PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Short Title:	A Phase 2 Study to Assess the Safety, Tolerability and Effectiveness of ATB1651 in Adults with Mild to Moderate Onychomycosis (Fungal Nail Infection)
Protocol Number:	ATB1651-102
Sponsor:	AmtixBio Co., Ltd. 2-606, 61, Madeul-ro, 13-gil Dobong-gu, Seoul, 01413 Republic of Korea
Principal Investigator:	Christchurch: Dr Cory Sellwood Auckland: Dr Aidan Cabezas-Hayes
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Phone Number:	Christchurch: 0800 862 278 Auckland: 0800 788 3437
Ethics Number:	2023 FULL 19342

This is the second time that ATB1651 will be studied in humans with mild to moderate Onychomycosis.
You may not get any health benefit from the drug used in this study; but there are risks of you having a drug reaction, injury, or illness.

You are invited to take part in a clinical research study. This study will test an experimental drug, named ATB1651, that may potentially be used for the treatment of mild to moderate onychomycosis. ATB1651 is an investigational product because it has not been approved by the New Zealand MedSafe or other drug regulatory authorities.

This Participant Information Sheet will help you decide if you'd like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. We expect this will take about 30-60 minutes. You do not have to decide today whether or not you will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

Whether or not you take part is your choice. If you don't want to take part, you don't have to give a reason, and it won't affect the care you receive. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

Please make sure you have read and understood all the pages of this document including the consent form.

1 WHY ARE WE DOING THE STUDY?

1.1 Purpose

Onychomycosis is contagious fungal infection of the fingernails or toenails that causes discoloration, thickening, and separation from the nail bed. It affects about 6% to 8% of the adult population contributing to almost half of all nail problems. Onychomycosis is predominantly a cosmetic problem but can be uncomfortable and can lead to cellulitis (bacterial skin infection) or in severe cases detachment can occur. Eradication of the infection is vital to improving appearance and avoiding these complications but is not easily accomplished due to the poor blood supply to nails. Current treatments have low effectiveness and low cure rates with a high chance of the infection returning. Therefore, there is an unmet need for effective treatment and eradication of onychomycosis.

ATB1651 is being developed for the treatment of mild to moderate onychomycosis. ATB1651 is an antifungal agent that is able to penetrate the affected nail, ultimately preventing further fungi growth and potentially eradicating the onychomycosis.

ATB1651 has already been tested in a smaller research study of patients with mild to moderate fungal nail infections who applied the treatment for 4 weeks. This larger study is to test the safety of ATB1651 and the effect of ATB1651 on your fungal nail infection when applied to the infected toenails for at least 12 weeks and up to 20 weeks. The researchers will also measure the amount of ATB1651 in your blood (called pharmacokinetics).

1.2 Study Design

This study will include approximately 90 participants with mild to moderate onychomycosis in 3 groups of 30 participants. After the results from these 3 groups have been reviewed, the Sponsor may also decide to include additional groups.

This is a randomised, blinded, placebo-controlled study:

Randomised means that the study medication you take (drug or placebo) will be assigned randomly (by chance).

Blinded means that neither you nor your study doctor will know whether you will be receiving ATB1651 or placebo. In an emergency, the study doctor can find out what you are receiving.

Every person in the study will receive multiple doses of ATB1651 or placebo (a substance that looks like ATB1651 but contains no active medication). Each application needs to completely cover the targeted toenail and the tip of the tube can be used to gently spread the solution to cover the entire all and only infected toenail.

Up to 6 dose groups (cohorts) are planned for the study, with 30 participants in each group. The group you are assigned to will depend on when you join the study. You will apply the study drug (ATB1651 or placebo) to all and only infected toenails either once a day or twice a day, according to your assigned study group. Details for the dosing groups are as follows:

Cohort	Dose of ATB1651 or Placebo	Dosing Frequency
1	3% solution (30 mg/mL)	Applied once daily (to all infected toenails for 12 weeks)
2		Applied once daily (to all infected toenails for 20 weeks)
3		Applied twice daily (to all infected toenails for 12 weeks)
4*	5% solution (50 mg/mL)	Applied once daily (to all infected toenails for 12 weeks)
5*	2% solution (20 mg/mL)	Applied once daily (to all infected toenails for 36 weeks)
6*	3% solution (30 mg/mL)	Applied once daily (to all infected toenails for 36 weeks)

*Optional cohorts 4, 5 and 6 may be enrolled at the sponsor's discretion

Whether you receive active study drug or placebo will be assigned randomly (by chance). You will have a 5 out of 6 (83 %) chance of receiving ATB1651.

Participants in Group 1 will start treatment first and Group 2 will start treatment at least 4 weeks later. A safety monitoring committee will review the study data for any unacceptable side effects, and decide if it is acceptable for Group 2 to continue treatment to 20 weeks and for Group 3 to start treatment twice a day. The safety monitoring committee and the Sponsor will review all of the study data and decide whether to proceed with Groups 4, 5 and/or 6. You will be told which dose group you will be in. You will also be told if any changes are made to the planned dose for your group.

While you take part in the study, you will be required to attend the study site for the visits and procedures described in section 2. These include:

- A Screening visit to determine if the study is suitable for you.
- Visits every 2 weeks while you are receiving study drug (the 'Treatment Period').
- Follow-up visits to check on your health.
- A visit at the end of the study.

Your study doctor may ask you to come for additional visits for your health and safety.

Blood samples and other tests to measure study drug levels and effects on the body will be collected at specific time points during the study, your safety will be monitored, and any changes in your health will be recorded.

1.3 Nature and Sources of Funding of the Study

This research project is being conducted and funded by AmtixBio Co., Ltd. and locally sponsored in New Zealand by Novotech, New Zealand a Contract Research Organisation (CRO) which help conduct and monitor the study in New Zealand.

By taking part in this research study, you agree that data generated from your assessments throughout the study, will be provided to the Sponsor. The knowledge gained from this data may lead to new discoveries, which would assist them in obtaining approval for a new drug and benefit the sponsor financially. There would be no financial benefit to you from these discoveries.

New Zealand Clinical Research (NZCR) will receive a payment from AmtixBio Co., Ltd. for undertaking this research project.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

1.4 Approval by Ethics Committee.

This study has been reviewed by an independent group of people called a Health and Disability Ethics Committee (HDEC). The ethical aspects of this research project have been approved by the **Northern A** Ethics Committee.

A description of this clinical study will be available on http://www.ClinicalTrials.gov. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

2 WHAT WOULD YOUR PARTICIPATION INVOLVE?

Participation in this study will last up to approximately 42 weeks (46 weeks in groups 5 and 6), including a screening, treatment, and follow-up period. If you wish to participate in this study, you will be asked to sign this consent form before any study assessments can be performed.

The details of the study and tests performed are discussed and shown below. During the screening period, assessments will be done to check whether the study is suitable for you. The day you have your first dose of ATB1651 (or placebo) is called Day 1 (week 1) and all other days are counted back or forward from this.

The results of the screening assessments will determine whether or not you can take part in the study. If you don't meet the screening criteria, the reasons will be explained. Your study doctor or treating physician will talk to you about other possible treatments.

Visit every 2 Weeks of Treatment Period:
If you are assigned to Group 1 or Group 4, you will apply study drug (ATB1651 or placebo) once a day for 12 weeks. During this treatment period, you must visit the study site every 2 weeks:

- *Week 2 (Day 14), Week 4 (Day 28), Week 6 (Day 42), Week 8 (Day 56), Week 10 (Day 70), and Week 12 (Day 84).*
- You must arrive at the study site before the time of day that you usually apply your study drug.

If you are assigned to Group 2, you will apply study drug (ATB1651 or placebo) once a day for 20 weeks. During this treatment period, you must visit the study site every 2 weeks:

- *Week 2 (Day 14), Week 4 (Day 28), Week 6 (Day 42), Week 8 (Day 56), Week 10 (Day 70), Week 12 (Day 84), Week 14 (Day 98), Week 16 (Day 112), Week 18 (Day 126), and Week 20 (Day 140).*
- You must arrive at the study site before the time of day that you usually apply your study drug.

If you are assigned to Group 3, you will apply study drug (ATB1651 or placebo) twice a day for 12 weeks. During this treatment period, you must visit the study site every 2 weeks:

- *Week 2 (Day 14), Week 4 (Day 28), Week 6 (Day 42), Week 8 (Day 56), Week 10 (Day 70), and Week 12 (Day 84).*
- You must arrive at the study site before the time of day that you usually apply your second study drug dose of the day.
- You will have assessments done before and after your morning and afternoon dose on clinic visit days. Each dose will be approximately 12 hours apart. You may be required to be at the clinic for a full day on your clinic visit days.

If you are assigned to Groups 5 or 6, you will apply study drug (ATB1651 or placebo) twice a day for 36 weeks. During this treatment period, you must visit the study site every 2 weeks:

- *Week 2 (Day 14), Week 4 (Day 28), Week 6 (Day 42), Week 8 (Day 56), Week 10 (Day 70), Week 12 (Day 84), Week 14 (Day 98) Week 16 (Day 112), Week 18 (Day 126), Week 20 (Day 140), Week 22 (Day 154), Week 24 (Day 168), Week 26 (Day 182), Week 28 (Day 196), Week 30 (Day 210), Week 32 (Day 224), Week 34 (Day 238) and Week 36 (Day 252)*
- You must arrive at the study site before the time of day that you usually apply your second study drug dose of the day.

Follow-up Period

After you have finished your Treatment Period, you must attend the study site for follow-up visits.

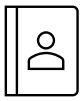
If you are assigned to Group 1, Group 3, or Group 4, you must visit the study site for follow-up visits every 2 weeks until Week 20 and then every 4 weeks until Week 36.

- *Week 14 (Day 98), Week 16 (Day 112), Week 18 (Day 126), Week 20 (Day 140), Week 24 (Day 168), Week 28 (Day 196), Week 32 (Day 224), and Week 36 (Day 252).*

If you are assigned to Group 2, you must visit the study site for follow-up visits every 4 weeks until Week 36. *Week 24 (Day 168), Week 28 (Day 196), Week 32 (Day 224), and Week 36 (Day 252).*If you are assigned to Group 5 or 6 you must visit the study site at Week 40 (Day 280)

You must bring your diary card to the study site at every visit. Your diary card will be reviewed by the study staff.

2.1 Tests and Procedures



Questions about your health and medications:
At Screening you will be asked demographic questions so we can identify you, as well as questions about your medical history, medications, social history (e.g., smoking, alcohol use, exercise, etc.). During the study, the doctor will ask questions about your health to determine whether you are having any side effects.

Physical Examination:
During the study, the doctor will perform a physical examination to check your health. Your height and weight will also be measured to calculate that your Body Mass Index (BMI) is within range for the study.

Electrocardiogram (ECG):
An ECG measures the electrical activity of your heart, using 12 wires attached to your chest and limbs with sticky pads.

Blood, Urine Samples:
At clinic visits, blood samples are taken by direct vein puncture. Blood, urine samples will be collected:

- To monitor your safety (blood cells, clotting, chemistry, fats, liver function, kidney function)
- To check whether you may be pregnant (for people of childbearing potential only) or to check hormone levels (in people who are post-menopausal)
- To screen for recreational drugs such as cannabis, methamphetamine, and opiates
- To screen for specific infections (HIV, Hepatitis B, Hepatitis C)
- To measure the amount of ATB1651 in the blood (pharmacokinetics)

Alcohol Breath Testing
You will be screened for the presence of alcohol via a breathalyser. You will blow into the mouthpiece for a few seconds to measure the presence of alcohol on your breath.

Diary Card:

- You will be given a diary card to take home with you. You will be instructed on how to complete the diary card to record details about when you apply the study drug, any medications you take, and any changes in your symptoms or health problems. You must bring the diary card to the study site at every visit.

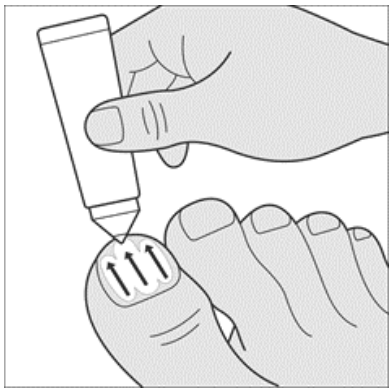
Toenail Examination, Nail Scrapings and Measurement of your infection:

- During the study, your toenails will be frequently photographed to assess and measure your onychomycosis, including the length and area of nail growth, infection status.
- Study staff will also assess the infected toenail for redness and irritation,
- Your toenails will be examined, and nail scrapings will be taken from your infected toenails to test for infections.
- A notch will be made at the base of your infected great toenail(s) near the cuticle and highlighted with a permanent marker pen; the notch will allow the study staff to measure the growth of your toenail(s).

Dosing Instructions:

You will be required to apply ATB1561 (or placebo) solution to only infected toenails (not including non-infected toenails) for:

Cohorts 1 and 4: once daily for 12 weeks
Cohort 2: once daily for 20 weeks
Cohort 3: twice daily for 12 weeks
Cohorts 5 and 6: once daily for 36 weeks



You will apply directly to the nail plate using a pinpoint applicator which enables accurate administration to the toenail, avoiding the skin, and eliminating concerns associated with contact with the skin and potential absorption through the skin. Each application needs to completely cover the toenail and the tip of the tube can be used to gently spread the solution to cover the entire toenail. Study staff will show you how to correctly do this. You will also be provided with step-by-step instructions that you will take home with you, as well as a diary card that you will need to complete each day following dosing. Study staff will show you how to complete your diary card correctly.

You should apply the solution at approximately the same time each day, and only after you have cleaned and carefully dried your toes. Once you have applied the solution to only your infected toenails, your toenails need to remain uncovered until they are completely dry. Once they are dry you will be able to complete your diary card.

Please wash your hands before and after application, avoid contact with eyes.

You must arrive for your clinic visit before the time of day you usually apply your study drug.

Study Schedule for Cohort 1, 3 and Optional Cohort 4

Period	Screening	Treatment Period							Follow-Up	
Study Day	**-42 to -1**	**1**		**14**	**28**	**42**	**56**	**70**	**84**	**98, 112, 126, 140, 168, 196, 224**	**252 (EOS) [a]**
Study week	**-6**	**Pre dose**	**Post dose**	**2**	**4**	**6**	**8**	**10**	**12**	**14, 16, 18, 20, 24, 28, 32**	**36**
Clinic Visit	X	X		X	X	X	X	X	X	X	X
Physical Exam [b]	X	X		X	X	X	X	X	X	X	X
Vital Signs	X	X				X				X	X
ECG	X	X	X	X		X			X	X (only 168)	X
BMI (Height & Weight)	X										
Dose of ATB1561 or Placebo			X[c]								
Blood Sampling [d]	X	X	X	X	X	X	X	X	X		
Urine Sampling	X	X		X	X	X	X	X	X	X	X
Urine Drug Screen and Alcohol Breath Test	X	X									
Diary Review Card			X								
Toenail Examination	X	X		X	X	X	X	X	X	X	X
Nail Scrapings	X			X	X	X	X	X	X	X	X
Measurement of your infection (Notch)		X		X	X	X	X	X	X	X[c]	X

Period	Screening	Treatment Period							Follow-Up	
Study Day	**-42 to -1**	**1**		**14**	**28**	**42**	**56**	**70**	**84**	**98, 112, 126, 140, 168, 196, 224**	**252 (EOS) [a]**
Study week	**-6**	**Pre dose**	**Post dose**	**2**	**4**	**6**	**8**	**10**	**12**	**14, 16, 18, 20, 24, 28, 32**	**36**
Questions about your health and medications:		X									

[a] EOS = End of Study

[b] Full Physical Exam at Screening. Symptom directed physical examination at other clinic visits.

[c] Cohort 1, 2, and 4 will dose once daily in the morning. Cohort 3 will dose once in the morning and once in the evening

[d] Cohort 3 will have blood samples and vital signs taken before and after dosing in the morning and evening at clinic visits. Each dose will be approximately 12 hours apart.

Study Schedule for Cohort 2

[a] EOS = End of Study

Period	Screening	Treatment												Follow-Up	
Study Day	**-42 to -1**	**1**		**14**	**28**	**42**	**56**	**70**	**84**	**98**	**112**	**126**	**140**	**168, 196, 224**	**252 EOS [a]**
Study Week	**-6**	**Pre dose**	**Post dose**	**2**	**4**	**6**	**8**	**10**	**12**	**14**	**16**	**18**	**20**	**24, 28, 32**	**36**
Clinic visit	X	X		X	X	X	X	X	X	X	X	X	X	X	X
Physical Exam[b]	X	X		X	X	X	X	X	X	X	X	X	X	X	X
Vital Signs	X	X												X	X
ECG	X	X	X	X		X			X					X (only 168)	X
BMI (Height & Weight)	X														
Dose of ATB1561 or Placebo			X												
Blood Sampling	X	X	X	X	X	X	X	X	X	X	X	X	X		
Urine Sampling	X	X		X	X	X	X	X	X	X	X	X	X	X	X
Urine Drug Screen and Alcohol Breath Test	X	X													
Diary Review Card			X												
Toenail Examination	X	X		X	X	X	X	X	X	X	X	X	X	X	X
Nail Scrapings	X			X	X	X	X	X	X	X	X	X	X	X	X
Measurement of your infection (Notch)		X		X	X	X	X	X	X	X	X	X	X	X	X
Questions about your health and medications:		X													

[b] Full Physical Exam at Screening. Symptom directed physical examination at other clinic visits.

Study Schedule for Optional Cohorts 5 and 6

Period	Screening	Treatment													Follow-Up
Study Day	**-42 to -1**	**1**		**14**	**28**	**42**	**56**	**70**	**84**	**98**	**112**	**126**	**140**	**168, 182, 196, 210, 224**	**238, 252**	**280 EOS [a]**
Study Week	**-6**	**Pre dose**	**Post dose**	**2**	**4**	**6**	**8**	**10**	**12**	**14**	**16**	**18**	**20**	**22, 24, 28, 30, 32, 34**	**36**	**40**
Clinic visit	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X
Physical Exam[b]	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X
ECG	X	X	X	X		X							X		X(only 252)	X
BMI (Height & Weight)	X															
Dose of ATB1561 or Placebo			X							X						
Blood Sampling	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Urine Sampling	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X
Urine Drug Screen and Alcohol Breath Test	X	X														
Diary Review Card			X							X						
Toenail Examination	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X
Nail Scrapings	X			X	X	X	X	X	X	X	X	X	X	X	X	X
Measurement of your infection (Notch)		X		X	X	X	X	X	X	X	X	X	X	X	X	X
Questions about your health and medications:		X								X						

[a] EOS = End of Study

[b] Full Physical Exam at Screening. Symptom directed physical examination at other clinic visits.

2.2 Who Can Take Part in this Study?

To take part in this study you must:	
✓	Be able to give informed consent and follow the study procedures.
✓	Be aged 18 – 70 years, inclusive.
✓	Have a BMI (Body Mass Index) between 17.5 kg/m^2 – 35.0 kg/m^2
✓	Have confirmed onychomycosis, with the appearance covering at least 20% to 60% of one or both your great toenail(s) – this will be determined by the study doctor following further examination at your screening visit.

You cannot take part in this study if you:	
✗	Are pregnant or breastfeeding
✗	Have taken any of the following medication or are not willing to stop using: • Topical antifungal treatment to the feet 4 weeks prior to dosing • Topical anti-inflammatory or corticosteroid treatment 2 weeks prior dosing • Systemic (ingested) corticosteroid (including injections), or other antifungal treatment 12 weeks prior to dosing.
✗	Have a history of a significant medical problem, mental health problem or severe allergy as determined by the study doctor – please speak with the study doctor to discuss whether any conditions you have may exclude you.
✗	Have history of either Type 1 or Type 2 diabetes that requires medication (i.e., not manageable through diet and exercise).
✗	Have received an investigational medication within at least 30 days prior to Screening
✗	Unwilling to refrain from the use of nail cosmetics from Screening until the end of the study (i.e., nail polish).
✗	Have nail abnormalities of the toe e.g., genetic nail disorders, pigment disorders, etc.

If you think that any of the above applies to you, or you have one of the conditions described, please discuss these with your study doctor for more thorough assessment to see if you can take part in this study or not. Additionally, there are other criteria that you will need to meet in order to be eligible for the study, but the study doctor will discuss this with you at your screening visit.

2.3 Study Instructions

It is important that you follow the instructions you are given and attend all scheduled clinic visits. It is also possible that the study doctor may schedule extra visits or tests for you, if considered necessary.

You will be given a Participant Identification Card if you participate in this study, stating the name of the study and the study doctor's contact information. This card should be carried with you at all times so that you can contact the study doctor at any time and so you can show it to any other doctor, dentist, or pharmacist that you might visit while in this study.

At each visit, the study staff will ask you questions about your health and the medications you are currently taking. You should always report any changes in your health, unusual feelings, or symptoms to the study staff. It is also important that you do not start, stop, or make changes to any of the medications you are currently taking without first discussing this with your study doctor.

Please inform the study doctor or staff if you decide to stop having the ATB1651 for any reason. If you stop receiving study drug for any reason (either your choice or on the advice of your study doctor) your study doctor will ask you to continue to attend the unit for follow-up assessments. If you decide to stop participating in the study for any reason your study doctor will discuss treatment choices with you.

Responsibilities and Restrictions:

- You need to attend the study site visits and cooperate in the study procedures as described in Section 3 above.
- You must apply your study drug (ATB1651 or placebo) as instructed.
- You must keep your study diary up to date and bring it to study visits when required.
- You must abstain from alcohol use for at least 48 hours before each study visit.
- You must not use any drugs of abuse during the study (from when you sign this consent form until the end of the study).
- You must not use any nail cosmetics such as clear and/or coloured nail lacquers during the study (from when you sign this consent form until the end of the study).
- You need to inform your study doctor about any health problems, accidents or medical interventions that happen while you are in the study, even if you think it is not important.
- You need to inform your study doctor before you start any new medication or stop any medication that you are already taking. This includes prescribed or over the counter products, vitamins, and herbal supplements, even if used short term (such as a pain relief for a headache).
  You need to inform the study doctor if you decide not to continue in the study. You don't have to give a reason for your decision.

3 WHAT ARE THE ALTERNATIVES TO PARTICIPATION?

You do not have to take part in this research project to receive treatment for mild to moderate onychomycosis. Your study doctor will discuss these options, including the risks and benefits of these options with you before you decide whether or not to take part in this research project. You can also discuss the options with your local doctor.

4 WHAT ARE THE POSSIBLE BENEFITS, COSTS AND RISKS TO YOU PARTICIPATING?

4.1 Benefits

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits may include an improvement in your fungal toenail infection.

Information from this study may help doctors learn more about ATB1651 and the treatment of fungal toenail infections. Others may benefit from the information learned in this study.

4.2 Reimbursement and Costs

All tests required to be done for this study will be paid for by AmtixBio Co., Ltd. And there will be no cost for you to participate in this study. You will still have to pay for the costs of your regular medical care that are not a part of this study.

You will be reimbursed the sum of $200 per clinic visit (for Cohorts 1, 2, 4, 5 & 6) or $300 per clinic visit (For Cohort 3) for your participation in this trial. However, the timing of reimbursement is flexible and can be adjusted to suit your needs – please discuss this with study staff if you have any concerns regarding your reimbursement. **We are required to deduct withholding tax at the applicable rate you have declared in the IR330C form**. You will be responsible for any other tax obligations (e.g., ACC). If you are GST registered, it may be possible for you to submit a GST invoice. Contact paymentforms@nzcr.co.nz if you would like to discuss this further.

The payment will be made after you complete the study, to cover your time and inconvenience. If you are receiving a benefit or allowance, your usual payments may be affected. Your tax statement will state that you were paid from your dosing day through to your final study visit.

To be able to participate in the clinical study you must be eligible to work in NZ for the entire duration of the study. If you are no longer eligible to work in NZ during the study, you will be withdrawn from the study and your reimbursement will be a pro-rata of the total amount.

You will be reimbursed for travel and parking for your study visits if you live in the metropolitan area. If you live outside this area, we will discuss your travel costs individually. Full reimbursement requires completion of all visits according to study requirements. If you are withdrawn from the study for medical reasons, having received trial medication, you will receive reimbursement in full.

If you leave the study of your own choice or are released from the study for non-medical reasons, you will receive a partial reimbursement (a pro-rata reimbursement) according to how far you contributed to the study.

If you complete the screening visit assessments and are found not eligible for the study, you will be appropriately reimbursed for any travel-associated costs.

4.3 Possible Risks and Disadvantages?

Medical treatments often cause side effects. You may have none, some or all the effects listed below, and they may be mild, moderate, or severe. There may also be unknown side effects from taking ATB1651 alone or with other drugs you may be taking. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you get.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you.

What are the Risks or Side Effects of ATB1651?

Animal studies have been done with ATB1651 to try and predict what type of side effects might occur in people. However, animal studies do not always predict human responses to drugs. When ATB1651 was applied to animals at doses higher than the maximum dose that will be given in this study, there was some skin irritation.

The condition of the skin around your toenails will be monitored in this study. Your study doctor and the safety monitoring committee will be checking for signs of skin irritation as well as any other side effects.

ATB1651 has been studied in 20 patients with mild to moderate fungal toenail infections. Side effects that were possibly related to use of ATB1651 in some patients were:

- Discolouration of the toenail
- Detachment of the toenail
- Removal of part or all of the toenail (avulsion)

ATB1651 may cause eye irritation if the solution comes into contact with eyes. Please ensure that you wash your hands before and after ATB1651 application and avoid contact with eyes. If the solution does come into contact with eyes, please wash with water and contact the study doctor if you experience any irritation.

As with other drugs, ATB1651 may cause an immune reaction or allergic reaction. Symptoms may include rash, flushing, itching, sneezing or runny nose, abdominal pain, diarrhea, swelling of face, tongue or throat, dizziness, lightheaded or fainting, trouble breathing, irregular or racing heart rate, and seizures. These reactions can be life-threatening / fatal.

If you believe you are having a severe allergic reaction, you should immediately seek emergency medical treatment by dialing the emergency phone number and alert the study doctor and study staff as soon as possible.

What are the Risks or Side Effects of Study Procedures?

Blood Sample Collection:
Risks include bruises, swelling with itching, and slight bleeding. The area may become inflamed. In rare cases, it may result in a blood clot, an infection or nerve damage. As needles can cause pain, you may feel light-headed or faint.

ECG Tests:
Sometimes the sticky pads used to attach the ECG leads can cause skin irritation (redness / itchiness).

Physical Examination:
During this examination you may be asked to remove some items of clothing so a full examination can be done. You can request a chaperone to be with you at the time of the physical examination, please ask one of our research nurses.

Photographs:
During the study, your toenails will be frequently photographed to assess and measure your onychomycosis, including the length and area of nail growth, infection status, and overall appearance. These photographs will be used to help the study doctors and study staff monitor your onychomycosis throughout the study. If you are not comfortable with these photographs of your toenails being taken, then please do not take part in this study. Your privacy will be protected by ensuring that these photographs have any identifying or revealing marks (i.e., scars and/or tattoos) removed so that you cannot be identified by any of these features.

Nail Scrapings and notches:
During the study, nail scrapings and notches using a scalpel will be taken/made in order to take biologic samples and measure the condition of your nail(s). These are painless procedures involving a small scratch to the nail and a notch made in the nail. There is a very small risk of injury to the skin from the scalpel.

COVID-19

There is the potential that while you are on the study you will want to receive the COVID-19 vaccination and/or booster vaccination if you have not received this already. You may receive the COVID-19 vaccination during the study but please discuss this with the study doctor to ensure your safety while on the study.

Additionally, COVID-19 testing may be done during the study if required. You will be informed if and when this will be performed.

4.4 Contraception

Reproductive Risks for Sexually Active Participants of Child-Bearing Potential

The effects of ATB1651 in pregnancy and breastfeeding are unknown, but there is a risk it may cause birth defects or foetal deaths, and/or be passed on in breast milk. If you are pregnant or breastfeeding, you cannot take part in this study.

If you are sexually active and of child-bearing potential (able to become pregnant), it is very important that you do not become pregnant during this study. A person of child-bearing potential is any pre-menopausal person who may become pregnant. If you are unsure if this applies to you, please check with the study doctor before you start the study medication. **You must use a of the method of contraception listed below**, from screening until at least 90 days after your final study visit:

A highly effective method (less than 1 pregnancy per 100 people using the method for one year) e.g.:

- Implant contraceptive (e.g., Jadelle®)
- Intra-uterine device (IUD) containing either copper or levonorgestrel (e.g., Mirena®)
- Sterilisation (e.g., vasectomy, bilateral tubal ligation ('clipping or tying tubes' or hysterectomy)

OR an effective method (5-10 pregnancies per 100 people using the method for one year) e.g.:

- Injectable contraceptive (e.g., Depo Provera)
- Oral Contraceptive Pill (combined hormonal pill or progestogen-only 'mini-pill')

You / your partner must also use a barrier form of contraception, from screening through until 90 days after your last study visit. Barrier methods of contraception include:

- Condoms (external or internal) – not to be used together due to increased risk of breakage
- Diaphragm ('cap')

Please note that barrier methods alone are not highly effective methods of birth control.

Total abstinence from heterosexual intercourse during the entire period of risk associated with the study drug (from Screening until at least 90 days after your last study visit) is considered an acceptable form of contraception if this is in line with your preferred and usual lifestyle. Periodic abstinence is not accepted as a form of contraception.

If you are unsure which method of birth control you are using (or want to start using) and whether it is acceptable for this study, please ask the study doctor for more information.

You must also agree to not donate eggs, from dosing until at least 90 days after your last study visit.

If you do become pregnant during the study, you must tell the study doctor as soon as possible. If you do become pregnant you will be asked to sign a separate consent form, to allow the Sponsor to collect information about your pregnancy and the outcome of your pregnancy.

Reproductive Risks for Sperm in Sexually Active Participants

The effects of ATB1651 if passed on through semen are unknown, but there is a risk it may cause birth defects or foetal deaths. **You are responsible for informing your sexual partner of these possible risks.**

If you are sexually active and have any partner who is of child-bearing potential (meaning a partner who may become pregnant) it is very important that you use contraception during this study. You and your partner must use one of the contraception options listed above for participants of child-bearing potential, from at screening through until at least 90 days after your final study visit.

You / your partner must also use a barrier method of contraception, from Screening through until 90 days after your last dose. Barrier methods of contraception include:

- Condoms (external or internal) – not to be used together due to increased risk of breakage
- Diaphragm ('cap')

Please note that barrier methods alone are not highly effective methods of contraception.

Total abstinence from heterosexual intercourse during the entire period of risk associated with the study drug (from Screening until at least 90 days after your last study visit) is considered an acceptable form of contraception if this is in line with your preferred and usual lifestyle.

Periodic abstinence is not accepted as a form of contraception.

If a pregnancy occurs, you must report this to the study doctor as soon as possible. Your partner will be asked to give consent for their information and their infant's information to be collected for monitoring purposes.

You must also agree not to donate sperm, from dosing until at least 90 days after your last study visit.

5 WHAT WOULD HAPPEN IF YOU WERE INJURED IN THE STUDY?

As this research study is for the principal benefit of its commercial sponsor AmtixBio Co., Ltd., if you are injured as a result of taking part in this study you **won't** be eligible for compensation from Accident Compensation Corporation (ACC).

However, AmtixBio Co., Ltd has satisfied the Northern A Health and Disability Ethics Committee that approved this study that it has up-to-date insurance for providing participants with compensation if they are injured as a result of taking part in this study.

New Zealand ethical guidelines for intervention studies require compensation for injury to be at least ACC equivalent. Compensation should be appropriate to the nature, severity and persistence of your injury and should be no less than would be awarded for similar injuries by New Zealand's ACC scheme.

Some sponsors voluntarily commit to providing compensation in accordance with guidelines that they have agreed between themselves, called the Medicines New Zealand Guidelines (Industry Guidelines). These are often referred to for information on compensation for commercial clinical trials. There are some important points to know about the Industry Guidelines:

- On their own they are not legally enforceable and may not provide ACC equivalent compensation.
- There are limitations on when compensation is available, for example compensation may be available for more serious, enduring injuries, and not for temporary pain or discomfort or less serious or curable complaints.
- Unlike ACC, the guidelines do not provide compensation on a no-fault basis:
- The Sponsor may not accept the compensation claim if:
    - Your injury was caused by the investigators, or;
    - There was a deviation from the proposed research plan, or;
    - Your injury was caused solely by you.

An initial decision whether to compensate you would be made the by the sponsor and/or its insurers.

If they decide not to compensate you, you may be able to take action through the Courts for compensation, but it could be expensive and lengthy, and you might require legal representation. You would need to be able to show that your injury was caused by participation in the trial.

You are strongly advised to read the Industry Guidelines and ask questions if you are unsure about what they mean for you.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

6 WHAT WILL HAPPEN TO MY TEST SAMPLES?

Blood, urine, and nail scraping samples will be collected throughout the study. These samples will be used for various tests. Some of the samples will be used for regular routine blood counts and blood chemistry, to monitor your general health. All these routine samples will be sent to Canterbury Health Laboratories (if you are in Christchurch) or LabPlus or Awanui (if you are in Auckland) for testing and destroyed after 3 months by internationally accepted means.

All other study samples (pharmacokinetics) will be sent to a central laboratory in Taipei, Taiwan (Novotech Labs) for testing and destroyed after 15 years by internationally accepted means.

The maximum amount of blood collected from each participant during the study will be up to approximately 220 mL. For comparison, a standard blood donation at a blood collection centre, is about 470 mL. Samples collected by NZCR will be identified by your study number, year of birth, initials, and sex, to allow study doctors to quickly respond to any abnormal results. Before the results of these tests are sent to the Sponsor, your identifiable information will be removed and replaced with a code.

The proposed blood tests include a screening test for HIV and for viral Hepatitis B and C, as well as a COVID-19 test. Signing the consent form means that you agree to have this testing performed. It is important to understand that a positive screening test does not necessarily mean you have the disease. Should you receive a positive screening result for HIV or either Hepatitis B or C, then the study doctors will provide initial counselling and medical advice and will assist in arranging any follow up tests that you require. HIV, Acute (newly diagnosed) Hepatitis B/C, and COVID-19 are all 'notifiable diseases', which means that it is required by law to notify government health authorities of any new cases.

6.1 Are There Any Cultural Considerations?

You may hold beliefs about sacred and shared values about your tissue samples and/or data originating from this tissue. The cultural issues associated with sending your tissue samples and data overseas and/or storing your tissue and data should be discussed with your family/whānau as appropriate. If you wish to know more about the study, we can arrange for an Investigator to come and talk to you and your whānau. NZCR are committed to preserving and upholding mauri through karakia and the handling of samples. You are invited to perform a karakia at the time of sample collection, please inform staff if you would like any assistance. However, due to your samples being sent to countries outside of New Zealand, a karakia will not be able to be performed at the time of your sample disposal.

Personal and health information is a tāonga and will be treated accordingly. The following data sovereignty principles are in place to ensure that the data generated from this research is protected and may benefit Māori now and into the future. The principles included are whakapapa, whanaungatanga, rangatiratanga, kotahitanga, manaakitanga and kaitiakitanga. Clinical trials are often driven by Sponsor companies overseas and involve very few Māori as participants.

Consideration of Tikanga and Tiriti obligations are highly valued at NZCR, whereby staff attend Tiriti and Tikanga workshops to acknowledge and understand Māori cultural values and principles. NZCR also maintain contact with the Office of the Chief Advisor Tikanga across Te Whatu Ora Waitemata and Te Toka Tumai Auckland and Te Puna Oranga Māori Research Review Committee for consultation of Māori health services. NZCR also have open dialogue with the chair of the Māori Governance Rōpu for Ira Tātai Whakaheke.

Before deciding whether to participate in this study or not, it may be appropriate to discuss your participation with your whanau/family/Kaumatua/hapu/Iwi and consider both the potential risks and benefits that may be involved. If you need cultural support, please let us know and we will arrange this for you. For additional cultural support or tikanga advice, please contact your local Māori support contact listed at the end of this document.

7 WHAT ARE THE RIGHTS OF PARTICIPANTS IN THE STUDY?

7.1 Participation is Voluntary

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage. This will not affect your routine treatment/medical care which you may otherwise receive, your relationship with NZCR or with those treating you.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

7.2 New Information

Sometimes during the course of a research project, new information becomes available about the medication that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project, you may be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, they will explain the reasons and arrange for your regular health care to continue.

7.3 Privacy and Confidentiality and Right to Access Information Collected During the Study

What will Happen to my Information?

During this study, the study doctors, researchers, nurses and other NZCR staff will record information about you and your study participation. This includes the results of any study. Your name, address and phone number will be on the demographics page for the study so we can identify you correctly at visits and contact you. This information may be used to obtain health records (detailed below) but is not supplied to anyone overseas.

If needed, **information from your hospital records and your usual doctor (GP) may also be collected**, and your GP will be notified about your participation in the study. You cannot take part in this study if you do not consent to the collection of this information.

Photographs will be transferred to a third-party photography vendor in the United States (Canfield Scientific, Inc., 4 Wood Hollow Road, Parsippany, NJ 07054) and will be handled according to Canfields' privacy policies and procedures. Every effort will be made to protect your confidentiality.

Type of information	Where is it stored?	Who can access it?
Identifiable Information – *this information can be traced back to you*		
• Information collected from you • Laboratory results • Photographs of toenails	• **Paper**: stored securely under restricted access at NZCR. Following study completion paper forms are transferred to a secure site and stored for 15 years, then destroyed • **Electronic**: stored on secure NZCR servers	• NZCR staff • Your GP / usual doctor • Local laboratory staff to process and report your screening and safety tests • Sponsor monitors to ensure the study is run properly and data is collected accurately • Representatives from the Sponsor if you make a compensation claim as a result of study-related injury. Identifiable information is required to assess your claim • Ethics committee, regulatory authorities, and sponsor representatives if the study or site is audited • Medical Officer of Health for positive test results for a notifiable disease (i.e., COVID-19, Hepatitis B/C) • The study doctor may share your information with other people, in the rare event of a serious threat to public health or safety, or to the life or health of you or another person OR if the information is required in certain legal situations
De-identified (coded) Information – *this information is only labelled with your unique study ID*		
• Study assessment results are uploaded into the study database to be analysed	• **Electronic**: will be stored-on a secure platform and will be retained indefinitely. Storage will comply with local and/or international data security guidelines.	• The Sponsor, for the purposes of this study. • People and companies working with or for the Sponsor, for the purposes of this study. • Regulatory or other governmental agencies worldwide.
Anonymised Information – *this information cannot be traced back to you (code removed)*		
• All de-identified information for which the code has been removed	• **Electronic**: stored on a secure sponsor-managed database	• Access not restricted

Future Research Using Your Information
Your coded information may be used for future research related to ATB1651 or onychomycosis.

This future research may be conducted overseas. You will not be told when future research is undertaken using your information. Your information may be shared widely with other researchers or companies. Your information may also be added to information from other studies, to form much larger sets of data.

You will not get reports or other information about any research that is done using your information.

Your information may be used indefinitely for future research unless you withdraw your consent. However, it may be extremely difficult or impossible to access your information or withdraw consent for its use once your information has been shared for future research.

Security and Storage of Your Information
During the study, your information will be stored on paper forms at NZCR and electronically on secure servers. When the study has finished, paper forms will be transferred to a secure site and stored for at least 15 years, then destroyed. De-identified information in electronic form will remain on a secure platform and will be retained indefinitely. Storage will comply with local and/or international data security guidelines.

Risks
Although efforts will be made to protect your privacy, absolute confidentiality of your information cannot be guaranteed. Even with coded and anonymised information, there is no guarantee that you cannot be identified. While the risk is currently very small, the chance that someone might access and misuse your information (for example, by making it harder for you to get or keep a job or health insurance) might increase in the future as people find new ways of tracing information.

Your coded information is being sent overseas. Other countries may have lower levels of data protection than New Zealand. There may be no New Zealand representation on overseas organisations which make decisions about the use of your information. There is a risk that overseas researchers may work with information in a way that is not culturally appropriate for New Zealanders.

Rights to Access Your Information and Results
You have the right to request access to your information held by the research team. You also have the right to request that any information you disagree with is corrected.

Please ask if you would like to access your screening and safety tests during the study. You may access other study-specific information before the study is over, but this could result in you being withdrawn from the study to protect the study's scientific integrity.

If you have any questions about the collection and use of information about you, you should ask a study doctor.

8 WHAT WILL HAPPEN AFTER THE STUDY ENDS, OR IF I WANT TO PULL OUT?

8.1 If You Decide to Withdraw

You may withdraw your consent for the collection and use of your information at any time, by informing your Study Doctor. Please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing, such as follow up visits.

If you withdraw your consent, your study participation will end, and the study team will stop collecting information from you. Information collected up until your withdrawal from the study will continue to be used and included in the study. This is to protect the quality of the study.

8.2 Why the Study Might be Unexpectedly Stopped

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

- Unacceptable side effects and safety issues
- The treatment being shown not to be effective.
- The treatment being shown to work and not need further testing.

8.3 Will the Study Medication Continue to be Available After the Study Finishes?

ATB1651 is at an early stage of development. When the study ends, the study doctor will discuss treatment choices with you. Therefore, after the research finishes, you will not be able to continue to receive ATB1651.

8.4 Results

When the research project ends the study data must be analysed, so the results of the study may not be available until about a year after the research finishes. The study doctors and/or Sponsor may decide to discuss or publish the results of the study. This may include publication in journals, presentation at conferences or other professional forums. In any publication, information will be provided in such a way that you cannot be identified. Results of the study will be provided to you. If you do not wish to receive a summary of the study results when they become available, then please inform NZCR staff.

9 WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns, or complaints about the study at any stage, you can contact:

Christchurch:
Dr Cory Sellwood
Phone: 0800 862 278
Email: hallux.christchurch@nzcr.co.nz

Auckland:
Dr Aidan Cabezas-Hayes
Phone: 0800 788 3437
Email: hallux.auckland@nzcr.co.nz

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone:	0800 555 050
Fax:	0800 2 SUPPORT (0800 2787 7678)
Email:	advocacy@advocacy.org.nz
Website:	https://www.advocacy.org.nz/

Māori cultural support is available through:

Christchurch:
Dr. Matea Gillies
Mobile: 027 4105 025
Email: gillies-lamb@xtra.co.nz

Auckland :
The Office of the Chief Advisor Tikanga, He Kamaka Waiora, Te Whatu Ora (Health New Zealand) – Waitemata and Auckland
Mobile: 021 0203 1167
Phone: 09 486 8320 ext 43204
Email: hkwresearch@waitematadhb.govt.nz

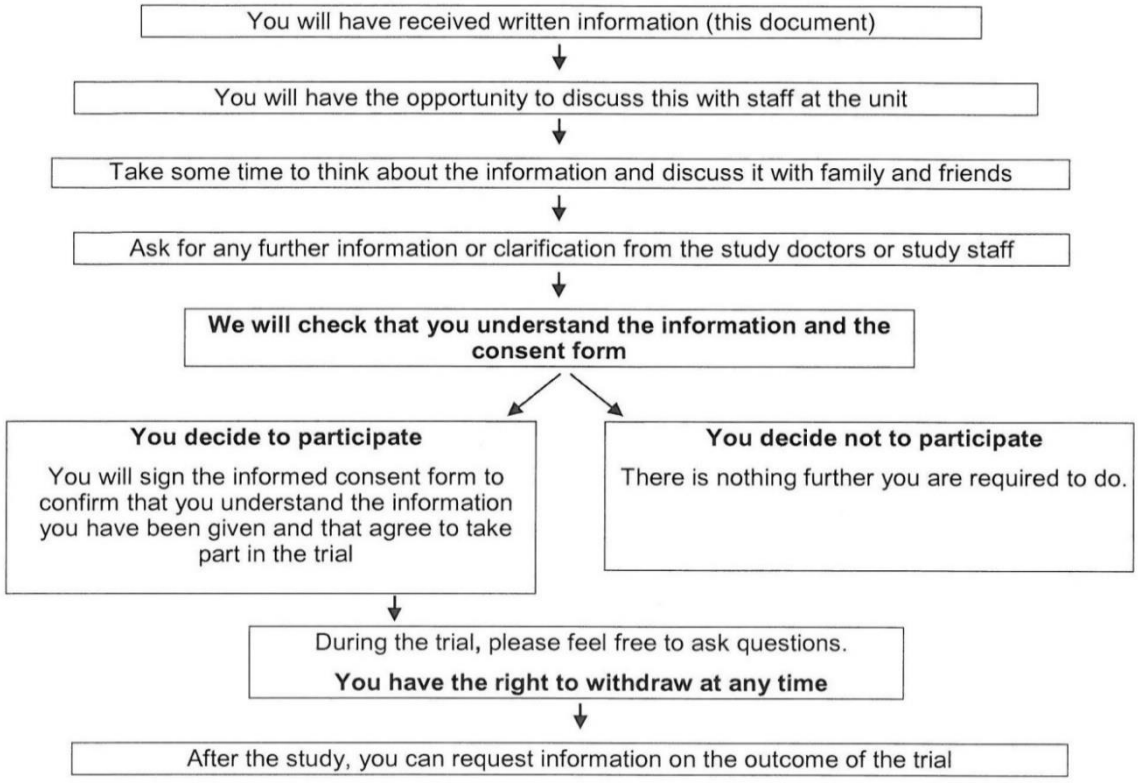
You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Email:	hdecs@health.govt.nz
Phone:	0800 400 569 (Ministry of Health general enquiries)

10 WHAT ABOUT ANY OTHER QUESTIONS I MAY HAVE?

11 DO I HAVE TO DECIDE STRAIGHT AWAY?

No, you do not have to decide straight away. You should take some time to consider whether or not to participate, we will be in touch in a week or so to discuss your decision**.** The following steps are useful in helping you reach a decision.



CONSENT FORM

Short Title:	A Phase 2 Study to Assess the Safety, Tolerability and Effectiveness of ATB1651 in Adults with Mild to Moderate Onychomycosis (Fungal Nail Infection).
Protocol Number:	ATB1651-102
Principal Investigator:	Christchurch: Dr. Cory Sellwood Auckland: Dr Aidan Cabezas-Hayes

***Please let study staff know if you require an interpreter*.**

Declaration by participant:

- I have read the Participant Information Sheet, or have had it read to me in a language I understand, and I fully comprehend what it says.
- I have been given sufficient time to consider whether or not to participate in this study.
- I have had the opportunity to use a legal representative, whanau/ family support or a friend 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 information sheet.
- I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.
- I consent to the research staff collecting and processing my information, including information about my health (including information collected from my GP and other Health Providers).
- 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 understand that there may be risks associated with the treatment in the event of myself or my partner becoming pregnant. I undertake to inform my partner of the risks and to take responsibility for the prevention of pregnancy.
- I agree to my tissue samples being sent overseas, and I am aware that these samples will be disposed of using established guidelines for discarding biohazard waste.
- I agree to an approved auditor appointed by the New Zealand Health and Disability Ethic Committees, 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 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 provisions in case of injury during the study.
- I know who to contact if I have any questions about the study in general.
- I understand my responsibilities as a study participant.
- I understand that I will receive a summary of the study results and if I do not wish to receive this, I will inform site staff.
- I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.