Division of Medicine
Middlemore Hospital
Counties Manukau Health
Private Bag 93311, Otahuhu
Auckland 1640

Participant Information Sheet

Study title:	**Oral resveratrol supplementation in bronchiectasis**		
Locality:		Ethics committee ref.:	
Lead Investigator:	**Dr Benjamin Diggins**	Contact phone number:	(09) 276 0044

INTRODUCTION

You are invited to take part in a clinical research study. Your participation is entirely voluntary (your choice). Before you decide to take part, you need to understand why we are doing the research and what it will involve. Please ask us if there is anything that is not clear or if you would like more information. We can provide you with an interpreter if you require one. Your family/whaanau is welcome to attend the study visits with you.

This study is funded by Counties Manukau Health. The ethical aspects of this study have been approved by the ___ Health and Disability Ethics Committee on the ____, reference ___.

PURPOSE OF THIS STUDY:

Bronchiectasis is a troublesome disease, due to inflammation and damage in the airways. Common symptoms are productive cough with sputum (phlegm) and feeling breathless. Patients often experience repeated chest infections. The **main aim** of this study is to assess whether resveratrol reduces inflammation in the lungs. We will also assess whether the effects in the bloodstream, and if resveratrol improves your quality of life. We will assess the effects of resveratrol on bacteria that live in your lungs.

This study will also provide important information that will help develop a larger study in future. This future study would assess whether resveratrol can prevent flare-ups of symptoms (exacerbations) in patients with bronchiectasis.

WHAT IS THE STUDY TREATMENT?

The study will use a nutritional supplement called “resveratrol”. Resveratrol is found naturally in a variety of foods. These foods include grapes, red wine, and berries. In laboratory studies resveratrol can reduce inflammation and kill harmful bacteria that commonly cause problems in bronchiectasis.

Transmax contains 98% resveratrol and comes as a capsule. It contains much higher levels of resveratrol than can be taken in the diet, and higher levels than in many resveratrol preparations.

In this study, eligible participants will take either one Transmax capsule twice a day (total 1000 mg a day) or two Transmax capsules twice a day (total 2000 mg a day), for 12 weeks. Transmax will be provided free of charge for the duration of the study.

STUDY DESIGN

Participants we be assigned randomly, with a 50 percent chance, to one of two options: either one capsule twice a day, or two capsules twice a day. You and the study investigators will know which treatment is given. The study will have a "Data Monitoring Committee". This committee will monitor side-effects and safety aspects to help ensure the safety of participants in the study.

Informed consent

In a research study, informed consent may be given when a person is informed of all the important points about the study, clearly understands this information, and signs and dates a consent form to acknowledge that they consent to take part.

This information sheet describes the purpose, procedures, potential benefits, known risks and potential adverse effects and precautions of the study. It is important to read and understand this information sheet. You can discuss any questions with the study doctor or study staff. Please feel free to discuss the study with your friends, family, whaanau, legal representative and/or general practitioner (GP) to help you decide.

If you agree to take part, you must sign and date the informed consent form before any study-related procedures are carried out. By signing this form, you show that you understand what the study involves and that you agree to take part. You will be given a copy of this information leaflet and consent form to keep.

We will also inform your GP that you are participating in this clinical trial and taking Transmax. They can contact the study team if there are any questions or concerns relating to the study. This is particularly important if you experience any side effects.

Qualifying for this study

If you meet all the inclusion criteria, and are willing to participate in this study, the study doctor will ask you questions about your health. This is to confirm that you qualify for the study.

You should tell the study doctor about all treatments and medications that you take. This includes any supplements, remedies and vitamins. You should also tell the study doctor about any other research studies or if you are enrolled in any other medical research projects.

WHY HAVE I BEEN ASKED TO TAKE PART?

You are being invited to take part in this study because you have a condition called bronchiectasis. All participants need to meet all of the inclusion criteria, but none of the exclusion criteria before they can take part (please see below).

WHO CAN TAKE PART IN THE STUDY?

Your study doctor will check that you meet the following inclusion requirements before you can enter the study.

You will be eligible for the study if you meet the inclusion criteria

- Are aged 18 years or more
- Are able to provide written informed consent
- Have bronchiectasis confirmed by a high-resolution CT scan of chest, done within the last 5 years
- Have stable lung symptoms and no antibiotic treatment during the 4-week period before visit 2
- Have had at least one chest infection requiring antibiotics in the past 12 months
- Produce a good sputum sample at visit 2

You will not be eligible for the study if you have any of the following exclusion criteria:

- Any serious co-existing illness affecting participation in the study
- Cystic fibrosis
- A chest infection requiring antibiotics or prednisone 4 weeks before starting Transmax
- Allergic bronchopulmonary aspergillosis
- Taking treatment for tuberculosis
- Active cancer (basal cell carcinoma of the skin is allowed)
- Taking oral or intravenous antibiotic treatment within 4 weeks before visit 1 (including macrolide antibiotics such as roxithromycin, erythromycin, and azithromycin)
- Currently taking, or have recently taken within the last 4 weeks, continuous oral steroids (e.g. prednisone) or other immune suppressing medications for more than 6 weeks
- Body mass index (BMI) < 18.5 kg/m^2
- Female patients who are pregnant or breast-feeding
- Cannot take medication regularly
- Cannot complete questionnaires
- Are already taking part in another clinical trial
- Allergy to any of the components of Transmax

HOW MANY PARTICIPANTS WILL BE INVOLVED?

We plan to recruit a total of 40 participants to take part in this study from the Counties Manukau region.

WHERE WILL THE STUDY BE CONDUCTED?

The study will be conducted at Middlemore Hospital.

HOW LONG WILL THE STUDY LAST?

The total amount of time that you will be involved in the study is 12 weeks. There is also a screening period, which takes place 2 to 4 weeks before the start of the study.

Following this, there are a total of 3 further visits or the study. You will also receive 2 telephone calls by research staff to check on your progress. Each visit will take 1.5 to 2 hours.

STUDY PROCEDURES

If you decide to take part, you will be asked to sign a consent form.

If, at any time during the study, it is not considered suitable for you to take part or continue, you will be withdrawn from the study and continue with your usual treatment.

You will be required to follow the following requests fully:

- Attend all study required clinic visits (4 visits in total)
- Take the study drug daily as requested for 12 weeks
- You should provide as accurate information as you can about your personal details, your health and medication history to study staff
- You will need to have a high-resolution CT scan of the chest if you have not had one within the past 5 years
- Have a physical examination at all study visits
- Have your vital signs (blood pressure, pulse rate, respiratory rate, temperature, and
- oxygen level) measured and recorded at all 4 visits
- Perform lung function tests (spirometry) at all 4 visits
- Have blood samples collected at visits 1, 2, 4.
- Have sputum samples collected at visits 2, 3 and 4. If you are unable to produce sputum, a sample can be "induced" by inhaling a salty solution via a nebulizer at visit 3 and 4
- Have a urine sample collected for pregnancy test (if applicable) at visit 2 and visit 4
- Complete daily diary cards for the duration of the study
- Complete questionnaires at visits 2, 3 and 4
- Respond to phone calls asking about flare-ups (exacerbation) & side-effects at weeks 2 and 8
- Bring completed daily diary cards with you to each visit
- Bring all study medication packages (used or un-used) with you to each follow-up visit

WHAT WILL HAPPEN TO MY TISSUE SAMPLES?

You will be asked to provide sputum samples at visits 2, 3 and 4 and blood samples at visits 1, 3 and 4 (10-20ml in total). We will send your sputum and blood samples to laboratories at the University of Auckland and Middlemore Hospital. These samples will only be used for the purpose of the study. At the end of the study, they will be destroyed by incineration by the laboratory. Blood will be used for safety tests (blood cell counts, kidney and liver function) and markers of inflammation. We will also measure levels of resveratrol and antioxidants in the blood. Sputum samples will be sent for analysis of markers of inflammation, resveratrol and antioxidant levels, and markers of antibacterial activity. We will also analyse sputum samples to determine what bacteria are present and if these change during the study.

You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with storing your tissue should be discussed with your family/whaanau as appropriate. There are a range of views held by Maaori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose.

POTENTIAL RISKS AND DISCOMFORTS

With any treatment, it is possible that there are complications and undesirable side effects (adverse effects) that are unknown at this time. While you are in this study, you should notify the study staff of any new symptoms that you experience and of any other medications that you use (over-the-counter, prescription, or recreational).

Safety of resveratrol

Resveratrol is found naturally in a range of foodstuffs at relatively low levels. A number of clinical trials have studied resveratrol and found it to be very safe, even at extremely high doses of up to 5 grams per day. In this study, the total daily dose is either 1 gram (one Transmax 500 mg capsule twice a day), or 2 grams (two 500 mg capsules twice a day).

At these doses, side effects are rare but include mild gastrointestinal disturbance, especially nausea (feeling sick). At very high doses, some people reported headache and muscle aching. In one study, some participants who took resveratrol lost weight. Therefore, we will measure your weight at each visit. If your body mass index is less than 18.5 kg/m^2 at the start of the study, you will not be eligible to participate.

Blood samples

Blood will be taken from a vein in your arm. This may cause discomfort and occasionally bruising.

Induced sputum samples by inhaling a high concentration salt solution

This involves breathing in nebulized air containing salt to induce coughing to produce a sputum sample. This can be uncomfortable. Most people do not have any side effects but in some people, a high concentration salt solution may cause narrowing of the breathing tubes (bronchospasm). We will give you 4 puffs of an inhaler (Salbutamol) prior to inhaling the solution to prevent this occurring.

POTENTIAL BENEFITS

There is no guarantee that you will receive any direct medical benefit from participating in this study. This study will be part of an effort to collect more information about the effect of resveratrol in patients with bronchiectasis. Some participants may benefit from having more frequent, regular visits to study staff and close monitoring of their bronchiectasis.

YOUR RESPONSIBILITIES AS A PARTICIPANT IN THIS STUDY

If you take part in this study, there are some things you are requested to do:

- Follow all instructions given to you by the study doctor and study staff.
- Attend all study follow up visits and take the supplied Transmax as instructed
- Complete diary cards daily
- Tell the study doctor or nurse about all medicines that you are currently taking including prescription, over-the-counter, vitamins, herbal and rongoa (traditional Maaori medicines) or any other treatments; and report any change in your medications

- Contact study staff for information related to the study if you are in doubt

WITHDRAWAL AND TERMINATION

Your participation in the study is voluntary (your choice). You can choose not to take part, or you can start the study and withdraw at any time, without giving a reason. If you choose not to participate, or to withdraw from the study, this will not affect your current or future treatment and it will have no effect on your rights or benefits to which you would otherwise be entitled.

Your study participation could be discontinued by the study doctor, without your consent, for any of the following reasons:

- The regulatory authority or ethics committee cancels the study
- The study doctor feels it is in your best interest to withdraw you from the study
- You do not meet the study requirements to continue
- You do not follow the directions given by the study doctor

If you decide to withdraw from the study, please notify the study doctor or nurse so that we can make sure you have the right ongoing health management.

COSTS, REIMBURSEMENTS AND PAYMENTS

You will not be paid for your participation in the study. However, parking costs related to study visits will be reimbursed, and travelling costs will be subsidized with a petrol voucher. If you use public transport, then reimbursement for this can also be discussed and provided.

CONFIDENTIALITY

If you agree to take part in the research, the study doctor and study staff will collect and record personal information about your health and your treatment. This includes medical information from hospital records and your GP, and information collected during the study.

Confidentiality is of great importance to the study team. All information collected about you is identified by a code number and your initials. Your name and address will be removed. The study team will maintain confidentiality when accessing, keeping, processing and in publication of information related to your participation in the study, i.e. your name will not be disclosed outside the clinic unless required by law.

Once raw data and your information has been analysed, it will be archived at Middlemore Hospital at a secure, restricted access archiving facility. After 10 years, the data will be securely destroyed.

Your study doctor is responsible for keeping a coded list to link your assigned number to your name. This will be kept in a safe place to ensure that in case of an emergency you can be identified and contacted. The code list will be kept for at least 10 years from the end of the study and after for as long as necessary to comply with legal, regulatory, scientific, or other requirements. It will then be securely destroyed.

Personal information about your health and treatment from the study may be processed by or transferred to other parties for clinical research and safety reporting purposes. This includes: (1) regulatory agencies and other health authorities; and (2) the ethics committee. This information will be de-identified.

Within New Zealand, all information collected during the study will be handled in accordance with New Zealand's privacy regime including the Privacy Act 1993 and the Health Information Privacy Code 1994.

The results of this research study may be presented at meetings or in publications. However, you will not be personally identified in any presentations or publications.

If you withdraw your consent, the study doctor will continue to use your health information collected up to that time under this consent, to preserve the scientific integrity of the study.

If you do not sign this consent form, you cannot participate in the study. If you cancel this consent in the future, you will no longer be able to participate in the study. For further information regarding cancellation, see the WITHDRAWAL AND TERMINATION section above. By signing this informed consent form, you are authorizing the uses and disclosures of personal information about your health and treatment identified in this informed consent form. You will not lose any of your legal rights as a research participant by signing this informed consent form.

COMPENSATION FOR INJURY

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Accident Compensation Act 2001. ACC cover is not automatic, and your case will need to be assessed by ACC according to the provisions of the Accident Compensation Act 2001. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors, such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses, and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators.

If you have any questions about ACC, contact your nearest ACC office or the investigator.

You are also advised to check whether participation in this study would affect any indemnity cover you have or are considering, such as medical insurance, life insurance and superannuation.

QUESTIONS / CONTACT

You are free to ask questions at any time. If you have any questions about this study or in case of any injury or illness, you should contact:

Principal Investigator: **Dr Benjamin Diggins**
Phone: **(09) 276 0044 extension 57956**

If you require Maaori cultural support, talk to your whaanau in the first instance. This study will be reviewed and approved by _____, who is able to address any study specific questions or any concerns relating to Tikanga or cultural issues.

If you have any questions or concerns about your rights as a participant in the study, you can contact an independent health and disability advocate. This is a free service provided under the Health and Disability Commissioner Act.

Telephone: (NZ wide): 0800 555 050
Free Fax (NZ wide): 0800 2787 7678
Email: advocacy@hdc.org.nz

If you are unsure of your legal rights, you should seek legal advice. This can be free from your community law centre, Citizens Advice Bureau or from your lawyer which would incur a fee.

STATEMENT OF APPROVAL

This study had received ethical approval from the Health and Disability Ethics Committee.

Thank you for reading this information

Consent Form

If you need an INTERPRETER, please tell us.

Study title:	**Oral resveratrol supplementation in Bronchiectasis**		
Locality:		Ethics committee ref.:	
Lead investigator:	**Dr Benjamin Diggins**	Contact phone number:	**(09) 276 0044**

Please tick to indicate consent to the following:

I agree to take part in the research study titled and have had time to consider participation.	
I have read and understand the participant information leaflet dated 9th March 2020 for volunteers taking part in this study. I have had the trial explained to me and been informed about what I am expected to do.	
I have had the opportunity to discuss this study with the study doctor. I am satisfied with the answers I have been given and that I have had sufficient time to consider whether to participate.	
I have had the opportunity to use whaanau / family support, a friend or legal representative to help me ask questions and understand the study.	
I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and the information sheet.	
I consent to the research staff collecting and processing my information, including information about my health.	
If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.	
I agree to an approved auditor appointed by the Health and Disability Ethics Committee, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.	
I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time. This will not affect my continuing health care.	
I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.	

I understand the compensation for injury provisions for this study.	
I understand that a sample of my tissue will be taken and stored for analysis at the Middlemore Hospital Laboratory.	
I understand that all blood and sputum collected from me during the trial for analysis will be destroyed after completion of analysis by incineration according to Good Laboratory Practice.	
I know who to contact if I have any questions about the study in general.	
I understand my responsibilities as a study participant.	
I consent to my GP being informed about my participation in the study	
I wish to see a copy of the published results from the study.	Yes / No

STATEMENT BY PARTICIPANT OR LEGAL REPRESENTATIVE: I hereby consent to take part in this study:

_____ _____

Name of participant (First and Last name in block capitals) Date

_____

Signature of participant or legal representative

STATEMENT BY INVESTIGATOR: I have explained and discussed with the participant the nature, purpose, demands and possible effects of the study:

_____ _____

Name of Investigator (co-investigator) (First and Last name in block capitals) Date

_____

Signature of Investigator / co-investigator