QCL118184 / BDM-2-C001

PARTICIPANT INFORMATION SHEET AND INFORMED CONSENT FORM

(Sponsor trial number; BDM-2-C001)

TITLE: A single ascending dose trial investigating the safety, tolerability and pharmacokinetics of orally administered BDM-2 in healthy male subjects.

(A study in healthy male volunteers to investigate the safety and tolerability of the test medicine [BDM-2]).

We're inviting you to take part in a research trial. This trial is for research purposes only and you will receive no medical benefit by taking part.

- Before you decide to volunteer it is important for you to understand why we're doing the research and what it involves.
- Please take time to read the following information carefully. Talk to your friends, relatives and whoever you feel is appropriate about the trial if you want to. When you visit the trial site one of our team will go through this information sheet with you to help you decide if you would like to take part or not.
- Please ask us if there is anything that is not clear or if you would like more information. Feel free to ask any questions at any time.
- It's entirely up to you if you want to take part in the trial. Take your time to decide whether you wish to take part.

We've split this information sheet into 3 Sections.

- Section A will tell you about the purpose of the trial and what will happen to you if you decide to take part.
- Section B will give you information on confidentiality, what will happen to the samples that you give, what to do if you have a problem (such as a side effect) and any contact details you may need.
- Section C contains the Informed Consent Form which you must sign if you would like to take part in the trial. This is a form to confirm that you have read and understand all of the information that we have given to you and that you want to take part in the research trial; it does not remove any of your statutory rights.

Out of Hours Medical Contact:

07774 017236

Quotient Sciences Recruitment Department Contact:

0330 303 1000

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Section A

1 Why Are We Doing This Trial?

HIVIH (the sponsor) is developing a new test medicine (BDM-2) for the treatment of human immunodeficiency virus (HIV) infections. HIV damages cells in the immune system and weakens the ability of the body to fight infections and disease. BDM-2 belongs to a new class of antiretrovirals (medicines that treat viruses). In this study you will be given either BDM-2 (test medicine) or placebo (dummy drug) in an oral suspension (liquid).

We will look at the safety and tolerability of the test medicine and also measure the amount of test medicine that reaches the blood circulation. You may also be involved in an investigation of the impact of food on the way the body processes the test medicine.

This will be the first time the test medicine has been dosed in humans.

2 Why Am I Being Asked To Take Part?

You have been invited to be screened to take part in this trial because the information we have about you on file seems to match the requirements for the trial. We still need to perform a medical check to make sure that you can take part (detailed in Section 3.1).

To be able to take part in this trial, you must:

- Be a healthy male;
- Be between 18 and 55 years of age;
- Be in good health and not have any abnormal laboratory values considered to be important by the site;
- Not have Gilbert's Syndrome (a harmless liver condition in which the liver doesn't properly process bilirubin);
- Not have a history of alcohol or drug abuse within the last 2 years before screening or positive test result(s) for alcohol and/or drugs of abuse at screening or on Day -1 of first session;
- Not consume more than 21 units of alcohol per week (1 Unit = ½ pint beer, a 25 mL shot of 40% spirit, or a 125 mL glass of wine);
- Not have donated blood or substantial loss of blood (more than 500 mL through surgery or an accident) in the last 3 months or the intention to donate blood or blood products during the trial;
- Follow the contraception requirements of the trial with your partner, as detailed in Section 12.3;
- Be a non-smoker/non-user of nicotine containing products, not be using e-cigarettes or should not have smoked in the last 3 months;
- Not have had a severe allergic reaction to anything or intolerance (including lactose);
- Not have major surgery, fracture, or prolonged immobilization (more than 2 weeks) within 3 months preceding screening, or surgery has been planned during the time you are expected to participate in the trial;
- Not have participated in an interventional clinical trial (i.e. one where you have received trial medication or involving a medical device) within 3 months before first dose of test medicine;
- Not be an employee, or an immediate relative of an employee, of either Quotient Sciences or the sponsor company;

- Not have any holidays planned for the time that the trial is happening (timing details can be obtained from the recruitment department);
- Avoid exposure to the sun or sunbathing, as well as the use of tanning devices (e.g., sunbed, solarium) and topical tanning products from 24 hours prior to first dose of test medicine until 72 hours after dosing in each session;
- Agree to attend all of the applicable dosing sessions;
- Agree to provide a mandatory blood sample for future DNA (deoxyribonucleic acid) research;
- Be capable of understanding and following the requirements of the trial.

3 What Will Happen To Me Before, During And After The Trial?

In this trial you will participate in 3 or 4 sessions, each separated by approximately 4 Weeks.

You will visit the Quotient Sciences unit as follows:

Visit	Fasting Required on Arrival
Screening Up to 28 days before your first clinical residency (Day -1)	Yes
↓	
Trial Visit 3 overnight stays (Day -1 to Day 3)	Yes
↓	
Follow-Up Visit 7 days post-final dose or 7 days after early withdrawal	Yes

The total time you will be involved in this trial (from the screening visit until the follow up visit) is expected to be 18 weeks for the group participating in 4 sessions and 14 weeks for the group participating in 3 sessions.

3.1 Screening Visit(s)

You will attend Quotient Sciences for a medical assessment to check you meet the criteria to take part in the trial, this is known as “screening”.

You should arrive at your screening visit having not eaten or drunk anything other than water for at least 10 hours.

The screening visit will be either 1 longer visit of up to 4 hours or 2 shorter visits of up to 2 hours to check if you are suitable for the trial. At this visit you will be introduced to the trial as a group with other volunteers and then you will also have the opportunity to ask any questions 1 to 1 with a trial doctor.

A trial doctor or nurse will explain the trial and then ask you to sign an informed consent form. This informed consent form is Section C of this information sheet. By signing this form, you are saying that you understand what will happen to you, what you will have to do during the trial and that you are happy to take part.

After this, a trial doctor will ask you questions about any medications you have taken, your surgical and medical history.

To confirm your surgical and medical history, we will need a medical report from your GP. If you are a new volunteer or the medical report we have for you is older than 12 months, we will request a (new) medical report from your GP.

This medical report will include, but is not limited to:

- Medical and surgical problems you have had in the past or ongoing
- Any allergies or intolerances you have
- Any medicines you have been given
- Any operations or procedures (e.g. X-rays) you have had
- Your reproductive status/contraception

This report might be a full print out of your records held by the GP and so might include everything recorded in your medical history. If you tell us of any visits to the GP or hospital or something is noted in your medical history that we think might be important, we will ask your GP for further details.

Tests will be done as listed in the table in Section 3.7. If the trial is delayed for more than 28 days after your screening visits, some or all of the tests described in the table in Section 3.7 might have to be repeated. If required, we will contact you to arrange an extra visit.

In cases where medical tests may be abnormal, for safety reasons we might have to perform extra tests to confirm or clarify the test result. Any extra tests will be discussed with you before we carry them out and your GP will be informed of any significant abnormal blood results during screening.

The screening procedures could possibly find underlying health conditions that you didn't know you had. If this happens, anything we find will be discussed with you and your trial doctor will arrange appropriate treatment and/or, with your permission, we will refer you to your GP.

If we find an unexpected problem during your medical check it could affect private healthcare or life insurance in the future.

Once you have had your medical check and all results and reports returned, the trial doctor will decide if you are suitable to take part in the trial. You will be contacted by the Recruitment Department to confirm that you should attend for admission to the trial visit (see section 3.2).

3.2 Admission

If you are suitable and accepted into the trial, you should arrive at the clinical trial site for admission at 08:00 (8am) (approximately 24 hours prior to dosing) on the day before dosing (Day -1). There are many factors which affect how the trial is organised, so sometimes we have to change the dates at short notice. If this happens we will discuss the new dates with you.

You should arrive having not eaten or drunk anything other than water for at least 10 hours.

On arrival to the clinical trial site we will need to do a bag search to check for any items that are not permitted in the trial site during the trial, such as medicines, food and drinks. Anything that you require for the trial while you are in the unit will be provided to you.

We will carry out some extra tests at admission to make sure that you are still suitable to take part in the trial. These tests are listed in the table in Section 3.7. We will ask for an update on your surgical and medical history. If there are any problems with these tests carried out on admission, the trial doctor may decide that you are not suitable to be dosed.

3.2.1 Reserve Volunteers

We need to have extra volunteers on standby just in case of non-attendance, exclusion or a last-minute withdrawal. All volunteers who are invited will be admitted to the clinical trial site on the day before dosing. Reserve volunteers are generally selected on a first-enrolled basis but may be selected for other logistical reasons for example, availability and willingness to participate in other groups or studies. We can't promise you a place on the trial.

You should not come to the trial site until a member of the Recruitment Department has spoken to you in person and confirmed that you should attend.

Most of the time, reserve volunteers only need to stay overnight until dosing is completed. **You must make sure you are available** for the whole time the trial is happening in case we need you to take part.

Reserve volunteers are still reimbursed for their time and inconvenience (see Section 11.1.1).

In every case, the final decision on "included" and "reserve" volunteers will be made by the trial doctor at Quotient Sciences.

3.3 Trial Visit(s)

If you are accepted into the trial, you will attend the trial site for one trial visits per session (from the day prior to dosing until 2 days after dosing). You will be dosed with the test medicine in either the fed or fasted state (see section 3.8 for further information on the trial design).

To ensure there is no detectable taste difference between the test medicine and the placebo, taste will be masked by administration of Bitrex® (the world's most bitter material). Immediately prior to administration of the test medicine or placebo, you will be asked to gargle with a 20 mL solution of Bitrex® which you will then spit out. Afterwards you will be asked to swallow the test medicine in the form of an oral suspension (liquid) of 100 mL.

If you are dosed in the fasted state, you will be given a light snack before bedtime on the day you arrive at the clinical unit and then you will not be allowed to eat or drink anything other than water until 4 hours after dosing, which will be the next day.

Lunch will be provided at approximately 4 hours post-dose, an evening meal at approximately 10 hours post-dose and an evening snack at approximately 12 hours post-dose. On the following days, meals will be provided at appropriate times.

If you are dosed in the fed state, you will be given a light snack just before bedtime on the day you arrive at the clinical unit and then you will not be allowed to eat or drink anything other than water until the following morning where you will be provided with a standardized breakfast.

You must eat the provided breakfast entirely within 25 minutes, and nothing else.

The standardized breakfast (or its equivalent) will consist of the following:

- 1 bowl of Kellogg's Cornflakes/Kellogg's Rice Krispies/Kellogg's Special K (25 g)
- 240 mL skimmed milk
- 1 sachet sugar
- 2 slices bread / bread roll and 1 pat of flora per slice
- 1 mug (200 mL) of decaffeinated tea or coffee plus 40 mL of skimmed milk and 1 sachet of sugar

You should only agree to take part in the trial if you agree to consume this breakfast.

Lunch will be provided at approximately 4 hours post-dose, an evening meal at approximately 10 hours post-dose and an evening snack at approximately 14 hours post-dose. On the following days, meals will be provided at appropriate times.

You must eat the food we give you, and nothing else.

On the morning of Day 1 of each session, you will be asked to gargle with a 20 mL solution of Bitrex® which you will then spit out. Afterwards you will be asked to swallow the test medicine in the form of an oral suspension (liquid) of 100 mL. After administration of the oral suspension, the dosing vessel will be rinsed twice with 50 mL of non-carbonated water and you will be asked to drink the rinse solution immediately after dosing. You will consume further water, to make a total volume of 240 mL which is equivalent to 1 cup (including the 100 mL suspension, and the 100 mL volume of water from the rinses of the dosing vessel.
Following dosing you will need to stay on site for 2 days for more trial procedures (see table in Section 3.7).

The trial doctor can withdraw you from the trial at any time. You can be withdrawn because of safety reasons or if you fail to follow the trial instructions or restrictions.

3.4 Blood Samples

We will collect blood samples (for measurement of the amount of test medicine in the blood and for safety assessments) at regular intervals for up to at least 48 hours after dosing. In total, we will collect approximately 63 (if you participate in 3 sessions) to 83 (if you participate in 4 sessions) samples from you, throughout the trial. The total amount of blood taken from you during the whole trial, including the screening visit and follow-up will not exceed 550 mL in any 4-week period. This maximum amount is about 20% more than the volume taken during a single blood donation (the amount taken during a single blood donation is about 470 mL, which is just under a pint).

Also, a blood sample for future genetic testing will be taken in this trial. If you participate in the trial, you are obliged to agree to the use of your DNA for future research. In your first treatment session (on Day 1) a blood sample will be collected (see section 18 for further information on future DNA blood testing).

3.5 Discharge

We will perform some tests before you leave the clinical trial site for your safety. These tests are listed in the table in Section 3.7. If we have any concerns about your safety, we may ask you to stay for extra safety tests.

3.6 Follow Up Visit

Once you have finished the dosing sessions, or if you withdraw from the trial, you must attend a follow up visit. This will take place 7 days (+/- 2 days) after your last intake of test medicine or after dropout/withdrawal. It will last about 30 minutes. A date and time will be arranged with you. At the follow-up visit the following tests will be done:

- heart monitoring using an ECG machine test;
- blood tests; urine tests;
- your blood pressure, pulse rate and aural body temperature (measuring your temperature from your ear) will be checked;
- physical examination including body weight measurement;
- respiratory rate
- check for concomitant medication and adverse events

If any results are outside the normal range or if you tell us that you feel unwell, you may be asked to return to the site for repeat tests. If the results remain outside the normal range, we may refer you to your GP for your ongoing care.

If the follow-up visit is completed, you have finished the trial.

3.7 Summary Of Trial Tests

Whilst at the clinical trial site, you will have the following tests.

Test	Screening	On Admission	Day 1	Day 2	Day 3 (Before Leaving)	Follow Up
Breath test for alcohol	✓	✓				
Urine test for smoking and drugs of abuse	✓	✓				
Blood and urine tests for safety*	✓	✓		✓		✓
Blood test to test for Hepatitis A/B/C/HIV-1 and 2 viruses	✓					
Blood tests to measure the amount of test medicine in the blood			✓	✓	✓	
Heart monitoring using ECG	✓		✓	✓	✓	✓
Blood pressure heart rate and aural body temperature	✓		✓	✓	✓	✓
Respiratory rate	✓		✓	✓	✓	✓
Blood sample for future genetic testing			✓**			
Physical Examination	✓	✓	✓	✓	✓	✓

*** Urine and blood tests for safety will be taken to ensure you are eligible to take part, and to monitor your health and wellbeing throughout the trial**
**** only in your first session**

3.8 Your Trial Design Explained

You will be one of up to 16 volunteers involved in this trial. You will be dosed in a group of up to 8 volunteers. There will be two groups in this trial (Cohorts A and B) and each cohort will receive the test medicine. One cohort will receive 4 doses on 4 occasions and the other cohort will receive 3 doses on 3 occasions.

You will have one dose of the test medicine during each treatment session. The dose level of the test medicine that is given to volunteers will change for each dosing session and will be different for each cohort. You will be informed of the dose you will be taking before the test medicine is given.

In the first session for Cohort A, the test medicine will be given under fasted conditions. The doses in the remaining sessions will take place under fasted or fed conditions. You will be told whether you are fasted or fed for dosing on your admission to the clinical unit.

This trial uses a placebo which is a “dummy test medicine”. It looks like the test medicine but contains no active medicine. You will not know if you are receiving the test medicine or the placebo. In each session, 6 subjects will receive the test medicine and 2 subjects will receive the placebo. This will be randomly allocated for each session, except for the last session (Session VII), where the same treatment allocation as a previous treatment session given in the fasted state will be repeated in the fed state.

If you are dosed in one of the first two sessions (Session 1 for cohort A and Session 2 for Cohort B) you will be dosed in a staggered “sentinel” dose design. This means that “sentinel” volunteers will be dosed 24 hours ahead so that the safety and tolerability of the trial drug is assessed by the trial doctor in the “sentinel” volunteer before we dose the remainder of the group. The “sentinel” volunteers will be randomly selected. After an evaluation of the first two sessions it will be decided if a sentinel approach will be followed in the next session(s). You will be advised if you will be one of the sentinel volunteers. In each of the sessions where sentinel volunteers are required one volunteer will be receive the active test medicine and one volunteer will receive placebo (see below). Neither you nor the site staff will know whether you have received active or placebo medication.

This is a First in Human (FIH) trial, which means that the investigational product has only previously been given to animals and will now be administered to humans for the first time.

This is a double-blind trial, which means that you will not know whether you are receiving the active test medicine or a matching placebo (with no active ingredient) and your trial staff will not know either. Only some of the researchers not directly involved in seeing or treating you will know. Blinding the trial means that the way in which you are treated at the site will be the same so that the results will not be affected by subjects or trial staff knowing which test medicine has been taken.

There will be a break of at least 7 days between each of your dosing days so that the test medicine is cleared from your body before you are given the next dose.

In all sessions, test medicine for oral administration (100 mL suspension) and placebo suspension will be administered. The doses of test medicine expected to be investigated in this trial range from 50 mg to 3600 mg as single doses of 100 mL suspension (liquid). You will be required to swallow the 100 mL oral suspension (liquid) on each dosing occasion.

There are a number of medications including over the counter products and herbal medications or dietary supplements that you must not use during participation in this study (for further details see Section 12.2).

4 Do I Have To Take Part?

It is entirely up to you if you take part or not. If you decide not to take part this will not affect whether we include you in future studies at Quotient Sciences.

5 What Happens If I Change My mind?

If you do decide to take part you can withdraw from the trial at any time without giving a reason, but you must attend a follow-up visit for your own benefit and to ensure your safety. This will not affect the standard of care you will receive. You should only volunteer if you have time to complete the whole trial.

6 Can I Be Taken Off The Trial?

The trial doctor can withdraw you from the trial at any time (from screening to final visit). You can be withdrawn because of safety reasons or if you fail to follow the trial instructions or restrictions which you have agreed to.

7 What If New Information Becomes Available?

Sometimes we may be given new information during the trial about the test medicine being studied after you have given consent or during the trial. If this happens your trial doctor will tell you about it and discuss with you if you want to continue in the trial. Your trial doctor might also decide you should not continue in the trial. If you and the doctor are happy for you to continue in the trial, you will be asked to sign an updated informed consent form.

8 Will There Be Any Side Effects?

8.1 Procedure Related Risks

See section 9 in this document.

8.2 Risks Related to the Investigational Product

Even though the risk of adverse effects from the test medicine as a single administration to humans is considered low based on animal data, the following adverse events are thought to be possible:

- A raise in liver function blood tests results
- A change in the levels of fat circulating in the blood
- A change in salt levels in the blood
- A change in body temperature
- A change in the rate of breathing

All drugs have the potential to cause severe isolated reactions, which may be life-threatening. As with any drugs there is a risk that a rare or previously unknown side effect will occur. Therefore, it is important that you report all symptoms and side effects that you experience as soon as they occur, whether or not you think they are caused by the trial product.

You should notify the trial staff immediately if you experience these side effects or any others during the trial.

The clinical trial site is fully equipped to care for you if you should suffer a severe reaction. Additionally, the trial site is very close to the Queen's Medical Centre, a large hospital in Nottingham and you can be taken here within 10 minutes in the case of an emergency.

With the information available at the time of this subject information sheet, it is not expected that there will be any significant changes to any of these measures from a single dose of the test medicine. If significant new information on side effects of the test medicine become available during the trial, you will be informed immediately. You will then be invited to the trial centre to receive an updated Subject Information Sheet. You will get time to decide if you still want to participate in the trial. If you want to continue, you will be asked to sign a new Informed Consent Form.

9 What Are The Possible Disadvantages And Risks Of Taking Part?

- **Attendance at all dosing sessions and adherence to trial restrictions** – As there are several dosing sessions separated by 4 weeks, your involvement in the study is quite lengthy during which time you have to adhere to the restrictions imposed by the study with regards to alcohol, medications and contraception.
- **Blood sampling** - During the trial you will have frequent blood samples taken. This is a standard procedure which is unlikely to cause you any problems but can sometimes cause discomfort. There is a risk of bruising, reddening and swelling of the vein, but this normally clears up with no further trouble. We prefer to take the blood samples using a cannula (plastic tube) placed in a vein in your arm and which stays there until we have finished taking the samples This is so that we don't have to keep using needles on days when we need a lot of blood samples.
- **ECG monitoring -** You may have minor discomfort, like removing a plaster, when the electrodes taped to your chest to measure your heart's electrical signals are removed. Rarely, a reaction to the electrode tape may cause redness or swelling of your skin.
- **Test medicine -** The dosage form(s) used for delivery of the test medicine in the trial is new and is still being tested to see if they behave as expected and are safe to use.
- **Loss of sleep -** During the trial we will have to perform some tests early in the morning or during the night, which we will have to wake you up for. You may be on a ward with up to 20 other people which could mean that your sleep is interrupted.
- **Private medical insurance -** If you have private medical insurance you should check with the company if taking part in the trial is considered a 'material fact' that should be reported to the insurance company before agreeing to take part in this trial. You will need to do this to ensure that taking part in the trial will not affect your medical insurance.

10 What Are The Possible Benefits Of Taking Part?

You will get no medical benefit from the test medicine, however development of a treatment for HIV may benefit the population as a whole. The screening tests might be of benefit to you if we find an important medical problem, but they could reveal something that you would prefer not to know.

11 What Expenses and Payments Will I Receive?

11.1 Inconvenience Allowance For Completing The Trial

You will be given an inconvenience allowance of up to £1,668.00 plus travel allowance for taking part in the whole trial if you complete 3 sessions (as compensation for your time, inconvenience and lifestyle restrictions). If you complete 4 sessions, you will be given an inconvenience allowance of up to £2,166.00 plus travel allowance.

This allowance will be reduced if;

- you do not complete the trial for non-medical reasons
- you do not follow the requirements and restrictions of the trial;
- you do not follow the rules of the clinic (please refer to your copy of the House Rules);

The allowance will not be increased if trial days are delayed.

This allowance may be reduced if you do not complete the trial for medical reasons.

The trial consists of 4 fixed sessions for one group and 3 fixed sessions for the other group.

11.1.1 Inconvenience Allowance For Reserve Volunteers

If you are a reserve volunteer, you will receive up to £252.00 plus travel allowance if you are not required for dosing.

11.1.2 Inconvenience Allowance For Volunteers Not Eligible At Screening

If you attend a screening visit but we can't offer you a place on this trial, you will receive a screening fee of up to £62 plus travel expenses. If you are offered a place, this is included within the trial/reserve expenses listed above.

11.2 If You Are In Receipt Of Any Benefits

If you are in receipt of any benefits, you should seek further advice from your benefits provider as to whether the payment that you receive from taking part in this trial will affect your eligibility for those benefits.

There may be circumstances when we are required by law to disclose such payments to the relevant authorities when requested.

11.3 If You Are A UK Taxpayer

This inconvenience payment may be taxable and further advice should be sought from HMRC.

If you test positive for drugs of abuse (illegal use of drugs) at any time during this trial, you will NOT be entitled to receive your inconvenience allowance or travel expenses and we reserve the right to remove you from the volunteer panel permanently.

12 What Restrictions Will I Have to Follow?

12.1 General Requirements

You must follow the restrictions we give you before and during the trial. This is for your safety and to ensure the data we collect from you during the trial is accurate:

- You should be able to attend all trial days and return visits and stay for the whole length of time;
- You should tell us about any special dietary requirements (e.g. vegetarian, vegan, dislike of certain foods) before you volunteer;
- Food (including sweets and chewing gum) and beverages not supplied by the clinical trial site will be forbidden during confinement to the trial site;
- If you are taking a medicine prescribed by your GP, you must not stop taking this in order to participate in this trial;
- You must use appropriate contraception (see Section 12.3).
- You should avoid exposure to sunlight or sunbathing, as well as the use of tanning devices (e.g., sunbed, solarium) and topical tanning products from 24 hours prior to dosing until 72 hours after dosing in each session. Exposure of skin and eyes to the sun should be avoided by using appropriate clothing (hat, gloves,...) and/or sun cream from 24 hours prior to dosing until 72 hours after dosing in each session. These precautions should be taken in all weather conditions; regardless if the sun is out or not.

12.2 Summary Of Trial Restrictions

Restricted Item / Activity	How Long For	Why?
Prescription or non-prescription medication except for irregular use of paracetamol	During the entire trial (from screening to discharge)	Other medicines might interfere with the test medicine
Over-the-counter medication and herbal medications or dietary supplements including products containing Hypericum perforatum (e.g., St. John's wort) except for sporadic use of paracetamol	Two weeks before dosing until the end of the trial	Other medicines might interfere with the test medicine
Use of paracetamol	You can take paracetamol up until one day before your first study visit (first dose of the test medicine). If needed, the study doctor may allow you to take paracetamol during the trial, but you will be allowed no more than 4x500 mg per day (intakes separated by 6 hours) and no more than 3 grams per week.	Other medicines might interfere with the test medicine. Higher doses can also affect the liver function tests.
Intake of water	On Day 1 of each session, you will be allowed to drink water until 1 hour before you are given the test medicine. From 1 hour after dosing, you will be allowed to drink water.	Drinking water may influence the break down and removal of the test medicine.
Intake of food	No food is allowed from the evening of Day -1 until 4 hours after dosing. You will receive a standard lunch approximately 4 hours after you take the test medicine on Day 1.	Eating food may influence the break down and removal of the test medicine
Food containing poppy seeds (i.e. poppy seed topped bread)	3 days before the screening visit and admission in each session and during the trial	This could show a positive result on our drugs of abuse test as it is very sensitive
• xanthine-containing products (e.g., caffeine, tea, cola, chocolate) • alcohol containing beverages, • grapefruit, grapefruit juice and Seville oranges • beverages containing quinine (e.g., tonic, bitter lemon, bitter alcoholic beverages containing quinine)	3 days prior to dosing until after the last time blood sample is taken to measure the level of test medicine in your blood in the last treatment session. In addition, the intake of xanthine-containing products should be limited to 3 cups per day during between treatment sessions and after the last treatment session but before the follow-up visit.	These chemicals can affect how long it takes your body to break down and remove the test medicine

Restricted Item / Activity	How Long For	Why?
Decaffeinated fluids	You cannot drink decaffeinated fluids until lunch time onwards on the day of dosing (Day 1)	Drinking fluids other than water can affect how long it takes your body to break down and remove the test medicine
Drugs that interact with body enzymes (e.g., CYP or transport inhibitor or inducer)	These should not have been taken within 30 days to your first study visit (first dose of the test medicine) and during the trial. **However, you should not stop taking treatments prescribed by your doctor**	Other medicines might interfere with the test medicine
Unaccustomed or strenuous exercise	3 days prior to admission to the trial site until after the last time blood sample is taken to measure the level of test medicine in your blood in the last treatment session	This is for reasons of your safety after having test medicine. Also, strenuous exercise may alter certain blood tests and give a false impression of your health.
Smoking and nicotine use	3 months prior to screening until after the last time blood sample is taken to measure the level of test medicine in your blood in the last treatment session	Smoke contains chemicals that can slow down how long it takes your body to break down and remove the test medicine and may also affect the vascular system.
Donation of blood	You should not have donated blood during the 3 months before screening and until at least two months after your last dose of the test medicine	The test medicine could still be in your bloodstream
Donation of sperm	You should not donate sperm from the first time you take the test medicine and for at least 3 months after receiving the last dose of test medicine	It is not yet known what the influence of the test medicine is on the reproduction
Recent fever (temperature above 38°C)	within 3 days of the scheduled test medicine intake	You must be healthy for this study and a recent illness may have residual effects in the body
Use of recreational drugs such as benzodiazepines, opiates, amphetamines, cocaine, cannabinoids, and barbiturates	We will check for traces in your urine at screening and they should not be used until completion of the trial	These drugs might interfere with the test medicine

Restricted Item / Activity	How Long For	Why?
Avoid exposure to sunlight or sunbathing, use of tanning devices and topical tanning products regardless of weather conditions	from 24 hours prior to dosing until 72 hours after dosing in each session.	The test medicine might cause an abnormal skin reaction in combination with UV light
Exposure of skin and eyes to sunlight should be avoided by using appropriate clothing (hat, gloves,...) and/or sun cream, regardless of weather conditions	from 24 hours prior to dosing until 72 hours after dosing in each session.	The test medicine might cause an abnormal skin reaction in combination with UV light

12.3 Contraception Requirements

There is no information about the effect of the test medicine on an unborn child and therefore may involve risk to the baby as it grows during pregnancy

All men who are sexually active must use a condom from the time of dosing until 90 days after your last dose of test medicine. Condoms must be used even if you have been sterilised or your partner is not of child bearing potential (e.g. if they are sterilised, post-menopausal, already pregnant or not female) you are still required to use condoms to prevent exposure of your partner to the test medicine.

Male volunteers should not donate sperm from the time of dosing until 90 after the last dose of test medicine.

If you are sexually active with a female partner that has the potential (able to have a baby) to become pregnant, you must use a condom and your female partner must use an additional effective method of contraception (from the list below,) from screening until 90 days after your last dose of the test medicine:

The Following Methods Are Considered Effective:

- Combined (oestrogen and progestogen-containing) hormonal contraception that stops the woman's eggs being released: These contraceptives may be given:
  - orally
  - into the vagina
  - patch
- Progestogen-only hormonal contraception. These contraceptives may be given:
  - orally
  - by injection / implant
  - as an intrauterine hormone-releasing system (IUS)
- Implantable intrauterine device (IUD)
- Surgical sterilisation (for example, documented bilateral tubal occlusion, hysterectomy for female volunteers or female partners; vasectomy for male volunteers or male partners)
- Male condom with either female cap or diaphragm (double barrier)

A male and female condom should not be used together due to risk of breakage or damage caused by latex friction.

Alternatively, if you do not normally have sex (abstinence), this will be acceptable, but only if this is what you normally do. Periodic abstinence (not having sex occasionally) and withdrawal are not acceptable methods of contraception.

There is no information about the effect of the test medicine on an unborn child and therefore may involve risk to the baby as it grows during pregnancy.

If you or your partner become pregnant in the time between you taking the test medicine until 90 days following the last dose of test medicine, you must inform the study doctor immediately. For the sake of safety, it is important for the sponsor and the study doctor to follow-up on the pregnancy until the end, to ensure that the test medicine does not influence your child.

Please note that you must discuss these contraception requirements with your partner.

13 HIV and Hepatitis A, B and C Testing

During the screening visit you will be tested for HIV and Hepatitis A, B and C.

13.1 HIV (Human Immunodeficiency Virus)

HIV is the virus which causes AIDS (Acquired Immune Deficiency Syndrome). It is a serious disease which decreases the body's resistance to infections and other illnesses.

13.2 Hepatitis A, B and C

Hepatitis A, B and C are viral infections that cause inflammation of the liver. They are serious diseases that both may lead to long term liver damage and eventually liver failure. These might also result in the development of liver cancer.

13.3 How are HIV and Hepatitis A, B and C Transmitted?

HIV and Hepatitis A, B and C are almost always transmitted from infected blood or other infected body fluids (e.g. semen, vaginal secretions, breast milk). The most common way of passing these on are through sexual intercourse or through contact with blood.

We need to test your blood for these viruses to ensure that you are healthy and to protect our staff, as they will be handling your blood samples. If you think that you are at risk of infection with HIV or Hepatitis A, B or C, you should discuss this matter with your own GP or by visiting the Genito-Urinary Medicine (GUM) clinic in Nottingham (located at Nottingham City Hospital; Tel: 0115 969 1169) or a clinic nearer to you.

13.3.1 How Will I Be Tested?

You will be asked to give your consent for a HIV and Hepatitis A, B and C test to be carried out. A sample of blood will be taken from your arm during your screening visit, which will be tested for all these viruses.

13.3.2 I've Never had Hepatitis. Why Do I Need To Be Tested For Hepatitis A, B or C?

The initial infection with Hepatitis A, B or C virus may cause only a very mild illness or even no illness at all. Some people may acquire the Hepatitis B infection from their mothers before birth and so never realise that they have been infected. Even if the initial infection was very mild, people can still become long term carriers of the virus. Infection can be difficult to detect without a blood test as carriers may appear to be perfectly fit and well for many years, although some of them may develop severe liver disease eventually.

13.3.3 What If I've Had a Hepatitis A or B Vaccine?

We will still need to check for infection as the vaccine is not always 100% effective. If you have had the vaccine, this won't interfere with the results of the test for infection.

13.3.4 Who Will Know The Result Of The HIV And Hepatitis Tests?

Your test results will be reviewed by the trial team. Your results will be filed with your trial notes and handled in a confidential manner. Your own GP will only be told if a result is positive. By signing the informed consent form (Section C), you are giving us your permission to notify your GP, but we would try to let you know first, before doing this. Only if we were unsuccessful in contacting you for follow up, would we notify your GP without speaking to you first. In this case, all correspondence with your GP will be strictly confidential.

13.3.5 What Happens If I Do Not Give Consent For The Test?

The test forms part of the trial requirements; therefore, if you do not want to have the sample taken or you are not willing to provide consent this would mean you will not be eligible to proceed onto the trial.

13.3.6 What Happens If A Result Is Positive?

If you have a positive result, you cannot take part in this trial. This is for your own safety and wellbeing as well as to minimise the risk to our staff of possible infection when handling your blood. You will be informed of the result by a trial doctor. The trial doctor will refer you to a GUM clinic or your GP as appropriate.

By signing the informed consent form (Section C), you are giving us your permission to notify your GP or other relevant party.

A negative HIV test does not necessarily mean that you are not infected, as a test may not reveal the presence of infection for 3 months after exposure.

14 What Happens When The Trial Stops?

There will be no continued provision for your care after the trial as this is a healthy volunteer trial. If you are interested in understanding whether you received active or placebo then we will be able to tell you, but only after the data has been processed, which may take some time. Please contact the recruitment department for further information.

Section B

15 What If There Is A Problem?

15.1 If You Feel Unwell

When you are discharged from the clinical trial site after you have been given the test medicine, you will be given a trial participation card which will have a 24hour phone number that you can use to contact the trial doctor.

Please carry this card with you and if you feel unwell at any time after discharge please contact the trial site in the first instance. If you prefer to visit your GP, please take your trial participation card with you and inform your GP that you have recently taken part in a trial at Quotient Sciences. If in the unlikely event that you need to attend the A&E Department of your nearest hospital, please ensure your Trial Participation Card is with you.

15.2 Complaints

If you have any medical queries in relation to this trial, you should contact 0330 303 1000 and ask to speak to the trial doctor. For any out of hours queries see Page 1 for contact telephone number.

If you have any concerns about the way you have been dealt with, please contact the Recruitment Department, Quotient Sciences, Mere Way, Ruddington Fields, Nottingham, NG11 6JS (see Page 1 for contact telephone number).

15.3 Harm

If your health or wellbeing is affected as a result of taking part in the trial the Sponsor will provide compensation to you in accordance with the Association of the British Pharmaceutical Industry "Guidelines for Phase I Clinical Trials (2012 Edition as amended in 2014)".

The sponsor will pay compensation where the injury probably resulted from:

- A drug being tested or given as part of the trial protocol;
- Any test or procedure you received as part of the trial;
- Any other significant negative change to your health or wellbeing as a result of taking part in the trial.

Any payment would be without legal commitment (please ask if you wish for more information on this). We would not be bound by these guidelines to pay compensation where the injury resulted from a drug or procedure outside the trial protocol or where you did not follow the restrictions in the protocol.

The amount of compensation shall be calculated by reference to the amount of damages that would commonly have been awarded for similar injuries by an English court had liability been admitted. The amount of compensation will be reduced if you are partly responsible for the injury or if you have been compensated under another insurance policy.

You and the Sponsor shall refer to an independent person any dispute or disagreement about the compensation undertaking. If you and the Sponsor cannot agree on the identity of an independent person, the President of the Royal College of Physicians, London will be invited to appoint an independent person with the power to consult an advocate of not less than 10 years standing on any issue of law including the amount of damages to be paid.

The contractual commitment to compensate you shall follow the laws in England and, subject to the provisions above, the English courts shall have sole jurisdiction over any dispute that may arise out of it.

If you would like an explanation of these legal terms, please feel free to ask.

If you want to contact us regarding a trial-related injury, please contact the Recruitment Department on 0330 303 1000.

For more information on insurance and compensation in the event of injury in Phase I clinical trials, please see the Association for the British Pharmaceutical Industry (APBI) guidelines that can be found online using the following link:

http://www.hra.nhs.uk/documents/2013/10/insurance-in-phase-i-trials.pdf

16 Will My Taking Part In This Trial Be Kept Confidential?

During this trial, some of your personal data including some medical notes kept by Quotient Sciences and the data collected for the trial will be looked at by authorised persons from the company sponsoring and/or the company organising the research, their representatives, Quotient Sciences Ltd or its group companies (the “Group”) and their representatives. It may also be looked at by people working for regulatory authorities and by other authorised people who check the data (these may be independent auditors or financial auditors) to check that the trial is or was being carried out correctly.

Representatives of the sponsor company (known as monitors) may be at Quotient Sciences to watch dosing and other procedures.

All these people will have a duty of confidentiality to you as a research participant and nothing that could reveal your identity will be disclosed outside the research site.

Your medical records and personal information will be treated in strictest confidence. If any results from the trial are published, your identity will be kept confidential. Quotient Sciences will take all reasonable steps to protect your privacy.

Data collected during the trial may be passed to associated researchers outside the European Union (EU) for processing and analysing. Some countries outside Europe may not have laws that protect your privacy to the same extent as the Data Protection Act in the UK or European Law. Any data which we send outside the EU will be identified (usually by a number or numbers) to make sure your personal details will not appear on any documents.

For your own safety your GP will be told if any of the test results from your blood or urine samples are significantly abnormal or if you become unwell as a result of taking part in the trial.

Quotient Sciences uses a national database called The Over Volunteering Prevention System (TOPS) to log your involvement in this trial. This information will be available to other clinical units and contains the following information:

- Your National Insurance number (if you're a UK citizen) or
- Your passport number and country of origin (if you're not a UK citizen); and
- The date of your last dose of trial medicine (but only if you go on to take part in a trial).

We may call other units, or they may call us, to check your details.

You have right to look at any personal data the Company holds about you. If you wish to see this information, please contact the recruitment department who will be able to talk you through the required steps. In the event of any inaccuracies about you recorded in the Trial Data, you have the right to request that such data be corrected.

17 What Will Happen To The Samples I Give?

All samples (for example, urine, blood, faeces) will be collected on the ward by a trained member of the clinical team. These samples are processed in a secure laboratory in the UK.

Samples may be stored for future research, if required. Blood will only be used for the development of this molecule and will be destroyed once they are no longer required.

Blood and urine samples for safety analysis are identified by the trial number, sample type, date of sample, date of birth, initials, gender and your volunteer panel number.

Blood samples for analysis of the amount of test medicine in your body are identified by the trial number, subject number, initials, date of sample and time point of blood draw.

If you withdraw your consent for participation in the trial, we will need to use the data collected up to your withdrawal. Any samples (e.g. blood) already sent off site for analysis are identified as described above. These samples may still be analysed and reported unless you ask for them to be destroyed following your withdrawal.

18 DNA Blood Testing

Collection of blood for future DNA research is part of the trial, important for understanding the results of the trial and will allow for genetic research to help understand BDM-2.

Genetic analysis will be conducted if it is thought that this may help resolve issues with the clinical data seen from BDM-2. DNA samples will only be used for genetic research related to BDM-2 and samples will be destroyed once they are no longer required.

The purpose of this section is to give you information about the blood sample which will be used in DNA research. If you do not agree to this part of the study, you will not be able to participate in the study.

18.1 Background of DNA Blood Testing

DNA (deoxyribonucleic acid) and RNA (riboxynucleic acid) make up the genetic material that provides the blueprint to tell our bodies how to grow and function. In our cells (the building blocks of our bodies) DNA is divided into short sections with specific instructions called genes. Copies of genes are made into RNA and these copies act as messengers to tell our cells how to behave. Therefore, our genetic material is fundamental to the working of our bodies.

Our DNA is unique to each of us and this means that different people can respond to drugs in different ways. DNA research can help us to understand how drugs work and even to understand disease processes themselves in more detail.

18.2 The Procedure and Your Sample

One blood sample of approximately 10 mL will be obtained from a vein in your arm.

18.3 Confidentiality

As with other samples taken from you in this study, multiple steps are taken to ensure that your blood sample, genetic material and data acquired from them are handled in a secure manner.

Your name, date of birth, address and phone number (or any other information which could uniquely identify you) will not be written on, or associated with, the samples that you donate. The investigator holds information that can personally identify you but neither the sponsor nor the scientists who conduct the DNA research have this personal information.

19 What Will Happen To The Results Of The Research Trial?

The results of the trial will be analysed and given to the sponsor company in the form of a report that is usually prepared by Quotient Sciences. Anonymised data (that doesn't identify you directly) from this trial may be used to support future development of the test medicine.

Trial data could be kept for 15 years or longer after completion or discontinuation of the trial. The trial data must also be kept for a minimum of 2 years following the discontinuation of drug development, or if all marketing authorisations planned for the test medicine are in place.

20 Who Has Approved The Trial?

The trial has been reviewed and approved by a recognised Ethics Committee.

The clinical trial has also been reviewed and approved by the Medicine and Healthcare products Regulatory Agency (MHRA), the government appointed agency for United Kingdom. The MHRA are also responsible for evaluating Quotient Sciences' s unit and granting the trial site approval to carry out clinical trial activity.

21 Contact Details For Further Information

If you want any further information on clinical research please see the UK Clinical Research Collaboration (UKCRC) booklet called 'Understanding Clinical Trials' (http://www.ukcrc.org/wp-content/uploads/2014/03/iCT_Booklet.pdf).

If you require any further information or advice on whether to participate in this trial you should contact the Recruitment Department at Quotient Sciences, the contact telephone number for this can be found on Page 1.

If you are unhappy with anything on the trial, please follow the complaints advice in Section 15.2.

You will be provided with a signed and dated copy of this information and consent form.

Thank you for considering taking part in this trial.

Volunteers's Alphadas Number | | | | | | |

Volunteer initials: | | | |

Section C

INFORMED CONSENT FORM (QCL118184, SPONSOR TRIAL NUMBER BDM-2-C001) **Initials**

1. I confirm that I have read and understood the information in this document for the above trial. I have had the opportunity to consider the information and ask questions. ☐
2. I understand that my participation is voluntary, and I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that relevant sections of my medical notes and data collected during the trial may be looked at as described in Section 15. ☐
4. I agree to my personal information being used in the manner and for the purposes set out in this document. This information may include my initials and date of birth and my full name and/or address. In particular, I understand and agree that information about me that is a result of me taking part in the trial will be processed by Quotient Sciences Ltd and data that does not identify me may be used to support future research. The Group will: ☐
   - Analyse my clinical data during and after the trial, to assess the test medicine and to produce reports (which may include my date of birth and initials, but not my full name and/or address);
   - Send clinical data to the Sponsor outside of the EEA where data protection laws are not as comprehensive as in the European Union, for central analysis. Such data may be seen by government regulatory authorities in the USA;
   - Hold my data on file and send it to government regulatory authorities in accordance with the government's requirements for clinical trials.
5. I understand that my GP is required to send a report of my medical history but may send a full print out which will be used by the trial team to assess my eligibility for the trial. ☐
6. I understand it is important to tell Quotient Sciences about all medical problems for which I needed to see a GP or nurse, and all medicines I have taken since the date of the last report from my GP. ☐
7. I understand that samples will be screened for HIV and Hepatitis A, B and C and the implications of a positive result. ☐
8. I consent to provide blood samples for this trial and understand what will happen to the samples I provide and the data they generate. ☐
9. I consent to provide a blood sample and understand that the blood sample may be used for future DNA research applicable to BDM-2 and will be destroyed once they are no longer required. This sample will always be used under full confidentiality, i.e., not be labelled with my name, date of birth or initials. ☐
10. I have understood that the Sponsor has taken out an insurance policy which can be effectuated in case of an event. ☐
11. I agree to take part in the above trial. ☐

		Time	Date
_____	_____	☐☐.☐☐	☐☐ ☐☐☐ ☐☐☐☐
Full Name of Volunteer	Signature	(24 h clock)	Day Month Year

		Date
_____	_____	☐☐ ☐☐☐ ☐☐☐☐
Name of Physician / Nurse Giving Information	Signature	Day Month Year

Volunteers's Alphadas Number						Volunteer initials:		

This information and consent form cannot be reproduced without the permission of Quotient Sciences. If you require extra copies to discuss with family, friends or your GP, please contact the recruitment department on 0330 303 1000.