment) options you might have if you leave the study; and
- the possible risks to you and your baby from your TB disease if you decide to stop taking TB treatment completely.

If the explanation is not clear, we want you to ask questions until everything is clear and you have sufficient information and time to take your decision.

What will happen during the study, if I decide to remain in the study?

You will be monitored to follow your TB using the same schedule you agreed to when you signed the original research consent form for endTB clinical trial.

If you decide to stay in the study, your study doctor will talk to you, and, if you permit, your gynaecologist and/or obstetrician (doctor in charge of pregnant women), to make sure the development of your baby is closely followed during the whole pregnancy.

We would also like to collect medical information about your pregnancy and the birth and health of your baby. We want to follow you and your baby during the pregnancy and until delivery to try to learn if the study medications have any effect on your pregnancy. We would like to follow the health of your baby at least at 6 and 12 months of age for any important medical issues.

What are the possible risks of staying in the study?

Your study doctor will explain the risks of the treatment for yourself, your pregnancy, your fetus and/or your future baby and you will be given a document entitled "participant information leaflet– pregnant patient" that summarizes the main side effects. The information about these risks is very limited; any known risks of abnormality will be described by your study doctor.

All the other risks (side effects) were explained to you when taking your consent for participation in the research study.

Your privacy will be protected as detailed in the research consent form you have already signed.

Are there benefits to staying in the study?

If your study doctor proposes that you stay in the study, s/he believes that the possible benefits of staying in the study and receiving the study treatment are bigger than the risks for you and your baby.

You will receive greater TB treatment support from the study team than during regular MDR-TB treatment and your pregnancy will be closely monitored.

Others with MDR-TB may benefit in the future from what we learn in this study**.** We hope that the information we gather about your pregnancy while taking the study drugs and after will help future patients and their children by increasing what we know about the possible of the study medications on pregnant women and developing babies.

What should I do if I want to stop taking part in the study?

If you decide you want to stop participating into this study, you should tell us. We will make sure you stop the study safely and we will invite you to make additional study visit(s) called "termination visit" and follow-up visits, as outlined into the research consent form you have already signed.

We will tell you if, at any time, we learn any new information that could make you change your mind and choose to leave the study.

If you decide to stop participating in the study, the study doctor will ask you for permission to collect information about the continuation and the outcome of your pregnancy, and the condition of your newborn (at least at 6 and 12 months of age for any important medical issues).

Information collected from you will be used to help answer study questions. When you leave the study, your information previously collected will still be used and stored during 20 years for the study and future TB research. However, if you prefer this information not to be used and destroyed, you can contact your study doctor or the email address endTB.clinicaltrial@paris.msf.org.

Also, your study doctor, at any point in time after your consent, might ask you to leave the study before you finish it. This may happen for example if s/he thinks that the risks of staying in the study are becoming higher than the expected benefits, or if s/he thinks that you need to receive treatment not allowed by the research study. If this happens, your study doctor will explain in detail all the reasons for his/her decision.

Will I be paid or have to pay additional expenses if I stay in this research study?

You will not receive reimbursements in addition to the ones you already receive for taking part into the study. This study will not cover any costs from your pregnancy, delivery or care of your baby *[to be adapted locally]*. There will be no cost [or payment] to you if you stay in the study.

What happens if my baby is injured or I am injured as a result of taking part in this research study?

The sponsor will pay for costs related to any injury to you,[or any miscarriage or damage to the fetus or your baby] that result from taking part in this study.

If you have a physical injury or you feel your pregnancy might be at risk because of participation in this study, please tell your study doctor and seek medical attention right away; the study team will make sure that you receive appropriate medical treatment and that your pregnancy course is closely monitored.

In an emergency, the study sponsor has made plans to pay for your visit to see a specialist, any related treatment, and/or your stay in the hospital. For non-urgent situations, the sponsor might pay for your visit to see a specialist. The study team will review your situation and decide whether the sponsor will pay for the resulting treatment if your condition is not the result of your participation in the study. You do not waive any of your legal rights by signing this consent form.

Who can I speak to if I have questions, concerns or complaints?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

[PI Name and title] is the person in charge of this research study. You can call him/her at [PI telephone number]. You can also call [Clinical Investigator] at [CI number] with questions about this research study. If you have questions about the scheduling of appointments, call [Study Coordinator] at [SC number].

If you want to speak with someone not directly involved in this research study, please contact the [Research Center IRB] office. You can call them at [Research Center IRB number].

Subject Identification

Version 3.5 Version Date: 15 December 2020

Informed Consent and Authorization

Your signature on this document means the following:

I have read this consent form. It has been explained to me why I'm being asked to sign this informed consent, the risks and the possible benefits for the fetus and for me resulting from staying in the study. I have had the opportunity to ask questions. I understand the information given to me. I recognize that my participation is voluntary and that I can refuse or end my participation at any time, without any loss of benefits that I would otherwise have. I recognize that by signing this document, I do not lose any of my legal rights as a study participant.

I will receive a complete, signed, dated copy of this informed consent form.

By signing below, I freely agree to continue my participation to the endTB clinical trial and I agree to take the treatments that will be prescribed to me.

Signature of Pregnant Participant

_____ _____ _____

Signature or thumbprint of pregnant participant Date (DD/MMM/YYYY) Time

_____

Name of pregnant participant, printed in capital letters

Witness (if applicable):

_____ _____ _____

Signature of witness Date (DD/MMM/YYYY) Time

_____

Name of witness, printed in capital letters

Subject Identification

Version 3.5 Version Date: 15 December 2020

Study representative who obtained informed consent:

I have explained to the pregnant participant why we are proposing that she continue to participate in the study and the risks for herself and the fetus deriving from the drugs intake and have answered all of her questions. She understands the information described in this document and accepts voluntarily to keep participating in the study.

_____ _____ _____

Signature of representative Date (DD/MMM/YYYY) Time

_____

Name of study representative, printed in capital letters

endTB Clinical Trial
Research Screening Adult Consent Form

Version 3.5 Version Date: 15 December 2020

Subject Identification

Protocol Title: endTB (Evaluating Newly approved Drugs for multidrug-resistant TB)

Sponsor: Médecins Sans Frontières (Doctors Without Borders) - France

Principal Investigators: Carole Mitnick, Sc.D. and Lorenzo Guglielmetti, M.D.

Site Principal Investigator: [Insert PI Name]

Research Center: [Insert Research Center Name]

Participant Name (please print): _____

Study Subject ID: _____

About this consent form

You have been diagnosed with multidrug-resistant tuberculosis (MDR-TB). We are conducting a study, called endTB, to see whether we can find a better treatment for MDR-TB. We would like to ask you whether you agree to be interviewed and examined to see whether you could be in our study.

Please read this form, called research screening consent form, carefully. It tells you important information about evaluating you for participation in the endTB study. This evaluation is called "screening". A member of our research team will talk to you about what it means to take part in the screening. People who agree to take part in screening are called "participants" in this consent form.

Introduction

TB is a disease caused by bacteria (or germ) that usually affects the lungs. It is passed from person to person through the air by droplets that come from the lungs of a person who is sick with TB. When the sick person coughs, sings, shouts, or spits, the TB bacteria can make others sick. Most people with TB can be treated and cured, if they complete all their treatment. Some types of TB bacteria cannot be killed by the regular drugs (rifampicin and isoniazid). These bacteria are called multidrug-resistant. People sick with multidrug-resistant TB need different drugs for their treatment.

Subject Identification

We are asking you to be screened for the endTB study because you are at least [18] years old and you have MDR-TB that is affecting your lungs. During this screening, we will do some laboratory tests and a doctor will examine you to see if you are eligible to be in the study. At least 2000 patients in 8 countries will be screened for this study. We expect about [number to be adapted locally] patients will be screened at [Research Center Name].

Médecins Sans Frontières (Doctors Without Borders) –France is the sponsor of this study.

If you have any questions about the screening or about this form, please ask us. Taking part in the screening for this study is up to you. You do not have to be screened if you do not want to. Screening is the first step. If you would like to take part in this screening, we will ask that you sign this form to confirm that you accept to be screened to see if you are eligible to be in the study. We will give you a signed copy of this research screening consent form to keep. You can decide not to take part in this screening at any time if you do not want to, even after signing this form.

If you are not able to sign the consent form, but you would like to participate, you can choose someone you know to sign for you and you can make a thumbprint to show that you understand the study and would like to be screened.

If you agree to be screened and are eligible to be in the study, we will give you more information about the study and ask you to sign another form to show you agree to take part in the study.

Why is this study being done?

Current treatment for MDR-TB includes 5-9 drugs taken daily for 18 to 24 months. Treatment may be oral or include a daily shot. In some cases, depending on the characteristics of your MDR-TB, a shorter treatment duration (9 to 12 months) with an all-oral standardized treatment regimen including 7 drugs may be a possible option. This treatment may cause many mild and very serious side effects, for example: nausea, vomiting, hearing loss, numbness/tingling in fingers and toes, kidney damage, mental illness/feeling sad, etc. Two new drugs (delamanid and bedaquiline) have recently become available. New regimens containing one of these drugs may be shorter for example, 9 months and/or simpler (without injection). Such regimens have to be tested to see if they are safe and effective for people with multidrug-resistant TB. We are asking to screen you for a study to test new 9-month-long, injection-free MDR-TB treatments. This research trial will compare new experimental treatment regimens to the current treatment for MDR-TB.

How long will the screening process take?

The complete screening process for this study could take 4 to 5 hours of your time. However, it is possible the doctors will need to see you at separate visits to finish all the screening procedures. If that happens, all visits should be done within 2 weeks.

What will happen during screening?

We will ask you to come to [Research Center Name]. We will ask you to sign this consent form before we do any screening procedures. Then, we will do some tests and procedures to see if you are eligible to take part in the study. The study doctor will review the results of these tests and procedures. If you cannot participate, the study doctor will tell you why and might ask if you will participate in another study.

Specifically, during screening, we will:

1. Answer all your questions and get your permission for screening.
2. Ask for your full name, contact information, sex, and age.
3. Review your medical history, including past or present illnesses, and information on drugs you are currently taking.

   The treatment you will receive for your TB may interact with some of the drugs that you are currently taking. The study doctor may review with you if some of your drugs need to be stopped or changed prior to receiving any MDR-TB treatment.
4. Perform a complete check-up and ask about your TB symptoms.
5. Collect 2 tablespoons of your blood for laboratory testing to check if your body is functioning well.
6. Unless recent results are available, we will also ask you to use the collected blood for viruses that might affect your treatment for TB, like hepatitis B and C, which affect your liver, and HIV, which affects your body's ability to fight infection.

   All test results will remain confidential. You have the right to decline these tests. Declining a test will not affect your participation to the study and the access to usual treatments that do not depend on knowledge of the test result. If the test result(s) is positive, you will be referred to appropriate care. If you have HIV infection, we will test CD4 count and HIV viral load to see if the disease is well controlled.
7. Ask you to cough up 3 sputum (or phlegm) samples. These will be used to test whether the TB bacteria can be treated with regular drugs and/or drugs in the study treatments. This is called testing for drug resistance.
8. Do a test, called an electrocardiogram, to check if your heart works normally.
9. Because we don’t know if some of these medications are safe in pregnancy:

   - The study doctor will discuss birth control methods to avoid pregnancy (yourself or your partner) if you are eligible and agree to participate in the study.
   - Pregnant patients cannot enter the study. So, if you are a woman who can get pregnant, we will collect a urine or blood sample for a pregnancy test. Your study

doctor will refer you to for TB treatment outside of the study if the test shows you are pregnant.

Depending on your test results:

- your study doctor may prescribe medications, for example to balance the level of salts in your blood, when possible;
- some of these tests may need to be repeated within the 2-week period; your study doctor will let you know which ones.

We will label all your samples and health information with a code instead of your name to keep all your information private. The key to the code connects your name to your samples and health information. The study doctor will keep the key to the code in a password-protected computer and/or locked file.

Storing Isolates (strains) and Health Information for Future Research

We would like to store some of the bacteria isolates (TB bug), and health information for future research related to TB, which will be collected during this screening. All your health information and bacteria isolates will be handled in a way to keep all your information private. Any use of stored bacteria isolates and your health information for other research inside your country or in other countries will be approved by the ethics committee of your country.

This future research is independent from being screened for the endTB study and your decision to participate in the future research will not affect your participation in the screening for endTB study.

The bacteria isolates found in your sputum samples and your health information may be stored for up to 20 years in a special place (bank or repository) created to safely store them. The stored isolates and your health information will be used only to help future research in TB and to improve diagnosis (including resistance testing) and treatment of TB. During your participation in the endTB study, and the following storage period of 20 years after completion of the study, you can contact your study doctor or the email address endTB.clinicaltrial@paris.msf.org to request any information regarding the use, storage and location of your health information and bacteria isolates.

Do you agree that your health information and bacteria isolates found in your sputum samples may be stored for 20 years and used only for future TB research? You are free to refuse such storage and further use for TB research of your health information and bacteria isolates and still take part in this screening.

☐ Yes ☐ No [Initials or signature, to be adapted locally]_____

You have the right to change your mind, and to later want your health information and/or bacteria isolates destroyed. In that case, during your participation in the endTB study, and the following storage period of 20 years after completion of the study, you can contact your study

doctor or the email address endTB.clinicaltrial@paris.msf.org to request any information regarding the use, storage and location of your health information and bacteria isolates and/or their destruction.

What are the risks and possible discomforts from being screened for this study?

Risks of Blood Draws

You may have a bruise (a black and blue mark) or pain where we take the blood samples. There is also a small risk of infection, light-headedness, and/or fainting.

What are the possible benefits from being screened for this study?

This screening evaluation has not been designed to give you direct benefits but it may help you to get treatment within the study, or get other appropriate treatment more quickly. Others with MDR-TB may benefit in the future from what we learn in this study**.**

Can I still receive TB treatment if I do not take part in this screening?

Yes. You will receive treatment through [local TB care provider/entity] if you do not take part in this screening. Taking part in this screening is up to you. You can decide not to take part. There will be no penalty, and you will not lose any benefits you receive now or have a right to receive.

What should I do if I want to stop taking part in this screening?

If you give your agreement for the screening, and you change your mind you should tell us.

Also, it is possible that we will have to ask you to drop out of the screening before you finish it. If this happens, we will tell you why.

And, we will tell you if we learn any new information that could make you change your mind and drop out later.

In any of these cases, we will discuss with you and refer you to other care, if needed.

Information collected during your screening will be used to help answer study questions. When you leave the study, your health information, and information obtained from sputum samples and bacteria isolates previously collected may still be used and stored for 20 years for the study and future TB research. However, if you prefer that this information is not used and that it is destroyed, you can contact your study doctor or the email address endTB.clinicaltrial@paris.msf.org.

Will I be paid to take part in this screening?

You will not be paid to take part in this screening. However, we will cover transportation costs for visiting the research center(s). We will pay or you will be reimbursed [local currency] _____ for transportation to and from the screening visit.

What will I have to pay for if I take part in this screening?

All screening procedures will be free of charge to you.

What happens if I am injured as a result of taking part in this screening?

If you suffer physical injury from the screening, _____ will give you immediate medical treatment.

_____ will not pay to treat a medical condition or disease you had before screening or expenses for injury, treatment, or hospitalization you may require that are not the result of your participation in the screening.

You do not waive any of your legal rights by signing this consent form.

Who can I speak to if I have questions, concerns or complaints?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want

[PI Name and title] is the person in charge of the screening and study. You can call him/her at [PI telephone number]. You can also call [Clinical Investigator] at [CI number] with questions. If you have questions about the scheduling of appointments or study visits, call [Study Coordinator] at [SC number].

If you want to speak with someone not directly involved in the screening or study, please contact the [Research Center IRB] office. You can call them at [Research Center IRB number].

If I take part in this screening, how will you protect my privacy?

We are careful to protect the identities of the people who are screened in this study to the extent permitted by law. We also keep your information secure and confidential. Electronic study information will be password-protected, and paper files will be stored in a locked office at [Research site]. Your screening records will be kept at the clinic/hospital for XX years [*to be adapted locally*] following the completion of the study. If needed to monitor the study quality, your information may be looked at by institutions responsible for quality and privacy such as the sponsor, Ethics Committee and Competent Authorities.

For the screening, we will store some non-medical information about you, such as your date of birth and city of residence. You can ask us to access, modify, complete, update, or delete this information. If you have any complaints about the protection of your data, you could contact your local/national Data Protection Authority [*Name and contact to be adapted locally*].

The information collected for screening will be used for the following purposes:

- For the purposes of this study. The sponsor, the study doctor, or other doctors involved in the study may publish reports or articles on the screening or present screening findings to scientific groups. After the study is completed, you may see your records, and you may be told the results of the study.
- Secondary use for TB research; your coded information may be used and shared with other institutions only for the purpose of further TB research during and after completion of the study and notably with the World Health Organization.

In all cases your identity will never be disclosed.

Your coded information may be sent electronically to other researchers or institutions. If sent, it will be encrypted (scrambled so it cannot be read by people who should not see it).
We guarantee that, when we send your coded information, it will be protected according to European Economic Area standards.

Subject Identification

Informed Consent and Authorization

Your signature on this document means the following:

I have read this consent form. The screening process has been explained to me, including risks and possible benefits, other possible treatments or procedures, and other important things about the study. I have had the opportunity to ask questions. I understand the information given to me. I recognize that my participation is voluntary and that I can refuse or end my participation at any time, without any loss of benefits that I would otherwise have.

I recognize that by signing this document, I do not lose any of my legal rights as a participant. I will receive a complete, signed, dated copy of this research screening consent form.

By signing below, I agree to take part in the screening.

Signature of Participant

_____ _____

Signature or thumbprint of participant Date (DD/MMM/YYYY) and Time

_____

Name of participant, printed in capital letters

Witness (if applicable):

_____ _____

Signature of witness Date (DD/MMM/YYYY) and Time

_____

Name of witness, printed in capital letters

Subject Identification

Study representative who obtained informed consent:

I have explained this study to the participant and have answered all of his/her questions. He/she understands the information described in this document and accepts voluntary participation in the study.

_____ _____

Signature of study representative Date (DD/MMM/YYYY) and Time

_____

Name of study representative, printed in capital letters

endTB Clinical Trial
Research Screening Assent Form

Version 3.5 Version Date: 15 December 2020

Subject Identification

Protocol Title: endTB (Evaluating Newly approved Drugs for multidrug-resistant TB)

Sponsor: Médecins Sans Frontières (Doctors Without Borders) - France

Principal Investigators: Carole Mitnick, Sc.D. and Lorenzo Guglielmetti, M.D.

Site Principal Investigator: [Insert PI Name]

Research Center: [Insert Research Center Name]

Participant Name (please print): _____

Study Subject ID: _____

About this assent form

You have been diagnosed with multidrug-resistant tuberculosis (MDR-TB). We are conducting a study, called endTB, to see whether we can find a better treatment for MDR-TB. We would like to ask you whether you agree to be interviewed and examined to see whether you could be in our study.

Please read this form, called research screening assent form, carefully. It tells you important information about evaluating you for participation in the endTB study. This evaluation is called "screening". A member of our research team will talk to you about what it means to take part in the screening. People who agree to take part in screening are called "participants" in this assent form.

Introduction

TB is a disease caused by bacteria (or germ) that usually affects the lungs. It is passed from person to person through the air by droplets that come from the lungs of a person who is sick with TB. When the sick person coughs, sings, shouts, or spits, the TB bacteria can make others sick. Most people with TB can be treated and cured, if they complete all their treatment. Some types of TB bacteria cannot be killed by the regular drugs (rifampicin and isoniazid). These bacteria are called multidrug-resistant. People sick with multidrug-resistant TB need different drugs for their treatment.

We are asking you to be screened for the endTB study because you are at least 15 years old and you have MDR-TB that is affecting your lungs. During this screening, we will do some laboratory tests and a doctor will examine you to see if you are eligible to be in the study. At least 2000 patients in 8 countries will be screened for this study. We expect about [number to be adapted locally] patients will be screened at [Research Center Name].

Médecins Sans Frontières (Doctors Without Borders) –France is the sponsor of this study.

If you have any questions about the screening or about this form, please ask us. Because you are a minor (between 15 and [17] years old), we will also ask your parent(s) or someone else who takes care of you (legal guardian) to give permission for you to be screened for the study, by signing a parental consent. Taking part in the screening for this study is up to you. You do not have to be screened if you do not want to. We will need both permissions from you and your parent(s) or legal guardian before you take part in this screening. Your decision not to take part cannot be over-ridden by your parent(s) or legal guardian. Your parents may be informed of results of the screening process [*to be adapted locally*].

Screening is the first step. If you would like to take part in this screening, we will ask that you sign this form to confirm that you accept to be screened to see if you are eligible to be in the study. We will give you a signed copy of this research screening assent form to keep. You can decide not to take part in this screening at any time if you do not want to, even after signing this form.

If you are not able to sign the consent form, but you would like to participate, you can choose someone you know to sign for you and you can make a thumbprint to show that you understand the study and would like to be screened.

If you agree to be screened, and you are eligible to be in the study, we will give you more information about the study and ask you to sign another form to show you agree to take part in the study.

Why is this study being done?

Current treatment for MDR-TB includes 5-9 drugs taken daily for 18 to 24 months. Treatment may be oral or include a daily shot. In some cases, depending on the characteristics of your MDR-TB, a shorter treatment duration (9 to 12 months) with an all-oral standardized treatment regimen including 7 drugs may be a possible option. This treatment may cause many mild and very serious side effects, for example: nausea, vomiting, hearing loss, numbness/tingling in fingers and toes, kidney damage, mental illness/feeling sad, etc. Two new drugs (delamanid and bedaquiline) have recently become available. New regimens containing one of these drugs may be shorter for example, 9 months and/or simpler (without injection). Such regimens have to be tested to see if they are safe and effective for people with multidrug-resistant TB. We are asking to screen you for a study to test new 9-month-long, injection-free MDR-TB treatments. This research trial will compare new experimental treatment regimens to the current treatment for MDR-TB.

How long will the screening process take?

The complete screening process for this study could take 4 to 5 hours of your time. However, it is possible the doctors will need to see you at separate visits to finish all the screening procedures. If that happens, all visits should be done within 2 weeks.

What will happen during screening?

We will ask you to come to [Research Center Name]. We will ask you to sign this consent form before we do any screening procedures. Then, we will do some tests and procedures to see if you are eligible to take part in the study. The study doctor will review the results of these tests and procedures. If you cannot participate, the study doctor will tell you why and might ask if you will participate in another study.

Specifically, during screening, we will:

1. Answer all your questions and get your and your parent/guardian's permission for screening.

2. Ask for your full name, contact information, sex, and age.

3. Review your medical history, including past or present illnesses, and information on drugs you are currently taking.

   The treatment you will receive for your TB may interact with some of the drugs that you are currently taking. The study doctor may review with you if some of your drugs need to be stopped or changed prior to receiving any MDR-TB treatment.

4. Perform a complete check-up and ask about your TB symptoms.

5. Collect 2 tablespoons of your blood for laboratory testing to check if your body is functioning well.

6. Unless recent results are available, we will also ask you to use the collected blood for viruses that might affect your treatment for TB, like hepatitis B and C, which affect your liver and HIV, which affects your body's ability to fight infection.

   All test results will remain confidential. You have the right to decline these tests. Declining a test will not affect your participation to the study and the access to usual treatments that do not depend on knowledge of the test result. If the test result(s) is positive, you will be referred to appropriate care. If you have HIV infection, we will test CD4 count and HIV viral load to see if the disease is well controlled.

7. Ask you to cough up 3 sputum (or phlegm) samples. These will be used to test whether the TB bacteria can be treated with regular drugs and/or drugs in the study treatments. This is called testing for drug resistance.

8. Do a test, called an electrocardiogram, to check if your heart works normally.

9. Because we don't know if some of these medications are safe in pregnancy:

   - The study doctor will discuss birth control methods to avoid pregnancy (yourself or your partner) if you are eligible and agree to participate in the study.
   - Pregnant patients cannot enter the study. So, if you are a girl who can get pregnant, we will collect a urine or blood sample for a pregnancy test. Your study doctor will refer you for TB treatment outside of the study if the test shows you are pregnant.

Depending on your test results:

- your study doctor may prescribe medications, for example to balance the level of salts in your blood, when possible;
- some of these tests may need to be repeated within the 2-week period; your study doctor will let you know which ones.

We will label all your samples and health information with a code instead of your name to keep all your information private. The key to the code connects your name to your samples and health information. The study doctor will keep the key to the code in a password protected computer and/or locked file.

Storing Isolates (strains) and Health Information for Future Research

We would like to store some of the bacteria isolates (TB bug) and health information for future research related to TB, which will be collected during this screening. All your health information and bacteria isolates will be handled in a way to keep all your information private. Any use of stored bacteria isolates and your health information for other research inside your country or in other countries will be approved by the ethics committee of your country.

This future research is independent from being screened for the endTB study and your decision to participate in the future research will not affect your participation in the screening for endTB study.

The bacteria isolates found in your sputum samples and your health information may be stored for up to 20 years in a special place (bank or repository) created to safely store them. The stored isolates and your health information will be used only to help future research in TB and to improve diagnosis (including resistance testing) and treatment of TB. During your participation in the endTB study, and the following storage period of 20 years after completion of the study, you can contact your study doctor or the email address endTB.clinicaltrial@paris.msf.org to request any information regarding the use, storage and location of your health information and bacteria isolates.

Do you agree that your health information and bacteria isolates found in your sputum samples may be stored for 20 years and used only for future TB research? You are free to refuse such

storage and further use for TB research of your health information and bacteria isolates and still take part in this screening.

☐ Yes ☐ No [Initials or signature, to be adapted locally]_____

You have the right to change your mind, and to later want your health information and/or bacteria isolates destroyed. In that case, during your participation in the endTB study, and the following storage period of 20 years after completion of the study, you can contact your study doctor or the email address endTB.clinicaltrial@paris.msf.org to request any information regarding the use, storage and location of your health information and bacteria isolates and/or their destruction.

What are the risks and possible discomforts from being screened for this study?

Risks of Blood Draws

You may have a bruise (a black and blue mark) or pain where we take the blood samples. There is also a small risk of infection, light-headedness, and/or fainting.

What are the possible benefits from being screened for this study?

This screening evaluation has not been designed to give you direct benefits but it may help you to get treatment within the study, or get other appropriate treatment more quickly. Others with MDR-TB may benefit in the future from what we learn in this study**.**

Can I still receive TB treatment if I do not take part in this screening?

Yes. You will receive treatment through [local TB care provider/entity] if you do not take part in this screening. Taking part in this screening is up to you. You can decide not to take part. There will be no penalty, and you will not lose any benefits you receive now or have a right to receive.

What should I do if I want to stop taking part in this screening?

If you give your agreement for the screening, and you change your mind you should tell us.

Also, it is possible that we will have to ask you to drop out of the screening before you finish it. If this happens, we will tell you why.

And, we will tell you if we learn any new information that could make you change your mind and drop out later.

In any of these cases, we will discuss with you and your parents/legal guardian and refer you to other care, if needed.

Information collected during your screening will be used to help answer study questions. When you leave the study, your health information, and information obtained from sputum samples and bacteria isolates previously collected may still be used and stored for 20 years for the study and future TB research. However, if you prefer that this information is not used and that it is destroyed, you can contact your study doctor or the email address endTB.clinicaltrial@paris.msf.org.

Will I be paid to take part in this screening?

You will not be paid to take part in this screening. However, we will cover transportation costs for visiting the research center(s). We will pay or you will be reimbursed [local currency] _____ for transportation to and from the screening visit.

What will I have to pay for if I take part in this screening?

All screening procedures will be free of charge to you.

What happens if I am injured as a result of taking part in this screening?

If you suffer physical injury from the screening, _____ will give you immediate medical treatment.

_____ will not pay to treat a medical condition or disease you had before screening or expenses for injury, treatment, or hospitalization you may require that are not the result of your participation in the screening.

You do not waive any of your legal rights by signing this consent form.

Who can I speak to if I have questions, concerns or complaints?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want

[PI Name and title] is the person in charge of the screening and study. You can call him/her at [PI telephone number]. You can also call [Clinical Investigator] at [CI number] with questions. If you have questions about the scheduling of appointments or study visits, call [Study Coordinator] at [SC number].

If you want to speak with someone not directly involved in the screening or study , please contact the [Research Center IRB] office. You can call them at [Research Center IRB number].

If I take part in this screening, how will you protect my privacy?

We are careful to protect the identities of the people who are screened in this study to the extent permitted by law. We also keep your information secure and confidential. Electronic study information will be password-protected, and paper files will be stored in a locked office at

[Research site]. Your screening records will be kept at the clinic/hospital for XX years [*to be adapted locally*] following the completion of the study. If needed to monitor the study quality, your information may be looked at by institutions responsible for quality and privacy such as the sponsor, Ethics Committee and Competent Authorities.

For the screening, we will store some non-medical information about you, such as your date of birth and city of residence. You can ask us to access, modify, complete, update, or delete this information. If you have any complaints about the protection of your data, you could contact your local/national Data Protection Authority [*Name and contact to be adapted locally*].

The information collected for screening will be used for the following purposes:

- For the purposes of this study. The sponsor, the study doctor, or other doctors involved in the study may publish reports or articles on the screening or present screening findings to scientific groups. After the study is completed, you may see your records, and you may be told the results of the study.
- Secondary use for TB research; your coded information may be used and shared with other institutions only for the purpose of further TB research during and after completion of the study and notably with the World Health Organization.

In all cases your identity will never be disclosed.

Your coded information may be sent electronically to other researchers or institutions. If sent, it will be encrypted (scrambled so it cannot be read by people who should not see it).
We guarantee that, when we send your coded information, it will be protected according to European Economic Area standards.

endTB Clinical Trial
Research Screening Assent Form

Subject Identification

Version 3.5 Version Date: 15 December 2020

Informed Assent and Authorization

Your signature on this document means the following:

I have read this assent form. The screening process has been explained to me, including risks and possible benefits, other possible treatments or procedures, and other important things about the study. I have had the opportunity to ask questions. I understand the information given to me. I recognize that my participation is voluntary and that I can refuse or end my participation at any time, without any loss of benefits that I would otherwise have.

I recognize that by signing this document, I do not lose any of my legal rights as a participant. I will receive a complete, signed, dated copy of this research screening assent form.

By signing below, I agree to take part in the screening.

Signature of Participant:

_____ _____

Signature or thumbprint of Participant Date (DD/MMM/YYYY) and Time

_____

Name of Participant, printed in capital letters

Witness (if applicable):

_____ _____

Signature of witness Date (DD/MMM/YYYY) and Time

_____

Name of witness, printed in capital letters

endTB Clinical Trial
Research Screening Assent Form

Subject Identification

Version 3.5 Version Date: 15 December 2020

Study representative who obtained informed assent:

I have explained this study to the participant and have answered all of his/her questions. He/she understands the information described in this document and accepts voluntary participation in the study.

_____ _____

Signature of study representative Date (DD/MMM/YYYY) and Time

_____

Name of study representative, printed in capital letters

endTB Clinical Trial
Research Screening Parental Consent Form

Version 3.5 Version Date: 15 December 2020

Subject Identification

Protocol Title: endTB (Evaluating Newly approved Drugs for multidrug-resistant TB)

Sponsor: Médecins Sans Frontières (Doctors Without Borders) - France

Principal Investigators: Carole Mitnick, Sc.D. and Lorenzo Guglielmetti, M.D.

Site Principal Investigator: [Insert PI Name]

Research Center: [Insert Research Center Name]

Participant Name (please print): _____

Study Subject ID: _____

About this consent form

Your child has been diagnosed with multidrug-resistant tuberculosis (MDR-TB). We are conducting a study, called endTB, to see whether we can find a better treatment for MDR-TB. We would like to ask you whether you agree for your child to be interviewed and examined to see whether he/she could be in our study.

Please read this form, called research screening parental consent form, carefully. It tells you important information about evaluating your child for participation in a the endTB study. This evaluation is called "screening". A member of our research team will talk to you and your child about what it means to take part in the screening. People who agree to take part in screening are called "participants" in this consent form.

Introduction

TB is a disease caused by bacteria (or germ) that usually affects the lungs. It is passed from person to person through the air by droplets that come from the lungs of a person who is sick with TB. When the sick person coughs, sings, shouts or spits, the TB bacteria can make others sick. Most people with TB can be treated and cured, if they complete all their treatment. Some types of TB bacteria cannot be killed by the regular drugs (rifampicin and isoniazid). These bacteria are called multidrug resistant. People sick with multidrug resistant TB need different drugs for their treatment.

We are asking you to give permission for your child to be screened for the endTB study because he/she is a minor (between 15 and [17] years old), and has MDR-TB that is affecting his/her lungs. During this screening, we will do some laboratory tests and a doctor will examine your

child to see if he/she is eligible to be in the study. We will need both permissions from you (by signing this consent form) and your child (by signing an assent form) before having your child take part in this screening. Your child does not have to take part in this screening if either you or your child does not want to.

At least 2000 patients in 8 countries will be screened for this study. We expect about [number to be adapted locally] patients will be screened at [Research Center Name].

Médecins Sans Frontières (Doctors Without Borders) - France is the sponsor of this study.

If you have any questions about the screening or about this form, please ask us. Because your child is less than [18] years of age (a minor), we will need both permissions from you and your child before having your child screened for this screening. Taking part in the screening for this study is up to you and your child. Your child does not have to be screened if you or your child does not want to. Screening is the first step. If you agree to let your child be screened, we will ask that you sign this form to confirm that you accept your child to be screened for this study. We will give you a signed copy of this research screening parental consent form to keep. We will also give your child the same information and ask for his/her permission to screening. Your child will be free to refuse even after you give permission for him/her to be screened. His/her decision not to take part cannot be over-ridden by your decision. Your child can also decide to stop screening for this study at any time if he/she does not want to, even after you sign this form. Likewise, you can also decide not to let your child take part in this study at any time if you do not want to, even after signing this form.

If you are not able to sign the consent form, but you would like your child to take part in the research study, you can choose someone you know to sign for you and you can make a thumbprint to show that you understand the study and would like your child to be screened.

If you agree your child to be screened and he/she is eligible to be in the study, we will give you more information about the study and ask you to sign another form to show you agree your child to take part in the study.

Why is this study being done?

Current treatment for MDR-TB includes 5-9 drugs taken daily for 18 to 24 months. Treatment may be oral or include a daily shot. In some cases, depending on the characteristics of your MDR-TB, a shorter treatment duration (9 to 12 months) with an all-oral standardized treatment regimen including 7 drugs may be a possible option. This treatment may cause many mild and very serious side effects, for example: nausea, vomiting, hearing loss, numbness/tingling in fingers and toes, kidney damage, mental illness/feeling sad, etc. Two new drugs (delamanid and bedaquiline) have recently become available. New regimens containing one of these drugs may be shorter for example, 9 months and/or simpler (without injection). Such regimens have to be tested to see if they are safe and effective for people with multidrug-resistant TB. We are asking to screen your child for a study to test new 9-month-long, injection-free MDR-TB treatments. This research trial will compare new experimental treatment regimens to the current treatment for MDR-TB.

How long will the screening process take?

The complete screening process for this study could take 4 to 5 hours of your time. However, it is possible the doctors will need to see your child at separate visits to finish all the screening procedures. If that happens, all visits should be done within 2 weeks.

What will happen during screening?

We will ask you and your child to come to [Research Center Name]. We will ask you to sign this consent form before we do any screening procedures. Then, we will do some tests and procedures to see if your child is eligible to take part in the study. The study doctor will review the results of these tests and procedures. If your child cannot participate, the study doctor will tell you why and might ask you if your child will participate in another study.

Specifically, during screening, we will:

1. Answer all your questions and get your and your child's permission for screening.
2. Ask for your child's full name, contact information, sex, and age.
3. Review your child's medical history, including past or present illnesses, and information on drugs he/she is currently taking.

   The treatment your child will receive for TB may interact with some of the drugs that he/she is currently taking. The study doctor may review with you and your child if some of his/her drugs need to be stopped or changed prior to receiving any MDR-TB treatment.
4. Perform a complete check-up and ask about your child's TB symptoms.
5. Collect 2 tablespoons of your child's blood for laboratory testing to check if his/her body is functioning well.
6. Unless recent results are available, we will also ask to use the collected blood from your child for viruses that might affect your child's treatment for TB, like hepatitis B and C, which affect his/her liver and HIV, which affects his/her body's ability to fight infection.

   All test results will remain confidential. You and your child will have the right to decline these tests. Declining a test will not affect your child's participation to the study and the access to usual treatments that do not depend on knowledge of the test result. If the test result(s) is positive, your child will be referred to appropriate care. If your child has HIV infection, we will test his/her CD4 count and HIV viral load to see if the disease is well controlled.
7. Ask your child to cough up 3 sputum (or phlegm) samples. These will be used to test whether the TB bacteria can be treated with regular drugs and/or drugs in the study treatments. This is called testing for drug resistance.

8. Do a test, called an electrocardiogram, to check if your child's heart works normally.

9. Because we don't know if some of these medications are safe in pregnancy:

    - The study doctor will discuss birth control methods to avoid pregnancy (of your child or his/her partner) if your child is eligible and you and your child agree to his/her participation in the study.
    - Pregnant patients cannot enter the study. So, if your child is a girl who can get pregnant, we will collect a urine or blood sample for a pregnancy test. The study doctor will refer your child for TB treatment outside of the study if the test shows she is pregnant.

Depending on your child's test results:

- the study doctor may prescribe medications, for example to balance the level of salts in his/her blood, when possible;
- some of these tests may need to be repeated within the 2-week period; the study doctor will let you know which ones.

We will label all your child's samples and health information with a code instead of his/her name to keep all his/her information private. The key to the code connects your child's name to his/her samples and health information. The study doctor will keep the key to the code in a password protected computer and/or locked file.

Storing Isolates (strains) and Health Information for Future Research

We would like to store some of the bacteria isolates (TB bug) and your child's health information for future research related to TB, which will be collected during this screening. All your child's health information and bacteria isolates will be handled in a way to keep all his/her information private. Any use of stored bacteria isolates and your child's health information for other research inside your country or in other countries will be approved by the ethics committee of your country.

This future research is independent from being screened for the endTB study and your decision to let your child participate in the future research will not affect your child's participation in the screening for endTB study.

The bacteria isolates found in his/her sputum samples and his/her health information may be stored for up to 20 years in a special place (bank or repository) created to safely store them. The stored isolates and your child's health information will be used only to help future research in TB and to improve diagnosis (including resistance testing) and treatment of TB. During your child's participation in the endTB study, and the following storage period of 20 years after completion of the study, you can contact the study doctor or the email address endTB.clinicaltrial@paris.msf.org to request any information regarding the use, storage and location of your child's health information and bacteria isolates.

Do you agree that your child's health information and the bacteria isolates found in his/her sputum samples may be stored for 20 years and used only for future TB research? You are free to refuse such storage and further use for TB research of your child's health information and bacteria isolates and your child can still take part in this screening.

☐ Yes ☐ No [Initials or signature, to be adapted locally]_____

You have the right to change your mind, and to later want your child's health information and/or bacteria isolates destroyed. In that case, during the participation of your child in the endTB study, and the following storage period of 20 years after completion of the study, you can contact the study doctor or the email address endTB.clinicaltrial@paris.msf.org to request any information regarding the use, storage and location of your child's health information and bacteria isolates and/or their destruction.

What are the risks and possible discomforts from being screened for this study?

Risks of Blood Draws

Your child may have a bruise (a black and blue mark) or pain where we take the blood samples. There is also a small risk of infection, light-headedness, and/or fainting.

What are the possible benefits from being screened for this study?

This screening evaluation has not been designed to give your child direct benefits but it may help your child to get treatment within the study, or get other appropriate treatment more quickly. Others with MDR-TB may benefit in the future from what we learn in this study**.**

Can my child still receive TB treatment if he/she does not take part in this screening?

Yes. Your child will receive treatment through [local TB care provider/entity] if he/she does not take part in this screening. Taking part in this screening is up to you and your child. You and your child can decide not to take part. There will be no penalty, and you and your child will not lose any benefits you receive now or have a right to receive.

What should I do if we want to stop taking part in this screening?

If you give your agreement for your child's screening and you change your mind, you should tell us.

Also, it is possible that we will have to ask your child to drop out of the screening before he/she finishes it. If this happens, we will tell you why.

And, we will tell you if we learn any new information that could make you change your mind and drop out later.

In any of these cases, we will discuss with you and your child and refer your child to other care, if needed.

Information collected during your child's screening will be used to help answer study questions. When your child leaves the study, his/her health information and information obtained from sputum samples and bacteria isolates previously collected may still be used and stored for 20 years for the study and future TB research. However, if you and your child prefer that this information is not used and that it is destroyed, you can contact your study doctor or the email address endTB.clinicaltrial@paris.msf.org.

Will we be paid to take part in this screening?

You or your child will not be paid to take part in this screening. However, we will cover transportation costs for visiting the research center(s). We will pay or you will be reimbursed [local currency] _____ for transportation to and from the screening visit.

What will we have to pay for if my child takes part in this screening?

All screening procedures will be free of charge to your child.

What happens if my child is injured as a result of taking part in this screening?

If your child suffers physical injury from the screening, _____ will give him/her immediate medical treatment.

_____ will not pay to treat a medical condition or disease your child had before screening or expenses for injury, treatment, or hospitalization your child may require that are not the result of your child's participation in the screening.

You do not waive any of your legal rights by signing this consent form.

Who can I speak to if I have questions, concerns or complaints?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want

[PI Name and title] is the person in charge of the screening and study. You can call him/her at [PI telephone number]. You can also call [Clinical Investigator] at [CI number] with questions. If you have questions about the scheduling of appointments or study visits, call [Study Coordinator] at [SC number].

If you want to speak with someone not directly involved in the screening or study , please contact the [Research Center IRB] office. You can call them at [Research Center IRB number].

If my child takes part in this screening, how will you protect our privacy?

Subject Identification

We are careful to protect the identities of the people who are screened in this study to the extent permitted by law. We also keep your child's information secure and confidential. Electronic study information will be password-protected, and paper files will be stored in a locked office at [Research site]. Your child's screening records will be kept at the clinic/hospital for XX years [*to be adapted locally*] following the completion of the study. If needed to monitor the study quality, your child's screening information may be looked at by institutions responsible for quality and privacy such as the sponsor, Ethics Committee and Competent Authorities.

For the screening, we will store some non-medical information about your child, such as his/her date of birth and city of residence. You can ask us to access, modify, complete, update, or delete this information. If you have any complaints about the protection of your data, you could contact your local/national Data Protection Authority [*Name and contact to be adapted locally*].

The information collected for screening will be used for the following purposes:

- For the purposes of this study. The sponsor, the study doctor, or other doctors involved in the study may publish reports or articles on the screening or present screening findings to scientific groups. After the study is completed, you may see your child's records, and you may be told the results of the study.
- Secondary use for TB research; your coded information may be used and shared with other institutions only for the purpose of further TB research during and after completion of the study and notably with the World Health Organization.

In all cases your child's identity will never be disclosed.

Your child's coded information may be sent electronically to other researchers or institutions. If sent, it will be encrypted (scrambled so it cannot be read by people who shouldn't see it).
We guarantee that, when we send your coded information, it will be protected according to European Economic Area standards.

Subject Identification

Informed Assent and Authorization

Your signature on this document means the following:

I have read this parental consent form. The screening process has been explained to me, including risks and possible benefits, other possible treatments or procedures, and other important things about the study. I have had the opportunity to ask questions. I understand the information given to me. I recognize that my child's participation is voluntary and that I can refuse or end my child's participation at any time, without any loss of benefits that we would otherwise have.

I recognize that by signing this document, I do not lose any of my legal rights as parent/guardian of the participant. I will receive a complete, signed, dated copy of this research screening parental consent form.

By signing below, I give my permission to let my child take part in the screening.

Signature of Parent/Guardian of the Participant:

_____ _____

Signature or thumbprint of parent/guardian of the participant Date (DD/MMM/YYYY) and Time

_____

Name of parent/guardian of the participant, printed in capital letters

Witness (if applicable):

_____ _____

Signature of witness Date (DD/MMM/YYYY) and Time

_____

Name of witness, printed in capital letters

Subject Identification

Study representative who obtained informed assent:

I have explained this study to the parent/guardian of the participant and have answered all of his/her questions. He/she understands the information described in this document and accepts voluntary participation of his/her child in the study.

_____ _____

Signature of study representative Date (DD/MMM/YYYY) and Time

_____

Name of study representative, printed in capital letters

endTB Clinical Trial
Research Adult Consent Form

Version 3.5 Version Date: 15 December 2020

Subject Identification

Protocol Title: endTB (Evaluating Newly approved Drugs for multidrug-resistant TB)

Sponsor: Médecins Sans Frontières (Doctors Without Borders) - France

Principal Investigators: Carole Mitnick, Sc.D. and Lorenzo Guglielmetti, M.D.

Site Principal Investigator: [Insert PI Name]

Research Center: [Insert Research Center Name]

Participant Name (please print): _____

Study Subject ID: _____

About this consent form

Please read this form, called research consent form, carefully. It tells you important information about this study, called endTB. A member of our research team will also talk to you about taking part in this study. People who agree to be in the study are called "participants" in this consent form. Recruitment of participants for this study has been approved by the [Research Center Ethics Committee] [and the applicable national regulatory authority].

If you have any questions about the study or about this form, please ask us. Taking part in this study is up to you. You do not have to be in the study if you do not want to. If you decide to take part in this study, we will ask that you sign this form to confirm that you want to take part. We will give you a signed copy of this research consent form to keep. You can decide not to take part in this study at any time if you do not want to, even after signing this form.

If you are not able to sign the consent form, but you would like to participate, you can ask someone you know to sign for you and you can make a thumbprint to show that you understand the study and would like to take part.

Introduction

You have been asked to join a study called endTB clinical trial. Researchers want to know what combinations of drugs work better for people who have multi-drug resistant tuberculosis (MDR-TB). Drugs work differently in different people, and it is not clear what combination of drugs is best for any one person. The new combinations of drugs used in this study are called "experimental"; they have been used before but we do not know how well they work together.

We are asking you to take part in this study because you are at least [18] years old and have tuberculosis that is affecting your lungs. You completed the screening process of this study and are eligible to take part. During the study, we will do some more tests to make sure that you may safely take part. 750 participants in 8 countries will participate in this study. About [number to be locally adapted] participants will take part at [Research Center Name].

Médecins Sans Frontières (Doctors Without Borders) –France is the sponsor of this study.

Why is this study being done?

Current treatment for MDR-TB has 5-9 drugs taken daily for 18 to 24 months. Treatment may be oral or include a daily shot. In some cases, depending on the characteristics of your MDR-TB, a shorter treatment duration (9 to 12 months) with an all-oral standardized treatment regimen including 7 drugs may be a possible option. This treatment may cause many mild and some serious side effects, for example: feeling sick to the stomach, throwing up, hearing loss, numbness/tingling in fingers and toes, kidney damage, mental illness/feeling sad, etc. Two new drugs (delamanid and bedaquiline) have recently become available. New treatments containing at least one of these drugs may be shorter for example, 9 months and/or simpler (without injection). Such treatments must be tested to see if they are safe and work well for people with MDR-TB. We are asking you to take part in this study to compare new experimental treatment regimens to the current treatment for MDR-TB.

How long will I take part in this study?

It will take you between 1.5 to 2 years (73 to 104 weeks) to complete this study. During this time, we will ask you to make 26 to 30 study visits to [Research Center Name]. All study visits will take place at [Research Center Name].

What will happen in this study?

If you choose to take part in this study, we will ask you to sign this consent form before we start the study with you. If you are currently taking any medications that can't be taken with your study drugs, you may need to stop these medications before you can start taking the study drugs. Your doctor may give you new drugs instead of your current medications. This could make you feel bad. If this happens, please tell the study doctor. If your medication cannot be replaced by other treatment or needs to be stopped for more than 2 weeks before taking study drugs, you may not be able to take part in this study.

At the beginning of the study, you will be assigned by chance (like rolling a dice) to one of 6 treatment groups described below. Most patients will get one of the experimental treatments. A smaller number will get the regular treatment for MDR-TB. We don't know exactly how many patients will get each treatment because, as we learn how the different treatments are performing, more patients will be assigned to the treatments that are helping more patients. You and the study doctor cannot choose your study treatment group.

If you are assigned to an experimental treatment, you will get 4 or 5 study drugs that will be taken by mouth. You will take the study drugs for 39 weeks (9 months).

If you are assigned to the control treatment, you will get the treatment used for MDR-TB according to current practice in your country and to international guidelines from World Health Organization. You will receive medications by mouth and, if needed, by needle shots. The treatment will last for 18 to 24 months, or in some cases from 9 to 12 months.

If you are receiving an experimental regimen with linezolid, one of the drugs used for MDR-TB, we will change your linezolid dose after about 4 months of treatment or earlier if you are having important side effects that might be caused by linezolid. We are looking at two ways to lower the total dose of linezolid: in one, we reduce the daily dosage (dose still daily but lower - for example, 1 pill instead of 2 pills every day) or by giving it less often (same dose but not every day; for example, 2 pills every 2 days instead of 2 pills every day). We do not know if one way is better than the other.

If you are receiving an experimental regimen with linezolid, one of the ways of lowering the linezolid dose will be assigned to you by chance. You and the study doctor cannot choose how your linezolid dose will be reduced.

For all your study drugs at all times during treatment, your study doctor will tell you how many pills of each drug you will take. Study staff will teach you how, how often and where you should take your medications and for how long. You must follow these instructions carefully and should not stop taking the study drugs without telling the study workers. A study worker *[to be adapted locally based on the setting for DOT/treatment support]* will be with you every time you take your study drugs and bring all the unused study drugs back to the [Research Center].

If you miss doses or a study visit, a study worker may call you or go to your home to check if you are well and discuss with you ways to help you keep taking your study drugs and go to your study visits. *[to be adapted locally based on the site set-up]*

With your agreement, the study doctor will inform your regular doctor or other doctors who may be treating you, of your participation in the study.

You will go to the [Research site name] for study visits until at least 73 weeks (17 months) and possibly as late as 104 weeks (24 months) after you start your study treatment. The exact time you spend in the study will depend on the overall progress of the study. You might still be on treatment at the end of the study; if so, we will help you talk to the regular TB doctors to make sure you can finish your treatment.

Visit procedures

All participants have the same visits. What happens at each visit is explained here:

Visit before starting treatment

At this visit, we will:

- Answer all your questions and get your consent to take part in the study.
- Ask about your job and schooling.
- Ask about any changes in your medical history or medicines being taken since the screening visit. The study doctor might change some of your medications and will discuss and recommend birth control methods so you can avoid pregnancy (yourself or your partner) while taking study medications.
- Ask about smoking or alcohol use.
- Perform a brief exam and ask you about TB symptoms.
- Check your vision, hearing, movement, mental health status, and ask about your daily activities.
- Collect ½ tablespoon of blood samples for laboratory testing (we might not do some of these tests if you have had these tests recently); and for a pregnancy test if you are woman who can get pregnant. The pregnancy test might be repeated if the study medications are started a few days after the first test.
- Do an electrocardiogram to check if your heart is working normally.
- Depending on what tests you have had recently, we might:
    - Collect ½ tablespoon of blood sample for CD4 and HIV viral load testing if you are HIV-infected.
    - Ask you to cough up two sputum specimens if you do not already have one test result from the study laboratory to show the TB germ is resistant to rifampin and susceptible to fluoroquinolone.
    - Perform a chest X-ray.

Follow-up Visits (Week 1 to Week 73-104)

After you start taking the study drugs, you will return to [Research site name] for your follow-up visits every week during the first 3 months, then approximately every month until the end. At each visit, our study worker will schedule the next visit and write the date on your study identification card. If you need to change a visit date, please let the study worker know as early as possible. Each visit will take about 1 ½ hours including waiting time.

If needed, your study doctor might call you for additional examinations.

Doctor's exams:

At each visit, we will:

- Ask about any changes in your medical history and any change in medicines you are taking since the last visit. The study doctor may change some of your prescriptions if you are taking medicines that can have interactions with drugs in your TB regimen.
- Perform a brief exam and ask you about TB symptoms and how you are feeling.
- Check if you are taking your study medications correctly and answer all your questions.
- If you are a woman who can get pregnant, we will ask you about your last menstrual period and use of birth control methods. The study doctor might do a pregnancy test.
- The study doctor will discuss and recommend birth control methods so you can avoid pregnancy (yourself or your partner) while taking study medications.
- If you are affected by other diseases, for example hepatitis C, we might collect the exam results that your doctor will prescribe according to clinical routine practice.

Other special exams

- An electrocardiogram will be done to check your heart at every visit until Month 12, then once again at Month 17 (25 times).
- Your vision, hearing, and movement status will be checked every 4 weeks until Month 8, then at Months 9, 10, 11, 17, and 24[1] (up to 15 times).
- Your ability to carry out your daily activities will be reviewed at Months 9, 17, and 24[1].
- Your mental health status will be checked at Months 17 and 24[1].
- A chest X-ray will be done at Months 2, 9, 17 and 24[1].

Collecting your sputum samples

- You will provide 2 sputum samples to our study workers every 2 weeks for the first month for the study, then at Month 2, and then at every visit after Month 3 until study completion.
- You must follow our study workers' instructions on how to collect and pack your samples properly.

[1] Exams after Month 17 will be conducted only if your study follow-up is still ongoing.

Collecting your blood samples

- One tablespoon of blood will be collected at the clinic to check for possible side effects approximately every 4 weeks until Month 11.
- 1/2 tablespoon of blood will be collected for CD4 and HIV viral load at Months 6, 11 and 17 if you are HIV-infected.
- 1/2 tablespoon of blood will be collected to check blood sugar at Months 6, 11, and 17 if you have abnormal blood sugar level at screening/baseline visit.

Stopping or withdrawing from the study early

If you start the study and decide you want to stop, you should tell us. We will make sure that you stop the study safely. We will ask you to make a termination visit. At this visit, we will:

- Ask about changes in your medical history and in medicines you are taking since the last visit.
- Perform a brief body exam and ask about TB-related symptoms and how you are feeling.
- Check your vision, hearing, movement, functional and mental health status.
- Obtain 2 tablespoons of blood for laboratory testing.
- If you are a woman who can get pregnant, we will ask you about your last menstrual period and use of birth control methods. The study doctor might prescribe you a pregnancy test.
- Collect 2 sputum specimens.
- Do an electrocardiogram to check your heart.
- Do a chest X-ray (unless recent results are available).

We will talk to you about follow-up care, if needed.

Also, the study doctor might decide to take you out of the study before you finish it. This might happen because:

- You are a female participant and become pregnant.
- The study doctor thinks it is best for you to stop taking the study drug.
- You can’t make the required study visits.
- We stop doing the study for any reason.

If this happens, the study doctor will explain why you need to stop taking part in the study. We will invite you to come in for the termination visit as described above. We will also help arrange other care for you, if needed.

If your study termination occurs before Week 39 (Month 9) or before Week 73 (Month 17), we will ask to come back for follow-up visits at the time of Week 39 and Week 73.

At this/these visit(s), we will:

- Ask about changes in your medical history and in medicines you are taking since the last visit.
- Perform a brief body exam and ask about TB-related symptoms and how you are feeling.
- Collect 2 sputum specimens.
- Unless recent results are available, we will:
    - Do a chest X-ray,
    - Collect up to 1/2 tablespoon of blood sample to measure your sugar level if it was abnormal when you started the study,
    - Collect up to 1/2 tablespoon of blood sample for CD4 and HIV viral load testing if you are HIV-infected.

The termination visit or the Week 73 follow-up visit will be your last visit for the study.

What will happen to me after the end of the study?

Once you complete your participation in the study, any follow-up of your disease will be done by your regular doctor.

If you complete the study with side effect(s) that are not yet resolved, your study doctor may contact you until the side effect goes away or is stable.

If you decide to leave or are taken out of the study early, and you still have ongoing side effect(s) at this time, your study doctor may contact you until the side effect goes away or is stable. You might also be contacted by your study doctor if you experience a new side effect.

Please let your study doctor know if you do not want to be contacted even for updates on the ongoing side effects. You do not have to give any information that you don't want to.

Managing your Samples and Health Information in the Study

We will label all your samples and health information with a code instead of your name to keep all your information private. The key to the code connects your name to your samples and health

information. The study doctor will keep the key to the code in a password-protected computer and/or locked file.

The samples and bacteria isolates obtained from your sputum samples might be tested for drug resistance confirmation and further analyses on the bacteria in a specialized laboratory in Belgium.

Storing Isolates (strains) and Health Information for Future Research

We would like to store some of the bacteria isolates (TB bug) and health information for future research related to TB, which will be collected during this study. All your health information and bacteria isolates will be handled in a way to keep all your information private. Any use of stored bacteria isolates and your health information for other research inside your country or in other countries will be approved by the ethics committee of your country.

This future research is independent from your participation in the endTB study and your decision to participate in the future research will not affect your participation in the study. The bacteria isolates found in your sputum samples and your health information may be stored for up to 20 years in a special place (bank or repository) created to safely store them. The stored isolates and your health information will be used only to help future research in TB and to improve diagnosis (including resistance testing) and treatment of TB. During your participation in the endTB study, and the following storage period of 20 years after completion of the study, you can contact your study doctor or the email address endTB.clinicaltrial@paris.msf.org to request any information regarding the use, storage and location of your health information and bacteria isolates.

Do you agree that your health information and bacteria isolates found in your sputum samples may be stored for 20 years and used only for future TB research? You are free to refuse such storage and further use for TB research of your health information and bacteria isolates and you will still be able to take part in the study.

☐Yes ☐No [Initials or signature, to be adapted locally]_____

You have the right to change your mind, and to later want your health information and/or bacteria isolates destroyed. In that case, during your participation in the endTB study, and the following storage period of 20 years after completion of the study, you can contact your study doctor or the email address endTB.clinicaltrial@paris.msf.org to request any information regarding the use, storage and location of your health information and bacteria isolates and/or their destruction.

Will anything bad happen to me from being in this study?

Risks of Taking Study Drugs:

You will take a combination of MDR-TB drugs when you are on this study, whether you get an experimental treatment or the control treatment. The drugs used in the control are the nation's standard MDR-TB medications, according to international guidelines from World Health Organization. Experimental treatments will use together 4 or 5 of the following drugs: bedaquiline, delamanid, clofazimine, linezolid, moxifloxacin, levofloxacin, and pyrazinamide.

Medications for MDR-TB have different side effects. We do not know which of the combinations is the easiest to take. Your doctor will tell you the most common side effects that you may have while taking study treatment and you will be given a document entitled "participant information leaflet" that summarizes the main side effects. There may be other risks of the study drugs that are not known yet. You will be closely followed through clinical, laboratory and other examinations (hearing test, heart test) in order to detect and treat promptly possible side effects. And, your doctor will explain more in detail when you should get in touch with him/her.

As with any drug, an **allergic reaction** can happen. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing.

Some of the drugs may have an effect on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant. It is possible that this effect is unknown and may be harmful. Because of these unknown risks, women cannot start this study if they are:

- known to be pregnant;
- trying to become pregnant;
- unwilling or unable to stop breastfeeding an infant.

If you are a menopausal woman and have not had a menstrual period for the past 12 months or more, you will not need to have a pregnancy test and are not considered able to become pregnant. Also, if you have had any well-documented method of surgical sterilization, you will not need to have a pregnancy test and are not considered able to become pregnant. Methods of surgical sterilization include having had a hysterectomy (removal of the uterus), bilateral oophorectomy (removal of both ovaries), a tubal ligation (having your tubes tied), and transvaginal occlusion (plugging the opening of the tubes with a coil). All other women must have a negative pregnancy test before starting the study drugs.

Regardless of your sex, if you are sexually active and able to become pregnant or father a child, you must agree to abstain from sex (have no sex) or use acceptable birth control (methods listed below) while taking study drugs. Your doctor may also discuss with you the use of birth control after you finish taking your study drugs. Acceptable birth control may be achieved by using a single "highly effective" method or by using a combination of other methods.

Acceptable "highly effective" single birth control methods for use in this study are:

- Hormonal method: birth control pills, patches, injections, vaginal rings, or implants.
- Intrauterine device (IUD).

An acceptable combination birth control method for use in this study is:

Condom (male or female)[2] used with or without a spermicide[3] AND one of the following used with a spermicide[3]: diaphragm, cap, or sponge;

These options are also summarized in the table below:

Method	**Use alone or in combination.**[2,4]
Hormonal method: birth control pills, patches, injections, vaginal rings, or implants.	Highly effective alone; needs no combination.
Intrauterine device (IUD).	Highly effective alone; needs no combination.
Condom (male) used with or without a spermicide. [3,2]	To be used in combination with one of the following: diaphragm, cap, or sponge AND spermicide.[3]
Condom (female) used with or without a spermicide.[2,3]	To be used in combination with one of the following: diaphragm, cap, or sponge AND spermicide.[3]
Diaphragm, cap, or sponge used with a spermicide.[3]	To be used in combination with male or female condom[2], with or without spermicide.

For female participants, if you miss a period, or think you might be pregnant during the study, you must tell the study doctor immediately. *[to be adapted locally]* If you become pregnant, your treatment might be changed and you might stop taking part in the study. The study doctor will ask for permission to collect information about the outcome of your pregnancy and the condition of your newborn.

For male participants, if your female partner becomes pregnant, we would like to follow the outcome of the pregnancy. You should let us know immediately if your partner becomes pregnant. You will not have to stop taking the study drugs or stop taking part in the study if your partner becomes pregnant.

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[2] Male and female condom should not be used together.
[3] Spermicide: a foam cream or gel that kills sperm.
[4] Withdrawal (coitus interruptus) and/or periodic abstinence during fertile times are unacceptable on their own but may be used in combination with any highly effective method or acceptable combination.

Risks of Taking the Study Drugs with Other Medications

Some drugs are not safe to be taken together with the study medications, or may not work when taken with the study medications. Please inform and consult your study doctor if, at any time of the study, you are prescribed or begin using any other medications.

For your safety during this study, call your study doctor BEFORE you take any:

- new medications prescribed by another doctor;
- other medications sold over-the-counter without a prescription;
- dietary or herbal supplements.

Risks of Blood Draws

You may have a bruise (a black and blue mark) or pain where we take the blood samples. There is also a small risk of infection, light-headedness, and/or fainting.

What are the possible benefits from being in this study?

By participating in the study, you may receive a shorter all-oral treatment compared to the current treatment recommended for MDR TB. There is no guarantee that any of these shorter treatments will work better than the current [18 to 24 – *to be adapted if short regimen available*] months standard treatment. During this study, we will learn more about the treatments and use the information to assign more patients to treatments that are helping other patients. When you receive the study drugs, we expect your medical condition/symptoms to improve. It is also possible that the TB bacteria are or become too strong to be killed by the study drugs you receive. If that happens, your study doctor will change your treatment. You will have more tests that allow the doctors to know what kind of anti-TB drugs they should use. The study doctors can also take care of your side effects sooner and better by having those extra tests. However, it may be harder for you to be cured if very few drugs work against your TB bacteria.

You will receive greater treatment support from the study team throughout the study than during regular MDR-TB treatment. Others with MDR-TB may benefit in the future from what we learn in this study**.**

What other treatments or procedures are available for my condition?

You do not have to take part in this study to be treated for MDR-TB. Other treatment is available to treat MDR-TB in your country through [local TB care provider/entity]. This treatment is similar to that in the control arm in the study. It is a combination treatment with several drugs. Your doctor will recommend treatment for either 18-24 months or for 9-12 months. In some cases, it will include a daily shot of about 6 months. Talk with the study doctor if you have questions about the other treatment.

Can I still receive TB treatment if I do not take part in this study?

Yes. Taking part in this study is up to you. You can decide not to take part. You will receive treatment through [local TB care provider/entity] if you do not take part in this study. There will be no penalty, and you will not lose any benefits you receive now or have a right to receive. The treatment outside the study is also free of charge.

What should I do if I want to stop taking part in the study?

If you take part in this study and decide you want to stop, you should tell us. We will make sure that you stop the study safely.

Also, it is possible that we will have to ask you to leave the study before you finish it. If this happens, we will tell you why.

We will tell you if we learn any new information that could make you change your mind and choose to leave the study.

If any of these happens, we will talk to you about follow-up care, if needed, and you will be encouraged to come back at least for one additional visit ("termination visit").

Information collected during your participation will be used to help answer study questions. When you leave the study, your health information, and information obtained from sputum samples and bacteria isolates previously collected may still be used and stored for 20 years for the study and future TB research. However, if you prefer this information is not used and that it is destroyed, you can contact your study doctor or the email address endTB.clinicaltrial@paris.msf.org.

Will I be paid to take part in this study?

You will not be paid to take part in this study. We will pay the transportation costs for study visits. You will also receive [local arrangement for monthly food supplements] when you take part in the study. In sum, you will be reimbursed [local currency] _____ for transportation for the baseline visit, [local currency] _____ for each follow-up visit, for any unscheduled visits, and [local currency] _____ for your final visit.

What will I have to pay for if I take part in this study?

You will not have to pay in order to take part in this study. You also will not have to pay for the study drugs, or for any study-related procedures and visits.

What happens if I am injured as a result of taking part in this study?

The sponsor has made insurance arrangements to pay for an injury you suffer due to your participation in the study.

If you suffer physical injury from this study please inform your doctor and seek medical attention right away, _____ will ensure that you receive appropriate medical treatment.

[Research site name] will not pay to treat a medical condition or disease you had before joining this study or expenses for injury, treatment, or hospitalization you may require that are not the result of your participation in the study.

In an emergency, the study sponsor has made plans to pay for your visit to see a specialist, the related treatment, and/or your stay in the hospital. For non-urgent situations, the sponsor may pay for your visit to see a specialist. The study team will review your situation and decide whether the sponsor will pay for the resulting treatment if your condition is not the result of your participation in the study.

Who can I speak to if I have questions, concerns or complaints?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

[PI Name and title] is the person in charge of this study. You can call him/her at [PI telephone number]. You can also call [Clinical Investigator] at [CI number] with questions about this study. If you have questions about the scheduling of appointments or study visits, call [Study Coordinator] at [SC number].

For medical emergencies outside business hours, please contact **[Must include 24/7 phone number of licensed site physician investigator here].**

If you want to speak with someone not directly involved in this study, please contact the [Research Center IRB] office. You can call them at [Research Center IRB number].

If I take part in this study, how will you protect my privacy?

We are careful to protect the identity of the people in this study to the extent permitted by law. We also keep your information secure and confidential. Electronic study information will be password-protected, and paper files will be stored in a locked office at [Research site]. Your study records will be kept at the clinic/hospital for XX years [*to be adapted locally*] following the completion of the study. If needed to monitor the study quality, your study information and other information about you may be looked at by institutions responsible for quality and privacy such as the sponsor, Ethics Committee and Competent Authorities.

For the study, we will store some non-medical information about you, such as your date of birth and city of residence. You can ask us to access, modify, complete, update, or delete this information. If you have any complaints about the protection of your data, you could contact your local/national Data Protection Authority [*Name and contact to be adapted locally*].

The information collected for this study will be used for the following purposes:

- For the purpose of this study. The sponsor, the study doctor, or other doctors involved in the study may publish reports or articles on the study or present the study findings

to scientific groups. After the study is completed you may see your records, and you may be told the results of the study.

- Secondary use for TB research; your coded information may be used and shared with other institutions only for the purpose of further TB research during and after completion of the study and notably with the World Health Organization.

In all cases your identity will never be disclosed.

Your coded information may be sent electronically to other researchers or institutions, If sent, it will be encrypted (scrambled so it cannot be read by people who should not see it).

We guarantee that, when we send your coded information, it will be protected according to European Economic Area standards.

Subject Identification

Informed Consent and Authorization

You completed the screening process for this study and are eligible to take part, or you completed the screening process for another study (endTB-Q) and were found to be eligible for this study (endTB). In the second case, you agree that your data and personal information collected during endTB-Q screening will be used for the endTB study.

Your signature on this document means the following:

I have read this consent form. This study has been explained to me, including risks and possible benefits, other possible treatments or procedures, and other important things about the study. I have had the opportunity to ask questions. I understand the information given to me. I recognize that my participation is voluntary and that I can refuse or end my participation at any time, without any loss of benefits that I would otherwise have. I recognize that by signing this document, I do not lose any of my legal rights as a participant. I will receive a complete, signed, dated copy of this research consent form.

By signing below, I agree to take part in this study.

Signature of Participant

_____ _____

Signature or thumbprint of participant Date (DD/MMM/YYYY) and Time

_____

Name of participant, printed in capital letters

Witness (if applicable):

_____ _____

Signature of witness Date (DD/MMM/YYYY) and Time

_____

Name of witness, printed in capital letters

Subject Identification

Study representative who obtained informed consent:

I have explained this study to the participant and have answered all of his/her questions. He/she understands the information described in this document and accepts voluntary participation in the study.

_____ _____

Signature of study representative Date (DD/MMM/YYYY) and Time

_____

Name of study representative, printed in capital letters

Schedule of Visits

Visit	Consent	Doctors' Exam	Nurses' Interview	Blood Collection	Sputum Collection	ECG	Chest X-ray
Baseline	✓	✓	✓	(✓)	(✓)	✓	(✓)
Week 1		✓	✓			✓	
Week 2		✓	✓		✓	✓	
Week 3		✓	✓			✓	
Month 1		✓	✓	✓	✓	✓	
Week 5, 6, 7		✓	✓			✓	
Month 2		✓	✓	✓	✓	✓	✓
Week 9, 10, 11		✓	✓			✓	
Month 3, 4, 5, 6, 6.5, 7, 8		✓	✓	✓	✓	✓	
Month 9		✓	✓	✓	✓	✓	✓
Month 10, 11		✓	✓	✓	✓	✓	
Month 12		✓	✓		✓	✓	
Month 13.5, 15		✓	✓		✓		
Month 17		✓	✓	(✓)	✓	✓	✓
Month 19, 20, 22[1]		✓	✓		✓		
Month 24[1]		✓	✓	✓	✓		✓