PARTICIPANT INFORMATION SHEET AND CONSENT FORM (Part B: Participants with HSV-2 Infection and Recurrent Genital Herpes)

Short Title:	A Study to Evaluate ABI-5366 in Healthy Participants and in Participants with HSV-2 Infection and Recurrent Genital Herpes
Protocol Number:	ABI-5366-101
Sponsor:	Assembly Biosciences, Inc. Two Tower Place, 7th Floor, South San Francisco, California 94080, USA
Principal Investigator:	Dr Cory Sellwood
Institution Address:	264 Antigua Street, Christchurch, New Zealand
Phone Number:	0800 862 278
Ethics Number:	**2024 FULL 19873**

This is the first time that ABI-5366 will be studied in humans with HSV-2 infection.
You may not get any health benefit from the medication used in this study; but there are risks of you having a medication reaction, injury, or illness.

You are invited to take part in a clinical research study. This study will test an experimental drug, named ABI-5366, that may potentially be used to prevent recurrent genital herpes (RGH). ABI-5366 is an investigational product because it has not been approved by the New Zealand MedSafe or other drug regulatory authorities.

There are two parts to this study, and you are being asked to take part in Part B. 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

ABI-5366 is being developed to prevent recurrence of genital lesions due to Herpes Simplex Virus Type 2 (HSV-2) infection. HSV-2 infection is spread through sexual contact and can cause painful genital blisters or ulcers (lesions). HSV-2 affects approximately 15% of New Zealanders and there is currently no cure for the infection. Treatments have been developed to reduce the recurrence and transmission; however, these are only partially effective.

It is hoped that ABI-5366 may control HSV-2 by preventing it from reproducing itself (making new copies of the virus) inside the body, to potentially reduce the levels of virus within the body, to hopefully prevent the recurrence of genital lesions.

This study will investigate the effects of ABI-5366 in healthy participants (Part A) and individuals who are infected with HSV-2 and experience recurrent genital lesions (Part B). You are being asked to take part in multiple ascending dose (Part B) of the study.

The purpose of Part B of this study is to:

- Evaluate how safe ABI-5366 is in participants with RGH.
- Measure levels of ABI-5366 in the blood over time in participants with RGH.
- Evaluate the effects of ABI-5366 to reduce levels of HSV-2 in participants with RGH.

1.2 Study Design

Approximately 146 participants will take part in this study. Part B of the study will consist of approximately 100 participants who are infected by HSV-2 and experiencing recurrent genital lesions. Part B of this study is being run in several sites across New Zealand and Australia. Part B of the study requires a Screening Visit to determine eligibility, and up to 22 scheduled study visits at the Auckland or Christchurch research unit.

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

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

Blinded means that neither you nor your study doctor will know whether you will be receiving ABI-5366 or placebo. In an emergency, the study doctor can find out what you are receiving.

Every person in Part B of this study will receive 2 or 5 doses of ABI-5366 or placebo (a substance that looks like ABI-5366 but contains no active medication). Each dose will be given by mouth, with a glass of water, in a fasted state (no food or drink, only water) in the morning.

Up to 4 dose groups (cohorts) are planned for the study. The group you are assigned to will depend on when you join the study. Details for the dosing groups are as follows:

Group (Cohort)	Dose of ABI-5366 or Placebo	Frequency
B1	TBD*	1 oral dose (tablet) per week for 5 weeks (5 doses total) or 1 oral dose (tablet) per month (2 doses total)
B2	TBD*	
B3	TBD*	
B4	TBD*	

TBD = To Be Determined

In each dosing group, up to 20 participants will receive ABI-5366 and 5 participants will receive placebo. Whether you receive active study medication or placebo will be assigned randomly (by chance). You will have a 4 out of 5 (80 %) chance of receiving ABI-5366.

Dose groups will be enrolled in order. You will be told which dose group you will be in and the exact dose level you will be receiving. You will also be told if any changes are made to the planned dose for your group.

Blood samples and other tests to measure study medication 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.

Depending on which dosing regime you are allocated to, your schedule may differ as per the tables below.

For weekly dosing: On Day 1 and Day 29 visits, you will be asked to stay on site for at least 8 hours for collection of PK blood samples at designated time points.

For monthly dosing: On Day 1 and Day 8 visits you will be asked to stay on site for at least 8 hours for collection of PK blood samples at designated timepoints.
You may have 1 or more additional visits on Days 2, 3, 5, 6 or 7 to receive loading doses (you will be informed ahead of time of your dosing days).

A loading dose is an initial dose of the study drug that may be initially given before dropping down to a lower, maintenance dose.

1.3 Nature and Sources of Funding of the Study

This research project is being conducted and funded by Assembly Bioscience Inc. ("the Sponsor") and locally sponsored in New Zealand by PPD, 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 medication and benefit the Sponsor financially. There would be no financial benefit to you from these discoveries.

NZCR will receive a payment from the Sponsor 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 B** 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 25 weeks, including screening, dosing, and up to 98 days of follow-up. The follow-up period is expected to be between 28 and 98 days. Study staff will inform you

of your follow up duration. 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 ABI-5366 or placebo is called Day 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. However, even if all your results are normal, you may not be guaranteed a place. There may be more screened participants than are needed and so you may be asked to be a reserve or enrol in a later dosing group. Your study doctor or treating physician will talk to you about other possible treatments.

2.1 Tests and Procedures

Physical Examination:
During the study, the doctor will perform a physical examination to check your health. This will include a physical examination of your anus and genital area. During this examination you can request a chaperone to be with you during this time, please ask one of our research nurses. Your height and weight will also be measured to calculate that your Body Mass Index (BMI) is within range for the study.

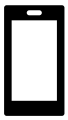
Electrocardiogram (ECG):
An ECG measures the electrical activity of your heart, using 12 wires attached to your chest and limbs with sticky pads.

Vital Signs:
Vital signs include recordings of your pulse, blood pressure, breathing rate, and temperature.

Blood and Urine Samples:
At study visits, blood samples are taken by direct vein puncture. On Day 1 and Day 29, a cannula (thin plastic tube) may be inserted into a vein in your arm to take blood samples. If your cannula stops working, direct vein punctures will be used.
Blood and urine samples will be collected to:

- Monitor your safety (blood cells, clotting, chemistry, fats, liver function, kidney function)
- Check whether you may be pregnant (for participants of childbearing potential only)
- Screen for recreational drugs such as cannabis, methamphetamine, and opiates
- Screen for specific infections (HIV, Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis E, HSV)
- Measure the amount of ABI-5366 in the blood (pharmacokinetics)
- Measure the effect of ABI-5366 on specific immune system cells and proteins

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.



Participant Swabbing and Symptoms Diary:
You will be asked to complete a diary at approximately the same time twice daily from Day 8 through Day 36. The diary can be accessed using the "eCOA" application on your mobile phone or other personal device. You will record when the swab is collected and any symptoms and their location. The doctor will review this diary during your scheduled visits.

Anus and Genital Swabbing – During the study, you will be required to complete twice daily swabbing of the anus and genital area from Day 8 through Day 36. If any new lesions occur in the anus or genital area, you will need to collect an additional swab from the lesion site twice daily. You will record the date and time of each swabbing sample in a diary. Each used swab will be stored in a vial and then stored at your home in a box provided by the site until your next scheduled visit. You will bring all collected swabs in their vials and turn them to the site staff. You will receive training on this swabbing procedure on Day 1 and Day 8. All supplies will be provided by the site including instructions to take home that you can review at any time. You can request for a chaperone to be with you during the training time by asking one of our research nurses. You can also request a specific gender for your study doctor. If your study doctor is the opposite gender, a chaperone will be present.
Swabbing samples will be collected to:

- Monitor if HSV-2 is resistant to ABI-5366
- Check if ABI-5366 is able to reduce levels of HSV-2 in participants with HSV-2 infection with RGH
- To screen for HSV DNA. This testing is specific to the HSV viral infection and is mandatory for the study.

Unscheduled Visits:
If any new lesions occur in the anus or genital area, you will need to return to the study site for an unscheduled visit within 48 hours, if possible, after appearance of the lesion. The study doctor will collect a swab from the lesion site, in addition to the genital swabs you have collected yourself over this time if the lesion occurs between Day 8 and 36.

Study Schedule (Weekly Dosing)

Period	Screening	Dosing						Follow-Up		Additional Follow-Up		
Study Day	**-45 to -1**	**1**	**4**	**8**	**15**	**22**	**29**	**36**	**43, 50, 57**	**64**	**71, 78, 85, 92, 99**	**127 EOS[a]**
In-Study Study Visit	X	X	X	X	X	X	X	X	X	X	X	X
Questions about my health	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
Vital Signs	X	X	X	X	X	X	X	X	X	X	X	X
ECG	X	X	X	X	X	X	X	X		X	X [c]	X
BMI (Height & Weight)	X	X [c]					X [d]			X [c, d]	X [c, d]	X [d]
Dose Administration		X		X	X	X	X					
Review of Participant Swabbing and Symptoms Diary					X	X	X	X	X[f]			
Participant Returns Collected Swabs					X	X	X	X	X[f]			
Blood Sampling	X	X	X	X	X	X	X	X	X	X	X	X
Urine Sampling	X	X	X		X	X	X	X	X [c]	X	X [c]	X
Pregnancy Test [e]	X	X			X		X		X [c]	X [c]	X [c]	X
Urine Drug and Alcohol Breath Test	X	X					X					
Training for Genital Swabbing		X		X								
Self-Swabbing of Genital area				*Twice daily from Day 8 through to Day 36*								

[a] EOS = End of Study. The last follow-up visit is expected to be between 28 to 98 days.
[b] A complete or symptom-directed physical exam will be performed at indicated visits and may be done at other points if needed
[c] Assessment will also be completed if this is your dosing group's final study visit

[d] Only weight will be measured on these days

[e]

A pregnancy test is required at Screening for female participants of childbearing potential. This will be performed on the blood sample provided at this visit. On Days 1, 15, 29, 57, 99, and 127 a urine pregnancy test will be performed. If positive on urine testing, a pregnancy test will be performed on the blood sample provided at the respective visits.

[f] Anogenital Swabbing Samples collected on Day 36 will be returned on Day 43. The Participant Swabbing & Symptoms 's study Diary will be reviewed for the final time on Day 43. You will collect 1 additional swab, twice a day, when you experience a lesion.

Study Schedule (Monthly dosing)

Period	Screening		Dosing						Follow-Up		Additional Follow-Up		
Study Day	**-45 to -1**	**1**	**4**	**Potential Additional Dose [f]**	**8**	**15**	**22**	**29**	**36**	**43, 50, 57**	**64**	**71, 78, 85, 92, 99**	**127 EOS[a]**
In-Study Study Visit	X	X	X	X	X	X	X	X	X	X	X	X	X
Questions about my health	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
Vital Signs	X	X	X	X	X	X	X	X	X	X	X	X	X
ECG	X	X	X		X	X	X	X	X		X	X [c]	X
BMI (Height & Weight)	X	X [c]						X [d]			X [c, d]	X [c, d]	X [d]
Dose Administration [f]		X		X	X								
Review of Participant Swabbing and Symptoms Diary						X	X	X	X	X[g]			
Participant Returns Collected Swabs						X	X	X	X	X[g]			
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 [c]	X	X [c]	X
Pregnancy Test [e]	X	X				X		X		X [c]	X [c]	X [c]	X
Urine Drug and Alcohol Breath Test	X	X						X					
Training for Genital Swabbing		X			X								

Period	Screening		Dosing						Follow-Up		Additional Follow-Up		
Study Day	**-45 to -1**	**1**	**4**	**Potential Additional Dose** [f]	**8**	**15**	**22**	**29**	**36**	**43, 50, 57**	**64**	**71, 78, 85, 92, 99**	**127 EOS**[a]
Self-Swabbing of Genital area					*Twice daily from Day 8 through to Day 36*								

[a] EOS = End of Study. The last follow-up visit is expected to be between 28 to 98 days

[b] A complete or symptom-directed physical exam will be performed at indicated visits and may be done at other points if needed

[c] Assessment will also be completed if this is your dosing group's final study visit

[d] Only weight will be measured on these days

[e]

A pregnancy test is required at Screening for female participants of childbearing potential. This will be performed on the blood sample provided at this visit. On Days 1, 15, 29, 57, 99, and 127 a urine pregnancy test will be performed. If positive on urine testing, a pregnancy test will be performed on the blood sample provided at the respective visits.

[f] For once-monthly treatment, study drug doses are administered on Days 1 and 8. You may have 1 or more additional doses between Days 1 – 8. You will be informed ahead of time of your dosing days.

[g] Anogenital Swabbing Samples collected on Day 36 will be returned on Day 43. The Participant Swabbing & Symptoms study Diary will be reviewed for the final time on Day 43. You will collect 1 additional swab, twice a day, when you experience a lesion.

Additional Follow-up:

You may be required to attend weekly additional follow-up visits if your group is selected for this. The extension into this additional follow-up period will be decided by the Sponsor and will be determined by reviewing study data. Study staff will inform you if you are required to attend these additional follow-up visits. If you are required for additional follow-up, you will be asked to visit the study site once a week until either the group is selected to end the study, or Day 127, whichever is earlier. You will be reimbursed $100 (less tax) per additional follow-up visit.

2.2 Who Can Take Part in this Study?

You have been invited to participate in this clinical trial as you have been diagnosed with HSV-2 infection with recurrent genital herpes.

To take part in this study you must:	
✓	Be able to give informed consent and follow the study procedures.
✓	Be aged 18 – 60 years, inclusive at the time of at the time of signing the informed consent form
✓	Have a BMI (Body Mass Index) between 18.0 kg/m^2 – 32.0 kg/m^2
✓	Have a history of HSV-2 infection with recurrent genital herpes (with 4-9 episodes in the last year or if currently on HSV-2 therapy, 4-9 times a year prior to starting HSV-2 therapy
✓	Be willing to stop taking any herpes treatment (on the skin or orally) beginning 7 days prior to Day 1 through until Day 36

You may not be able to take part in this study if you:	
✗	Are pregnant or breastfeeding
✗	Have taken certain prescription medication, herbal/dietary supplements or over the counter medications (except for paracetamol) within 14 days or more prior to Day 1.
✗	Have a history of drug or alcohol abuse within 3 years prior to screening.
✗	Have a history of a significant medical problem, mental health problem or medication-related severe allergy.
✗	Have donated more than 500mL of blood within 60 days prior to screening or plasma within 7 days of screening.
✗	Have an episode of genital herpes on Day 1 prior to dosing.
✗	Have had cancer in the last 5 years, with exceptions – please ask the study doctor
✗	Have received an investigational agent within the last 30 days prior to Screening,
✗	Have an illness (such as the flu, common cold or COVID-19) within 5 days prior to receiving the first dose of study medication.
✗	Have had long-term (ie > 14 days) treatment with systemic steroids or other agents that regulate the immune system with 6 months prior to screening.

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 study visits. It is also possible that the study doctor may schedule extra visits or tests for you, if considered necessary. In the event that an assessment is not performed on the day outlined within the Schedule of Activities within this document, the assessment may be performed at your next study visit, as needed.

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 that you no longer want to take ABI-5366 or placebo for any reason. If you stop receiving study medication 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.

Restrictions:

- You must be willing to stop any herpes therapy (on the skin or orally) at least 7 days prior to Day 1 dosing, through to Day 36.
- You must be willing to obtain the required genital swabs during the study.
- You must be willing to maintain a diary of swabbing details and symptoms during the study.
- You must not consume any alcohol for at least 48 hours prior to the first dose, through to Day 29.
- You must not use illicit drugs (including marijuana) before screening until your last study visit.
- You must refrain from consuming grapefruit, pomelo, or Seville oranges whole fruits or juice for 7 days prior to dosing on Day 1 until Day 29.
- You must not donate blood or plasma until your last study visit.
- You must not engage in strenuous exercise beyond what you are used to from Day 1 until your last study visit.
- You must be fasted (no food, only water) for at least 8 hours prior to your screening visit and some of your follow up visits. You may need to fast at least 10 hours prior to a dosing visit. You will be asked to continue fasting for an additional 4 hours after you take the study medication. Study staff will remind you prior to each visit that you need to be fasted.
- You should keep away from excessive sun light/ultraviolet (UV) light from Day 1 through Day 36 since studies have not been conducted to evaluate the effect of UV light on ABI-5366.
- You should not take any herbal/dietary supplements (i.e. vitamins, St. John's Wort, ginkgo biloba, garlic supplements), over the counter (except paracetamol) or prescription medications that may not be allowed for at least 14 days or more before Day 1 and through your final study visit. Your study doctor will tell you which of your medications and supplements must be stopped for the study.

3 WHAT ARE THE ALTERNATIVES TO PARTICIPATION?

You do not have to take part in this research project to receive treatment for recurrent genital lesions due to HSV-2 infection. Other options are available. Your study doctor can discuss the risks and benefits of other 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. Your condition may get better, but it could stay the same or even get worse. The information from this study might help to develop better treatments in the future for HSV-2 infection.

4.2 Reimbursement and Costs

All tests required to be done for this study will be paid for by the Sponsor 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 $3,900, following the final study visit**.** You will also be reimbursed and additional $150 (before tax) for any additional visit required to the site to receive these loading doses. 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?

Medication often causes 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 ABI-5366 alone or with other medications 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.

What are the Risks or Side Effects of ABI-5366?

ABI-5366 is an experimental medication being studied for the suppression of RGH. There is no information yet on the use of ABI-5366 in humans. At this stage of development, the risk considerations for ABI-5366 are based only on nonclinical data, meaning data from laboratory and animal studies. ABI-5366 could potentially benefit patients with RGH in the future.

ABI-5366 was studied in animals. The results show that there is no significant risk of genetic mutations or damage from exposure to ABI-5366. No harmful medication-related events to the central nervous (brain and spinal cord) system, respiratory (breathing) system, or circulatory (heart) system were observed in the animal studies. Overall, ABI-5366 was clinically tolerated in animals for 28 days of dosing. There were no medication-related clinical signs or changes in mean body weights. In animals, buildup of crystalline material (thought to be precipitated ABI-5366) was observed under a microscope in tissues at high ABI-5366 blood levels, which are higher than the anticipated ABI-5366 blood levels in this current study in humans. In some animals, this was accompanied by inflammation in a number of tissues with additional changes in the bone marrow, adrenal gland, and spleen. These changes were not considered harmful. In some animals, harmful effects to the kidney occurred at the highest dose tested and were accompanied by monitorable changes in body fluids. These harmful effects were reversible when ABI-5366 was discontinued. In other animals no harmful effects occurred at any dose tested.

In order to ensure participant safety, the study is designed to increase in dose between subsequent participant groups over the study period, including a maximum dose and a maximum step-up between doses. There are also stopping rules for individual participants and for the overall study. You will undergo complete and frequent clinical and laboratory safety monitoring. A Data Review Committee (DRC) and the study Investigators will perform ongoing safety data reviews.

If you feel you may be experiencing any side effects or new signs or symptoms during the study, or you are worried about potential side effects, talk with your study doctor, who will be looking out for side effects throughout your study participation.

It is currently not possible to know whether taking ABI-5366 may cause cancer or birth defects in humans. The risks for ABI-5366 in pregnancy are unknown. Do not participate in this study unless you understand and accept this risk and are willing to take appropriate measures to avoid pregnancy. To be in this study, highly effective birth control is required; your study doctor can provide details on recommended types of birth control.

If new findings develop during this study that might suggest a chance for significant side effects when taking ABI-5366, or that might affect your willingness to participate, your study doctor will inform you and your legally authorized representative (if applicable) as soon as possible.

Some medications may not be safe when taken with ABI-5366. You should contact the study doctor before starting any new medications or supplements (including vitamins or herbal medicines).
Talk to your study doctor if you have any questions or would like more details on possible side effects.

What are the Risks or Side Effects of Study Procedures?

Blood Sample Collection & Cannulas:
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:

The physical examination will include examination of your anus and genital area. This means you will 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. Please note that if the doctor is of the opposite gender, a chaperone will be present. You may request a specific gender for your study doctor.

Genital Swabbing:
After a swab test you may have a little bit of bleeding or discomfort where your skin was swabbed.

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 not receive the COVID-19 vaccination 7 days before dosing till your last study visit.

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 ABI-5366 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 one of the methods of contraception listed below**, from screening through your last study visit:

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

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

Hormonal methods of contraception other than the Mirena®, are not acceptable forms of contraception for this study. If you are using a hormonal methos (other than the Mirena®) you will not be able to participate in this study.

You / your partner are encouraged to also use a barrier form of contraception, from screening through until the end of follow up. 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.
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 screening until at least your last study visit.

If you do become pregnant during the study, you must tell the study doctor as soon as possible and you will not continue with the study. 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 ABI-5366 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 Screening through until at least your final study visit.

A hormonal method of contraception (e.g., pill, implant, injection) is also acceptable.

You / your partner must also use a barrier method of contraception, from screening through until the end of the follow-up. 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 unless you've had a vasectomy at least 6 months prior to the first study medication administration and/or your partner is using an effective contraceptive method as stated earlier in this document.

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

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 screening 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, if you are injured as a result of taking part in this study you **will not** be eligible for compensation from Accident Compensation Corporation (ACC).

However, the Sponsor has satisfied the **Northern B** 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 will not affect your cover.

6 WHAT WILL HAPPEN TO MY TEST SAMPLES?

Blood, urine and genital swab 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 LabCorp Central Lab (Singapore) for testing and destroyed after testing or 5 years after the study is completed by internationally accepted means.

All other study samples (pharmacokinetics and HSV serology, and genital swabs) will be sent to central laboratories (Aliri Bioanalysis) in Utah, USA, (University of Washington) in Washington, USA and (Signature Diagnostics) Pittsburgh, USA, for testing and destroyed after 5 years after the study is completed by internationally accepted means.

The maximum amount of blood collected from each participant during the study will be up to approximately 153 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 participant ID number, year of birth, 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 A, B, C and E. 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 are ‘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 assessments. 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.

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 Participant Symptoms and Swabbing Diary	• **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 • Symptoms and Swabbing diary information recorded in the eCOA application.	• **Electronic**: will be stored-on a secure platform and will be retained indefinitely. Storage will comply with local and/or international data security guidelines. • Electronic: stored on a secure platform for a minimum of 25years.	• 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 ABI-5366 or HSV-2.

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 / some 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
- Poor recruitment
- Poor study conduct

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

ABI-5366 is at an early stage of development. Therefore, after the research finishes, you will not be able to continue to receive ABI-5366. When the research project ends the study doctor will discuss treatment choices with you.

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 Use of New Technologies

During the study, the use of technology will be a mandatory requirement.

My Application:

While you are enrolled in this study you will be required to record detailed information for morning and evening symptoms and swabbing in a diary from Day 8 till Day 36. You will also be asked to report any new lesions.

In order to complete this diary, you will need to log in to an App called “eCOA” using your smartphone or other personal device. If you do not own a smartphone, one can be provided for this use. The App is made by a company called eResearch Technology. Study staff will help set up the diary and show you how to use it.

Information you need to provide in the diary are as follows:

- If you are currently experiencing any signs or symptoms related to genital herpes.
- A description of symptoms experienced, including location/s.
- Confirmation of swab collections

During your scheduled clinic visits, study staff will review the diary information with you and collect additional information as necessary to accurately document.

The Sponsor will see the data collected. However, the Sponsor will not see any of your identifiable information.

Your de-identified information will be added to the data of other study participants and made available to groups of certified Investigators working on the study for analysis.

How is your data protected when using this diary?

The information you enter in the diary will be stored in the secure eResearch Technology servers hosted in USA and Germany. All eResearch Technology locations that will be used are secured and compliant with the regulations to protect the privacy and security of your information.

All of your information that is collected will be encrypted (unreadable form) while being transferred from the diary on your personal device to the study server. This will help to prevent unauthorised access and keep your identity safe, although the risk of unauthorised access cannot be eliminated entirely.

Additionally, the diary will be password protected and only you can access your own login. For the protection of your privacy, you must not give your login information to anyone. If you are aware, or think that your login information has been compromised, change your password immediately and notify the study staff.

What are the risks?

The system has been designed to protect your privacy and personal health information. However, because your personal information is being transferred over the internet, there is still some risk of accidental disclosure of your identifiable medical information.

10 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:

Dr Cory Sellwood
Phone: (03) 372 9477 or 0800 862 278
Email: quail.christchurch@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:

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

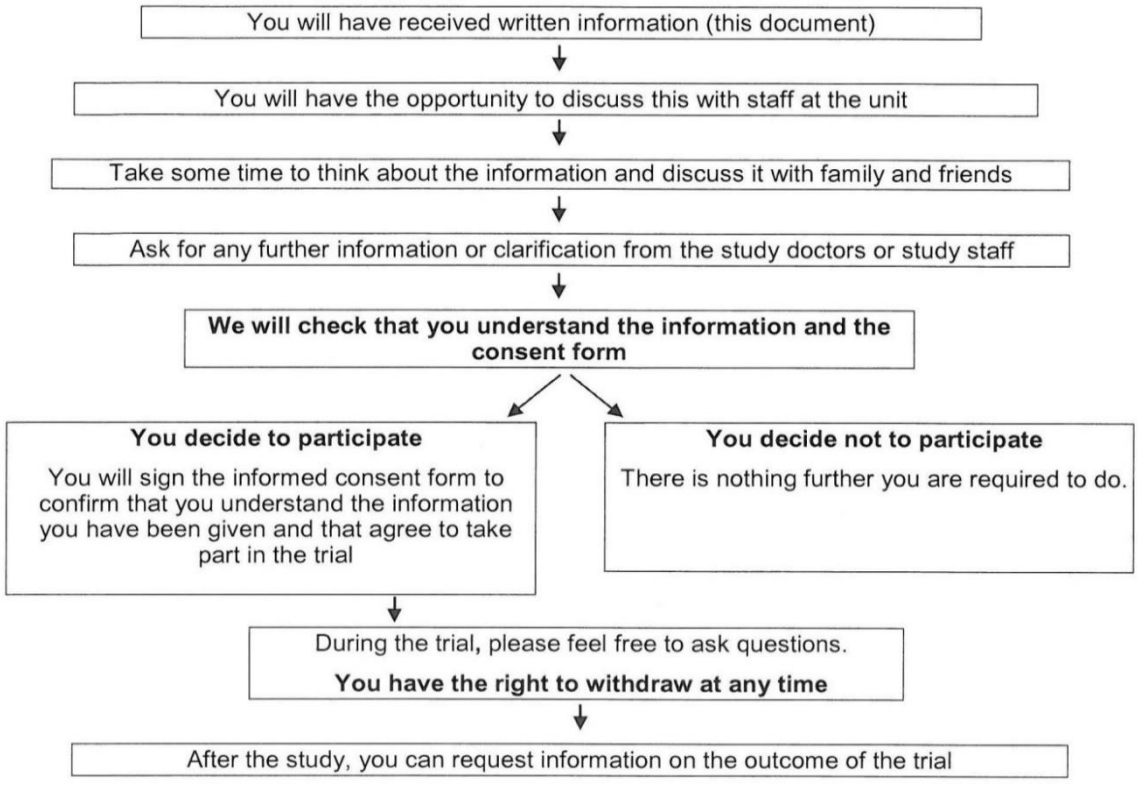
You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Email: hdecs@health.govt.nz

11 WHAT ABOUT ANY OTHER QUESTIONS I MAY HAVE?

12 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
(Part B: Participants with HSV-2 Infection and Recurrent Genital Herpes)

Short Title:	A Study to Evaluate ABI-5366 in Healthy Participants and in Participants with HSV-2 Infection who have Recurrent Genital Herpes
Protocol Number:	ABI-5366-101
Principal Investigator:	Dr Cory Sellwood

***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 study medication 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 the usage of an external App called “eCOA” to record any symptoms, swabbing or new lesions.
- 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.

Statement by Participant	I hereby consent to take part in this study. I understand that I will receive a signed copy of this consent form for my records. _____ (full name) _____ (signature) __ __ / __ __ __ / __ __ __ __ (Date DD/MMM/YYYY) Time: __ __ : __ __

Statement by Consenter (Investigator/designee) I have discussed this study with the above-named participant. The participant appeared to fully understand the information provided about the study. _____ (full name) _____ (signature) _____ (project role) __ __ / __ __ __ / __ __ __ __ (Date DD/MMM/YYYY) Time: __ __ : __ __