

**Appendix 1.1**  
**Christian Medical College, Vellore**  
**Department of Psychiatry**

**A randomized controlled trial comparing drug GVV278 with placebo in to reduce stress-related symptoms in people with psychiatric disorders (RCT 1)**

**Information sheet**

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**Invitation to participate in a randomized controlled trial (RCT)**

You are being requested to participate in a study to see if a new medicine called GVV278 can help reduce some of the symptoms of the psychiatric condition that you are admitted here for. This study aims to recruit a minimum of 30 patients from this hospital and is also being conducted in other institutions in India and other countries to achieve a target sample size of 800 participants.

[This study has been approved by the Institutional Review Board (Research and Ethics Committees) of the Christian Medical College, Vellore, as a hypothetical study (imaginary study) done as part of another study evaluating the attitudes of patients and participants on participating in clinical trials]

**What is the new medicine supposed to do?**

GVV278 has been shown in laboratory research to reverse the effects of stress in laboratory animals. It has been tried in research involving 20 people with no psychological problems who took GVV278 for over one year and experienced no troubling side effects at doses of 10 mg, 20 mg, and 30 mg taken orally in the morning after breakfast. Analysis of the effects of the different doses on psychological test performance of these people indicates that the 20 mg per day dose is the dose that is most likely to help reduce symptoms of stress.

In one clinical trial involving 25 people from Brazil with different psychiatric conditions but who were also experiencing symptoms related to stress such as tiredness, headaches, sleep disturbance, and irritability, GVV278 was shown to be useful in reducing symptoms and reducing scores on psychiatric tests for symptoms of the underlying disorder. However, because this study involved only a small number of people and because GVV278 was not compared with a dummy tablet, doctors are not certain if the improvement seen in those given GVV278 in addition to their usual treatment was due to GVV278 or due to their usual treatment or due to chance.

There are also other drugs that can help in your problem and you may already be taking medication for your problem that is prescribed by your doctor.

**How does GVV278 act to help reduce stress related symptoms?**

It is not entirely clear how this drug acts as there are many chemical changes that take place in the brain that seem to work together to result in the effects that GVV 278 has.

**Does GVV278 have any side effects?**

Some people on GVV278 have experienced some side effects such as headache, feeling anxious, feeling like vomiting, loose motion and stomach discomfort, but these were usually mild and temporary. GVV278 does not cause addiction or any problems when it is stopped suddenly. It may cause mild increases in blood pressure but these are usually not serious. It is not known to cause any problems to the heart.

**How is this research study designed to prove the effects of GVV278?**

This study will use a research design called a randomized controlled trial (or RCT) where every patient who is eligible and who consent to participate will be given an identical looking tablet to take after breakfast daily for 8 weeks. Half the participants in the trial will actually get GVV278 for the 8 weeks and the other half will get an identical looking tablet that does not contain GVV278 but contains only a small amount of sucrose (like sugar) that is unlikely to have any effect in the person taking it. The choice of who gets GVV278 or the dummy tablet has been decided by a computer that provided a code to the pharmacist of the company sponsoring this study in Switzerland. They have prepared serially-numbered containers containing one week's supply of GVV or the dummy tablet, according to the randomization code. The doctors in this hospital conducting the study do not have access to this code and do not know what is in any of the tablets. This information is only known to the company sponsoring the trial. The doctors in this hospital are only provided with the serially numbered, coded medicine containers that have identical looking medicines for 8 weeks of treatment for the patients who will be recruited to the trial from this hospital.

Since the selection of who gets which tablet will be decided by the code, we expect that this will result into equal selection of people in both groups especially with relation to severity of symptoms. If this is not done, this may result in more sick people being selected to take GVV278 or the dummy tablet and we will not be sure if any difference in the results were due to any of the tablets or due to that fact that there were more sick people who got one of the tablets. We expect that by this method all people irrespective of the severity of symptoms will get an equal chance to get GVV278 or the dummy tablet

In addition, since both tablets are identical, the doctors who will decide if GVV278 or the dummy tablet causes more improvement, and patients who are taking part in the study will not be influenced by what they expect either tablet to do with regard to improvement in symptoms or in causing side effects, since nobody in this hospital knows who is taking GVV278 or the dummy tablet. Every week for the first month and at the end of 8 weeks, all participants in the study will be assessed for improvement in symptoms or the presence of side effects. Once these assessments are over the code will be opened and then statistical tests will be done to see if the differences in the results shows that GVV

was better than the dummy tablet in improving symptoms and if there were more side effects with GVV or with the dummy tablet.

This method is the best method to be sure of the effects of GVV on stress-related symptoms in people with psychiatric disorders.

**What will be expected of you if you agree to take part in this study?**

Once you agree to take part in this study, and have signed the informed consent form, your regular treatment will be changed during the period of this study and you will be given only a mild sedative for week, if you have sleep disturbance. This is to be sure that all your previous medicines are no longer in your body. At the end of one week, I will assess you for your symptoms in a clinical interview and if you do not have enough symptoms your participation in the study will end and you will be requested to discuss with your treating team about whether you should continue on your usual medicines.

If you still have troubling symptoms after a week, you will be asked to take one tablet every morning after breakfast for 8 weeks. This tablet will have either GVV or the dummy tablet but neither you nor I will know what is in the tablet you will be given. I will see you every day for the first four weeks during which you are expected to stay in the hospital as an in-patient. I will ask you for any side-effects due to the medicine you are taking.

During this time you may experience worsening of your condition, including increased symptoms such as agitation, restlessness or decreased sleep. I will carefully monitor your condition and report it to your treating doctors as well. If your symptoms worsen and make you uncomfortable, you can withdraw from the study. You can do this at any time during the study, and you will be put back on your previous medicine. I will also ask you questions daily about your sleep, activities, and how you feel, in addition to asking you about any side effects. Your weight and blood pressure will also be recorded daily for as long as you are in hospital. No additional procedures or blood tests will be conducted routinely for this study.

If at any time you experience any problems, you will be expected to report this to me, or the nurses or to your doctor. If I or the other doctors in this study or your treating doctor feel that you are not showing satisfactory improvement or are getting worse on the tablet you are taking, we shall withdraw you from the study and you will be put back on your previous medicine.

At the end of four weeks, you will be discharged if you are at least 50% better than when you started the new tablet. You will be contacted by telephone once a week by me or one of the doctors in this study who will ask you about any side effects that you are experiencing and rate your improvement by asking you questions about your sleep, appetite, mood, energy, and daily routine.

At the end of 8 weeks, you will be expected to return for a final visit for the study where you will have all the assessments that were done on you at the start repeated and your weight and blood pressure monitored.

If you are not at least 50% better by the end of four weeks, you will be expected to stay on as an inpatient and assessed every week. If you achieve 50% improvement at any of the weekly assessment, you will be discharged and followed up as described above.

### **Can you withdraw from this study after it starts?**

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study, for any reason. If you do so, this will not affect your usual treatment at this hospital in any way. In addition, if you experience any serious side effects or your condition worsens, the study tablets will be stopped and you may be given additional treatment.

### **What will happen if you develop any study related injury?**

We do not expect any serious injury to happen to you but if you do develop any side effects or problems due to the study, these will be treated at no cost to you. We are unable to provide any monetary compensation, however.

### **Will you have to pay for the study tablets?**

Both GVV278 and the dummy tablets will be given free for a total period of 8 weeks. Your hospital charges for these eight weeks will also be made free, but you will have to pay for your food, if this is the usual arrangement you have with your treating doctor. In addition, you will also be reimbursed 250 Rs for any outpatient visit you make for the purposes of this study from the time you were discharged till the end of the study. If the cost you incur is more, this additional amount will also be reimbursed if you provide us the receipts or tickets. We will also reimburse 250 Rs (or any additional amount supported by tickets or receipts) for one family member to accompany you on these visits.

### **What happens after the study is over?**

You may or may not benefit from the study medicine that you are given. Once the study is over, if the tablet you were given is GVV278 and if it has helped you and you wish to continue, then your doctor may prescribe it for you. Otherwise, your treating doctor will help you decide on the best treatment for you to continue after the study is over. If you were given the dummy tablet and GVV278 has helped the people in this study who took it, then your doctor will give you the choice of taking GVV278. However, this will not be part of the study and you may have to pay for it. It may also take up to a year after the study for the government to approve GVV278 for sale in India as the results of treating people from all over India who take part in this trial will have to be analyzed. We may not be able to assure you a ready supply of GVV278 from the company till then, although the company has promised to give us stocks of the medicine.

**Will your personal details be kept confidential?**

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

**Who can you call if you have questions?**

You can call me Dr. Donae George on my mobile XXXXXXXXXXXX at any time, or you can call Psychiatry Unit II office: XXXXXXXXXXXX during working hours and ask for me by name. You can also call the Psychiatry Unit II Office and ask to speak to Dr. Saumil Dholakia or Dr Prathap Tharyan.

## INFORMED CONSENT FORM

**Title of the study:**

**A randomized controlled trial comparing drug GVV278 with placebo in to reduce stress-related symptoms in people with psychiatric disorders**

**Name of the investigators and institution:**

Dr. Donae George, Dr. Saumil Dholakia, Dr. Prathap Tharyan; Christian Medical College, Vellore

**Study Number:**

**Participant's name:**

**Date of Birth / Age (in years):**

I \_\_\_\_\_, \_\_\_\_\_ son/daughter \_\_\_\_\_ of \_\_\_\_\_ declare that I have read the information sheet in \_\_\_\_\_ provided to me/ had this information read out to me regarding this study and have clarified any doubts that I had.

I understand that I am being invited to participate in a research study that involves changing my current medicines, and being on no medicines for a week, except a mild sedative if needed. I understand that I will be invited to take the study medicines only if I continue to have troubling symptoms after a week of stopping my current medicines.

I understand that my participation in this study is entirely voluntary and that I am free to withdraw my decision to continue to participate at any time without affecting my medical care or my legal rights.

I understand that during this study I will be required to take remain as an inpatient for 4 weeks at least and take one tablet every day for a total of 8 weeks.

I understand that neither I nor any of the doctors in this hospital will have any choice in whether I am given GVV278 or a dummy tablet that looks identical to GVV278. This selection will occur by chance, as in a lottery, and I will have an equal chance of getting GVV278 or the dummy tablet.

I understand that I will also have to cooperate with assessments for this study as explained to me in the information sheet.

I understand that I may or may not benefit by participation in this trial and that if I develop any study related injury, I will not receive any compensation, though I will be not be charged for the treatment of study related injury.

I understand that the study medicines will be provided free of charge for 8 weeks and that if I chose to continue any of the study medicines after 8 weeks, I shall have to bear the costs. I also understand that a regular supply of the study medicine cannot be assured.

I understand that all information about me will be kept confidential and that my identity will not be revealed in any information released to third parties or if published in medical journals.

I also understand that the study staff and, if needed, the institutional ethics committee members, will not need my permission to look at my health records /my relative's health records even if I withdraw from the trial.

I consent to participate in this study and to the conditions described in the information sheet.

Name:

Signature:

Date:

Name of witness

Relation to participant:

Date:

Key relatives consent:

I, \_\_\_\_\_, relative of \_\_\_\_\_, have read the information provided and clarified my doubts. I consent to my relative participating in the trial as described in the information sheet.

I consent to participate in this study and to the conditions described in the information sheet.

Name:

Signature:

Date:

Relation to participant:

**Appendix 1.2**  
**Comprehension of information for the Hypothetical RCT on GVV278 versus placebo: RCT 1**

*I shall ask you some questions to assess whether you have understood essential details about the RCT you were invited to participate in. If you are unsure of the answer to any of the questions, I shall clarify this information for you.*

*I shall read out the questions loud and I will record your answers. This interview is also being recorded by voice recorder to make sure your replies are correctly understood.*

1. The new drug GVV278 has been found in previous research to be better than currently used medicines in treating symptoms of psychiatric conditions.  
True / False / Unsure / Other
2. If you agree to take part in this study, your treating doctor or I will decide whether you will get GV278 or the dummy tablet  
True / False / Unsure / Other
3. If you agree to take part in this study, you will be given the study medicine as well as you usual medicines that you are now taking.  
True / False / Unsure / Other
4. If you agree to take part in the study, you will be able to find out what medicine you have been given by asking one of the doctors or nurses in this hospital or the pharmacist at this hospital.  
True / False / Unsure / Other
5. If you agree to take part in this study, you will be expected to take the study medicine for period of 4 weeks.  
True / False / Unsure / Other
6. If you agree to take part in this study, you are likely to feel better whatever the medicine you are given.  
True / False / Unsure / Other
7. If you agree to take part in this study, you are not likely to feel worse in any way, if you are actually given the new medicine GVV278.  
True / False / Unsure / Other
8. If you agree to take part in this study, you will be given free food and 200 Rs per day  
True / False / Unsure / Other



9. If you agree to take part in this study, you will have blood tests done every week while you are in hospital  
True / False / Unsure / Other
10. If you agree to take part in this study, and if you are given the dummy tablet, you are likely to feel worse than if you were given the new medicine GVV278.  
True / False / Unsure / Other

Thank you for your time and for answering my questions. I will now discuss your answers with you.

**Appendix 1.3**  
**Clarifying questions and probes to assess barriers and facilitators to participation in a hypothetical RCT: RCT 1**

**1. Willingness to participate in the RCT of GVV278 versus placebo**

Now that you have understood the information provided about the RCT comparing the new medicine GVV278, how likely is it that you will be willing to sign the informed consent document to participate in the study?

Most unlikely to participate	Probably unlikely to participate	Unsure	Probably likely to participate	Very likely to participate
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**2. Open ended questions to clarify the choice**

What are the reasons for you to make the choice that you did?

General probes:

Were there any elements in the information provided about the study that influenced your choice?

Were there any elements in the information not provided about the study that influenced your choice?

Specific probes:

Did the fact that your usual medicines would be withdrawn give you concerns?

Did the fact that you would not have any choice in the drug you received cause concern?

Did the fact that your doctor would not have a choice in what medicine you got cause concern?

Did the fact that a dummy tablet was used cause concern?

Were there any other aspects of this trial that caused concern?

If this had been a real trial, would you have changed your choice?

Do you think trials like this should be done?

Do you think that if your treating doctor recommended that you should take part in the trial, you would be more likely to agree to participate?

**Appendix 2.1**  
**Christian Medical College, Vellore**  
**Department of Psychiatry**

**Information sheet and consent form**

**A randomized controlled trial comparing drug GVV278 with placebo in to reduce stress-related symptoms in people with psychiatric disorders-RCT 2**

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The detailed information regarding the new medicine GVV278 was discussed with you during the first part of the study. Do you want me to repeat any of the information? In case the details are not clear to you, I would like to repeat it as follows. If it is clear to you, than we may move on to understanding what will be expected out of you if you decide to take part in this study extension.

**How is this research study designed to prove the effects of GVV278?**

This study will use a research design called a randomized controlled trial (or RCT) where every patient who fulfills the criteria for inclusion in the study and who consent to participate will be given an identical looking tablet to take after breakfast daily for 8 weeks. Half the participants in the trial will actually get GVV278 for the 8 weeks and the other half will get an identical looking tablet that does not contain GVV278 but contains only a small amount of sucrose (like sugar) that is unlikely to have any effect in the person taking it. The choice of who gets GVV278 or the dummy tablet has been decided by a computer that provided a code to the pharmacist of the company sponsoring this study in Switzerland who prepared serially-numbered containers containing one week's supply of GVV or the dummy tablet, according to the randomization code. The doctors in this hospital conducting the study do not have access to this code and do not know what is in any of the tablets. This information is only known to the company sponsoring the trial. The doctors in this hospital are only provided with the serially numbered, coded medicine containers that have identical looking medicines for 8 weeks of treatment for the patients who will be recruited to the trial from this hospital.

Since the selection of who gets which tablet will be decided by the code, this will prevent anyone selecting sicker (people with more severe symptoms) to take either GVV27 or the dummy tablet for any reason. If this is not done, this may result in more sick people being selected to take GVV278 or the dummy tablet and we will not be sure if any difference in the results were due to any of the tablets or due to that fact that there were more sick people who got one of the tablets. We expect that by this method there

will be equal numbers of people who have more severe symptoms and those who have less severe symptoms who will get GVV278 and the dummy tablet

In addition, since both tablets are identical, the doctors who will decide if GVV278 or the dummy tablet causes more improvement, and patients in the study who are taking the tablets and who will report to the doctors about any benefits or side effects of the treatment, will not be influenced by what they expect either tablet to do with regard to improvement in symptoms or in causing side effects, since nobody in this hospital knows who is taking GVV278 or the dummy tablet. Every week for the first month and at the end of 8 weeks, all participants in the study will be assessed for improvement in symptoms or the presence of side effects. Once these assessments are over the code will be opened and then statistical tests will be done to see if the differences in the results shows that GVV was better than the dummy tablet in improving symptoms and if there were more side effects with GVV or with the dummy tablet.

This method is the best method to be sure of the effects of GVV on stress-related symptoms in people with psychiatric disorders.

### **What will be expected of you if you agree to take part in this study?**

Once you agree to take part in this study, and have signed the informed consent form, your regular treatment will continue as prescribed by your treating doctor during the period of this study and you will not be expected to make any changes to these medicines for the 8 weeks of the trial.

At the start of the study, you will be asked to take one tablet every morning after breakfast for 8 weeks. This tablet will have either GVV or the dummy tablet but neither you nor I will know what is in the tablet you will be given. I will see you every day for the first four weeks during which you are expected to stay in the hospital as an in-patient. I will ask you for any side-effects due to the medicine you are taking.

During this time you may experience worsening of your condition although we are uncertain whether this will occur or what symptoms might be caused. I will carefully monitor your condition and report it to your treating doctors as well. If your symptoms worsen and make you uncomfortable, you can withdraw from the study. You can do this at any time during the study, and you will be put back on your previous medicine. I will also ask you questions daily about your sleep, activities, and how you feel, in addition to asking you about any side effects. Your weight and blood pressure will also be recorded daily for as long as you are in hospital.

Since we wish to make sure that the combination of GVV278 and your usual medicines will not cause any problems, if you agree to take part in this study, we will perform blood tests to check your liver functions, kidney functions etc. at the start of the study and weekly for the first four weeks and at the end of 8 weeks. We will withdraw about 10 ml

of blood each time. Any remaining blood after the tests will be discarded. In addition, we will perform an EEG to assess your brain electrical activity and an ECG to assess your heart's electrical activity at the beginning and the end of the study. The EEG and the ECG will be done in the laboratories of the main CMC Hospital by special appointment and will be painless procedures. We will provide more information about these procedures once you agree to participate.

If at any time you experience any problems, you will be expected to report this to me, or the nurses or to your doctor. If I or the other doctors in this study or your treating doctor feel that you are not showing satisfactory improvement or are getting worse on the tablet you are taking, we shall withdraw you from the study and you will be put back on your previous medicine.

At the end of four weeks, you will be discharged if you are at least 50% better than when you started the new tablet. You will be contacted by telephone once a week by me or one of the doctors in this study who will ask you about any side effects that you are experiencing and rate your improvement by asking you questions about your sleep, appetite, mood, energy, and daily routine.

At the end of 8 weeks, you will be expected to return for a final visit for the study where you will have all the assessments that were done on you at the start repeated and your weight and blood pressure monitored.

If you are not at least 50% better by the end of four weeks, you will be expected to stay on as an inpatient and assessed every week. If you achieve 50% improvement at any of the weekly assessment, you will be discharged and followed up as described above.

### **Can you withdraw from this study after it starts?**

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study, for any reason. If you do so, this will not affect your usual treatment at this hospital in any way. In addition, if you experience any serious side effects or your condition worsens, the study tablets will be stopped and you may be given additional treatment.

### **What will happen if you develop any study related injury?**

We do not expect any serious injury to happen to you but if you do develop any side effects or problems due to the study, these will be treated at no cost to you. We are unable to provide any monetary compensation, however.

### **Will you have to pay for the study tablets?**

Both GVV278 and the dummy tablets will be given free for a total period of 8 weeks. Your hospital charges for these eight weeks will also be made free, but you will have to pay for your food, if this is the usual arrangement you have with your treating doctor. In addition, whatever medicine you are being prescribed at the start of the study will also be

paid for and you will not have to pay for them. All the investigations associated with the study will also be done free of cost.

You will also be reimbursed 250 Rs for any outpatient visit you make for the purposes of this study from the time you were discharged till the end of the study. If the cost you incur is more, this additional amount will also be reimbursed if you provide us the receipts or tickets. We will also reimburse 250 Rs (or any additional amount supported by tickets or receipts) for one family member to accompany you on these visits.

### **What happens after the study is over?**

You may or may not benefit from the study medicine that you are given. Once the study is over, if the tablet you were given is GVV278 and if it has helped you and you wish to continue, then your doctor may prescribe it for you. Otherwise, your treating doctor will help you decide on the best treatment for you to continue after the study is over. In all cases once the study is over, the decision to continue your medicine will be made by your treating doctor in collaboration with you. If you were given the dummy tablet and GVV278 has helped the people in this study who took it, then your doctor will give you the choice of taking GVV278. However, this will not be part of the study and you may have to pay for it. It may also take up to a year after the study for the government to approve GVV278 for sale in India as the results of treating people from all over India who take part in this trial will have to be analyzed. We may not be able to assure you a ready supply of GVV278 from the company till then, although the company has promised to give us stocks of the medicine.

### **Will your personal details be kept confidential?**

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

### **Who can you call if you have questions?**

You can call me Dr. Donae George on my mobile XXXXXXXXXXXX at any time, or you can call Psychiatry Unit II office: XXXXXXXXXXXX during working hours and ask for me by name. You can also call the Psychiatry Unit II Office and ask to speak to Dr. Saumil Dholakia or Dr Prathap Tharyan.

## INFORMED CONSENT FORM

**Title of the study:**

**A randomized controlled trial comparing drug GVV278 with placebo in to reduce stress-related symptoms in people with psychiatric disorders- RCT 2**

**Name of the investigators and institution:**

Dr. Donae George, Dr. Saumil Dholakia, Dr. Prathap Tharyan; Christian Medical College, Vellore

**Study Number:**

**Participant's name:**

**Date of Birth / Age (in years):**

I \_\_\_\_\_, \_\_\_\_\_ son/daughter \_\_\_\_\_ of \_\_\_\_\_ declare that I have read the information sheet in \_\_\_\_\_ provided to me/ had this information read out to me regarding this study and have clarified any doubts that I had.

I understand that I am being invited to participate in a research study that involves continuing on my current medicines and adding a new medicine GVV278 or a dummy tablet for a period of 8 weeks.

I understand that my participation in this study is entirely voluntary and that I am free to withdraw my decision to continue to participate at any time without affecting my medical care or my legal rights.

I understand that during this study I will be required to take remain as an inpatient for 4 weeks at least and take one tablet every day for a total of 8 weeks.

I understand that neither I nor any of the doctors in this hospital will have any choice in whether I am given GVV278 or a dummy tablet that looks identical to GVV278. This selection will occur by chance, as in a lottery, and I will have an equal chance of getting GVV278 or the dummy tablet.

I understand that I will also have to cooperate with assessments for this study as explained to me in the information sheet. These assessments include blood tests and EEG and ECG tests as described in the information sheet.

I understand that I may or may not benefit by participation in this trial and that if I develop any study related injury, I will not receive any compensation, though I will be not be charged for the treatment of study related injury.

I understand that the study medicines and my regular medicines will be provided free of charge for 8 weeks and that if I chose to continue any of the medicines after 8 weeks, I shall have to bear the costs, or discuss this with my treating doctor. I also understand that a regular supply of the study medicine cannot be assured.

I understand that all information about me will be kept confidential and that my identity will not be revealed in any information released to third parties or if published in medical journals.

I also understand that the study staff and, if needed, the institutional ethics committee members, will not need my permission to look at my health records even if I withdraw from the trial.

I consent to participate in this study and to the conditions described in the information sheet.

Name:

Signature:

Date:

Name of witness

Relation to participant:

Date:

Key relatives consent:

I, \_\_\_\_\_, relative of \_\_\_\_\_, have read the information provided and clarified my doubts. I consent to my relative participating in the trial as described in the information sheet.

I consent to participate in this study and to the conditions described in the information sheet.

Name:

Signature:

Date:

Relation to participant:



**Appendix 2.2**  
**Comprehension of information for the Hypothetical RCT on GVV278 versus placebo-RCT 2**

*I shall ask you some questions to assess whether you have understood essential details about the RCT you were invited to participate in. If you are unsure of the answer to any of the questions, I shall clarify this information for you.*

*I shall read out the questions loud and I will record your answers. This interview is also being recorded by voice recorder to make sure your replies are correctly understood.*

1. The new drug GVV278 has been found in previous research to safe when given along with your currently used medicines in treating symptoms of psychiatric conditions.

True / False / Unsure / Other

2. If you agree to take part in this study, you will be given the study medicine as well as you usual medicines that you are now taking.

True / False / Unsure / Other

3. If you agree to take part in this study, you are not likely to feel worse in any way, if you are actually given the new medicine GVV278.

True / False / Unsure / Other

4. If you agree to take part in this study, you will not have to pay for your usual medicines for the period of the study.

True / False / Unsure / Other

5. If you agree to take part in this study, you will have an EEG and an ECG done every week while you are in hospital

True / False / Unsure / Other

Thank you for your time and for answering my questions. I will now discuss your answers with you.

### Appendix 2.3

#### Clarifying questions and probes to assess barriers and facilitators to participation in a hypothetical RCT- RCT 2

1. Willingness to participate in the RCT of GVV278 versus placebo- RCT 2  
Now that you have understood the information provided about the RCT comparing the new medicine GVV278, in this extension study how likely is it that you will be willing to sign the informed consent document to participate in the study?

Most unlikely to participate- probably unlikely—unsure---probably likely--- most likely to participate

2. Open ended questions to clarify the choice

What are the reasons for you to make the choice that you did?

General probes:

Were there any elements in the information provided about the study that influenced your choice?

Were there any elements in the information not provided about the study that influenced your choice?

Specific probes:

Did the fact that your usual medicines would be continued influence your decision?

Did the fact that you would have to undergo blood tests cause concern?

Did the fact that you would have to undergo an ECG cause concern?

Did the fact that you would have to have an EEG cause concern?

Were there any other aspects of this trial that caused concern?

If this had been a real trial, would you have changed your choice?

Would you prefer to participate in this trial or the previous trial?

Do you think patients and relatives should be involved in helping to design research studies?