Participant Information and Informed Consent

Study Title: **A Prospective, Single-Blinded, Dose-Response Study of SCS Therapy using Paraesthesia-Free Waveform Patterns in Patients with Chronic Neuropathic Low Back Pain**

Protocol Number: **GRS2017-001**

Investigator: **Dr Marc Russo**

Location: **Genesis Clinical Research Services**
220 Denison Street
Broadmeadow NSW 2292

1 Invitation

You are being invited to take part in a research Clinical Study to investigate a potential new treatment for Chronic Neuropathic Low Back Pain (low back pain of long duration). You have been selected for consideration because you have been diagnosed with chronic neuropathic low back pain and the Study Doctor has recommended that you trial a commercially available treatment. The potential new treatment uses a TGA approved and commercially available Spinal Cord Stimulation (SCS) device (also called a neurostimulator). The Intellis Neurostimulator is manufactured by a US company called Medtronic. We hope to learn more about different types of paraesthesia-free based stimulation programs delivered by this device in treating people with chronic neuropathic low back pain. This means that unlike traditional stimulation, which produces a tingling or pins-and-needles sensation (paraesthesia), you should not feel anything (paraesthesia-free). This trial is testing the use of these new stimulation regime types and not the actual implant for which you are intended to trial.

Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. The study team will go through this information sheet with you and answer any questions you have. Please take time to read the following information carefully and discuss it with others if you wish.

Ask us if there is anything that is not clear, or if you would like more information. Take time to decide whether or not you wish to take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to taking part in the research project
- Consent to having the tests and treatments that are described
- Consent to the use of your personal and health information as described.

2 What is the purpose of the study?

You are being invited to participate in a data collection study to evaluate the safety and effectiveness of paraesthesia-free waveform patterns delivered by a Spinal Cord Stimulator device in patients like you as per the clinic's routine practice. The study is about the data collected on your experience with this device. The Intellis Neurostimulator device is not investigational and will be provided to you as per the clinic's routine and commercial

practice. The device is approved by the Therapeutic Goods Administration (TGA) for the treatment of your type of pain. Consenting to be part of this study will enable your Study Doctor and associated researchers to monitor the device and your progress more closely which is a part of routine practice. Your participation in this study is absolutely voluntary. The expected length of your participation in this study is approximately 14 months. Approximately 20 participants from the study site with a permanent Intellis Neurostimulator System will be followed up.

Your Study Doctor and associated researcher will explain Spinal Cord Stimulation procedures to you in detail and you will be given a detailed manual that describes the device system. You will also be shown a sample of the device parts. Your Study Doctor will show you how each part works and where it will be placed in your body. This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way without bias.

3 Why have I been invited?

You have been invited to participate in the Clinical Study because you have been diagnosed with chronic neuropathic low back pain, and all treatments that have been offered to you so far have not helped you. Therefore, the treatment proposed in this study may be of benefit to you.

4 Who is organising and funding this Clinical Study?

Your Study Doctor and Genesis Research Services have received a grant from Medtronic to independently conduct the study. This grant is to cover some of the costs associated with conducting this research study, such as Ethics Committee fees, rights for the use of questionnaires, etc. The research team will not allow a conflict of interest to compromise their position or this research study.

5 What is the treatment that is being tested?

This study uses a Medtronic SCS device, the Intellis Neurostimulator System, for Spinal Cord Stimulation. The treatment will involve the application of different types of paraesthesia-free based spinal cord stimulation programs, under the supervision of your Study Doctor to allow for clinical investigation of reported pain outcomes associated with these unique applications of stimulation. The device will be programmed to deliver the new stimulation regime at doses of 80%, 60%, and 40% of what you were aware of during your initial programming session and you will not know which you are receiving at each reprograming session. This allows us to accurately assess what patients believe may be most effective. The study staff, programmer and the study doctor (by necessity) will not be blinded to each treatment period dose. If the stimulation program is associated with effective pain relief, it is believed that this could significantly reduce the device recharge requirements for SCS patients and therefore prove less burdensome and easier to use. This trial is testing the use of these new stimulation regime types and not the actual implant for which you are intended to trial.

6 Do I have to take part?

Participation in the study is entirely voluntary. It is up to you to decide whether or not to take part. If you agree to take part, you will be asked to sign an Informed Consent Form to confirm that you understand what is involved when taking part in this study. You are free to leave the study at any time and without giving a reason. If you withdraw from the study, unless you object, we will still keep records relating to the treatment given to you, as this is valuable to the study. A decision to withdraw at any time, or a decision not to take part, will not affect the quality of care you receive or your relationship with your Study Doctors or the hospital.

It is possible that after satisfying the eligibility requirements to be included in the study, you decide that you do not wish to proceed with the study, trial or implant. There is no obligation to proceed.

7 What will happen to me if I take part?

Before the study starts, you will be asked to sign this consent form. Once you have signed this form, you are enrolled in the study.

There may be reasons why you cannot participate in this study. Your Study Doctor will discuss these with you

Baseline, Screening and Enrolment – Part of Study

You will be asked to complete a series of patient questionnaires to gather information on your condition and current level of pain, disability, previous treatments and affected lifestyle metrics. Your Study Doctor may perform some physical examinations. Your medication use will be recorded.

The Study Doctor's staff will schedule you for implantation of the trial devices.

This visit may take up to 1 hour.

Trial SCS Implant - Part of Standard Care

You will undergo a surgical procedure to place two leads into the space around your spinal cord. The leads are connected to an external device with an extension cable, if needed. The external device, called the external neurostimulator (ENS), is a handheld, battery-operated device that serves as a temporary stimulator.

Your Study Doctor, with the support of Medtronic personnel, will try to find the stimulation program that best covers your pain areas. Once the program is set, the Study Doctor and Medtronic personnel will teach you how to use the ENS and a handheld remote-control device. You will be asked to use this program for the first 3-5days.

You will be discharged from the clinic and go home the same or next day as per hospital procedure. Your Study Doctor may give you antibiotics to help avoid an infection and discuss any other medications for you to take. Additional visits may be scheduled and settings may be changed depending on how you are feeling. During this period, you will be asked to complete daily a diary to record your pain.

After the initial 3-5 days you will be asked to return to the clinic to be reprogrammed to a second and final form of stimulation program for the following 3-5 days with the support of the Medtronic technician using the parameters that best cover your pain areas.

Prior to your next visit, if you are continuing to experience pain or are uncomfortable with the stimulation, you are asked to contact your Study Doctor. Your Study Doctor, with the support of the Medtronic technician, may reprogram your device to try to find a setting that provides pain relief or lessens the discomfort. They may not be able to find a program that covers your pain areas or that is comfortable for you. If this occurs, an X-ray will be taken to determine if the leads have moved from their original position. If they have moved, your Study Doctor may need to adjust the location of the leads by performing a surgery. After the leads are adjusted, the ENS is reconnected and the device is reprogrammed.

End of Trial Visit – Part of Standard Care

At the end of the Trial phase, you will return for a clinic visit. During this visit, you will be asked to complete a series of patient questionnaires to gather information on your condition and current level of pain, disability and affected lifestyle metrics. Your Study Doctor may perform some physical examinations. Your medication use will be recorded. You will be asked to tell the Study Doctor if you are experiencing any problems.

Together with your Study Doctor, you will discuss your experience over the past week using the two different programmes and decide whether or not move forward with a Medtronic SCS implant. If the stimulation helped reduce your pain, you will be scheduled to receive a smaller, implantable (internal) version of the ENS. If you choose not to move ahead, you will be given alternative treatment options by your Study Doctor, and no further follow up study procedures will be required.

If your Study Doctor and Medtronic technician were not able to find a stimulation program that reduces your pain, the Study Doctor will disconnect the ENS and surgically remove the leads. If you are not having any problems, your study record will be closed and your participation in the study is complete. If you are having any problems from the lead removal, you will be seen by your Study Doctor or staff until it is resolved. This visit may take up to 1 hour.

Permanent Implant – Part of Standard Care

The Study Doctor will implant the permanent system via the pain clinic's standard procedure. The procedure may be performed with a combination of pain medication, sedation and anaesthesia to make sure that you are comfortable during the procedure. Your Study Doctor may prescribe pre-surgery antibiotics to help prevent infection and additional medications to help with after-surgery pain. At the end of this procedure, no part of your device will be outside of your skin; it will be completely implanted. This implant may take up 1 to 2 hour(s).

Prior to going home, you will be told how to care for your surgery wounds. Once the stimulator is activated, this phase of the study will last approximately 12 months. The stimulator and leads will remain implanted at the end of the study, unless otherwise indicated by your condition and as determined by your Study Doctor.

Post-Operative Follow Up/Device Activation

During hospital recovery after the permanent implant, your permanent stimulator will be turned on. The stimulator will be programmed by your Study Doctor, in support with Medtronic personnel. The settings will be based on where you have pain and how much pain you have. This will begin the study investigation period, which involves planned progressive reprogramming intervals regarding your stimulation. You will be asked some questions about how the stimulation feels and be shown how to use the stimulator charger and remote control (that controls the stimulator) to change programs and turn stimulation on and off. Once the stimulator is activated, this phase of the study will last approximately 6 weeks. The stimulator and leads will remain implanted at the end of the study, unless otherwise indicated by your condition and as determined by your Study Doctor.

Follow-Up Visits (Part of Study):

At 6, 10, 14, 26 and 52 weeks after receiving the permanent implant, you will return to the Study Doctor's site for a visit. During these visits you will be asked to complete a series of patient questionnaires to gather information on your condition and current level of pain, disability and affected lifestyle metrics. Your medication use will be recorded. You will be asked to tell the Study Doctor if you are experiencing any problems.

Your stimulator function programs will be purposefully adjusted at each study visit and optimized to try to help you get better pain relief without affecting the amount of pain relief you are experiencing.

These visits may take up to 2 hours.

Stimulation Dosing Plan

6 Week Visit (Part of Study):

After experiencing your initial device stimulation program over 6 weeks, your device will be reprogrammed to a new stimulation setting for the next 4 weeks. You will be required to maintain this program setting throughout the treatment period.

10 Week Visit (Part of Study):

After experiencing your second device stimulation program over 4 weeks, your device will be reprogrammed to a new stimulation setting for the next 4 weeks. You will be required to maintain this program setting throughout the treatment period.

14 Week Visit (Part of Study):

After experiencing your third device stimulation program over 4 weeks, your device will be reprogrammed to your preferred treatment period stimulation setting. You will be able to change your stimulation settings from this time onwards. You will also be asked some new questions at this visit about how you would rate your change since the beginning of the study, your satisfaction with the therapy, and what your preferred stimulation program settings were. This visit ends any programming restrictions.

26 Week Visit (Part of Study):

You will be asked some questions at this visit about how you would rate your change since the beginning of the study and your satisfaction with the therapy.

52 Week Visit (Part of Study):

You will be asked some new questions at this visit about how you would rate your change since the beginning of the study and your satisfaction with the therapy. If you are not having any problems, your study record will be closed and your participation in the study is complete. If you are having problems, we will follow you until you are recovered or have determined that your condition is stable.

Other Tests, Visits and Phone calls

At any time during the study, if you experience pain, are not feeling well or are having any problems, please contact your Study Doctor or research staff. If you discover significant changes in your overall health, they should be discussed with your Study Doctor.

You may be asked to come in to the Study Doctor's office/clinic for an extra study visit(s) of about an hour to change the settings of your stimulator to give you better pain relief.

If needed, additional testing may also be done. An x-ray may be taken at any time during the study to see the position of the leads.

Finally, you may be contacted by telephone by study staff to see how you are doing.

You may be contacted directly by a representative of the company that makes the device you received to see if you are having problems with the equipment and answer questions related to the use of the device.

All medically related matters should be discussed only with your Study Doctor or research staff. If you have any questions about your device or your pain relief, please contact your Study Doctor or research staff.

8 Expenses and Payments

You will not be paid to participate in this study. The 12 months of follow-up consultations (including the monitoring, programming and any extra medical assessments as part of the study) will not incur a cost to you. All costs of your medical care (e.g.: drugs, device and procedures) will continue to be your responsibility. All reasonable travel expenses related to your attending the study visits will be reimbursed. You will be compensated $50 per study visit to contribute to your transport costs.

9 What are the alternatives for participation in the study?

If you choose not to participate in this Clinical Study, there may be other treatments available to you. Some of the other possible treatments include pain medications, commercial SCS devices outside of the study, including the Intellis implantable device as standard of care, physiotherapy, chiropractic, surgery, nerve block, counselling, massage, meditation, and some alternative medicine therapies. If you participate in this study, the only therapies for your back pain you will be permitted to use during the study will be those approved by your Study Doctor and required by participation in the study.

10 What are other possible disadvantages and risks of taking part?

The Medtronic Intellis System has received TGA approval for use in the treatment of chronic pain. In addition to the standard of care, you will need to undergo extra medical assessments and complete questionnaires at regular intervals as part of this study. There are no risks associated with these assessments and questionnaires. The devices will be used per the clinic's routine and commercial practice and possible risks will be discussed by your Study Doctor or site staff.

The known risks associated with the implantation and use of a spinal cord stimulation system are shown below:

- Undesirable changes in stimulation sensation and/or location may occur frequently (between 10% and 15% of patients)
- Uncomfortable changes in stimulation (over and/or under stimulation) may occur frequently (between 10% and 15% of patients)
- The study prescribed stimulation regimes may not result in adequate pain relief that you may otherwise receive with standard stimulation regimes prescribed off study.
- You will be required to undergo extra study assessments (compared to standard of care) associated with follow up visits.
- Some participants may become distressed while answering quality of life questionnaires. **(Should this occur, clinical and psychological support will be offered to participants by both study staff and psychology support staff).**

You may require surgery (including revision, explant and replacement) as a result of any of the above.

You will receive a Medtronic Patient Manual. We will tell you if there is new information about the safety of the Medtronic Spinal Cord Stimulator that we learn while you are participating in the study. You can then decide if you want to still be in the study.
You must tell the Study Doctor or study staff about all side effects or problems that you have. If you are not honest about your side effects or problems, it may not be safe for you to stay in the study.

Pregnancy Clause:

If female, it is preferable to confirm to the investigator that, to the best of your knowledge, you are not pregnant on the date of the study. Any subsequent radiation received from fluoroscopy during SCS implantation as part of your standard care may pose a risk.

11 Ionising Radiation

This research study involves exposure to ionising radiation which reflects standard care. You will have 2 fluoroscopies of your back (at Trial and Permanent phase). Fluoroscopies are required for correct positioning of the leads in your body. These scans will expose you to a medically acceptable dose of radiation.

12 What are the possible benefits of taking part?

You have been proposed to participate in this study because your Study Doctor has determined that the Intellis Neurostimulator System may be able to help reduce your pain. It is unknown whether or not you will benefit from participation in this Clinical Study. Your pain may improve, worsen or stay the same.

You have a chance to be in a research study that may help others find a spinal cord stimulation that provides better pain relief for some types of pain. We are expecting that this study will help us understand more in the area of spinal cord stimulation for the treatment of chronic pain of the lower back and leg and will give us the opportunity to improve the therapy.

By participating in this study, you will also contribute to providing valuable information for medical science, which could lead to future treatments for other people who have the same condition as you.

13 Voluntary Participation/Right to Refuse or Withdraw

There is no obligation for you to be involved in this study. If you do not participate, your normal treatment plan will be followed.

If you first agree to participate and then change your mind, you are free to withdraw your consent and discontinue your participation at any time. Your decision will not affect your ability to receive medical care for your disease and you will not lose any benefits to which you would otherwise be entitled.

If there are no problems, your participation in the study will be complete. If you are having problems, we will follow you until you are recovered or have determined that your condition is stable.

You may also be withdrawn from the study, and have the device taken out, without your consent for one or more of the following reasons:

- If your pain relief in the "trial phase" indicates that the therapy is not effective for you
- If your pain relief in the "permanent implant phase" indicates that the therapy is not effective for you

- If you do not follow the Study Doctor's instructions
- If the Study Doctor decides that continuing your participation could be harmful to you
- If the study is stopped by the Study Doctor or Ethics Committee
- Other administrative reasons or unanticipated circumstances

14 Illness or Injury

If, as a result of being in this study, you become ill or are injured, please immediately contact your Study Doctor. He will then give you all necessary information and treatment and will inform the device manufacturer.

15 Compensation for injury

If you are injured as a result of your participation in this trial, you have a legal right to seek compensation. If, as a result of your participation in this study, you become ill or get injured, immediately advise your study investigator of your condition. In the first instance your Study Doctor will evaluate your condition and then discuss treatment with both you and your regular treating Study Doctor.

Since you are participating in a non-sponsored trial, any question about compensation must initially be directed to the study investigator, who will advise their insurer to the matter. However, it would be prudent to seek independent legal advice before accepting any offer of monetary compensation.

16 Termination of the Study

This research project may be stopped for a variety of reasons. These may include the unacceptable side effects, and unanticipated changes in the funding of the study.

17 Investigator Benefits

As noted in section 4, your Study Doctor is not being remunerated to conduct this study. Your Study Doctor and Genesis Research Services have received a grant from Medtronic to independently conduct the study. This grant is to cover some of the costs associated with conducting this research study, such as Ethics Committee fees, rights for the use of questionnaires, etc. The research team will not allow a conflict of interest to compromise their position or this research study.

18 What happens when the Clinical Study is complete?

When the Clinical Study is complete, you may continue to use the Medtronic SCS system as needed.

19 New Information Arising During the Project

During the research project, new information about the risks and benefits of the project may become known to the researchers. If this occurs, you will be told about this new information. This new information may mean that you can no longer participate in this research. If this occurs, the person(s) supervising the research will stop your participation. In all cases, you will be offered all available care to suit your needs and medical condition.

If you have a concern about any aspect of this study, you should ask to speak with your Study Doctor, who will do their best to answer your questions.

20 Will my Taking Part in this Study be Kept Confidential?

Yes. All the information about your participation in this study will be kept confidential. Your identity will be kept confidential at all times.

Your records relating to this study and any other information received will be kept strictly confidential. However, staff participating in your care and other agencies authorised by law, may inspect the records related to the study.

In the event that you are admitted to hospital as a result of an adverse event resulting from this study, your primary care physician may require access to your study records. Your identity will not be revealed and your confidentiality will be protected in any reviews and reports of this study which may be published.

The data will be kept for the duration of the study and for an additional period of at least 15 years.

Data collected throughout the study may be presented at medical conferences or published in medical journals after the completion of the study. It will not be possible to identify you personally from any of this material.

A publicly-accessible description of this clinical trial will be available on http://www.anzctr.org.au/ as required by the National Statement on Ethical Conduct in Human Research (2007), section 3.3.12. These web sites will not include information that can identify you. At most, the web sites will include a summary of the results. You can search these websites at any time.

21 Results of the Project

The results of the project will be communicated at Australian and International conferences and in peer-reviewed journals. The results will be communicated to participants via a patient letter and/or copy of conference posters.

22 Consent

Your Study Doctor is required to provide you with all information regarding the nature and purpose of the research study, risks/benefits and the possibility of alternative treatment and you should be given the opportunity to discuss these. It must be stated that you are free to withdraw anytime and that if you do not participate you will not suffer any prejudice.

23 Who has reviewed the study?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC).

The Bellberry Human Research Ethics Committee has reviewed and approved this study in accordance with the National Statement on Ethical Conduct in Human Research (2007) incorporating all updates. This Statement has been developed to protect the interests of people who agree to participate in human research studies. Should you wish to discuss the study or view a copy of the Complaint procedure with someone not directly involved, particularly in relation to matters concerning policies, information or complaints about the conduct of the study or your rights as a participant, you may contact the Committee chair, Bellberry Human Research Ethics Committee 08 8361 3222.

23 Advice and Information

If you have any further questions regarding this study, please do not hesitate to contact

Your Study Doctor / Investigator: Dr Marc Russo Tel Number: (02) 4985 1860
Your Research Coordinator: Michael Holt Tel Number: (02) 4985 1860

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if the participant has any medical problems which may be related to their involvement in the project (for example,

any side effects), you can contact the principal Study Doctor on (02) 4985 1860 or any of the following people:

Clinical contact person

Name	Michael Holt
Position	Clinical Trial Coordinator
Telephone	(02) 4985 1860
Email	michael@genesisresearchservices.com

For matters relating to research at the site at which the participant is participating, the details of the local site complaints person are:

Complaints contact person

Name	Dominic Bailey
Position	Chief Executive Officer
Telephone	(02) 4985 1860
Email	dom@genesisresearchservices.com

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

HREC Office contact

Name	Trina O'Donnell
Position	Operations Manager
Telephone	(08) 8361 3222
Email	Bellberry@bellberry.com.au

Participant Informed Consent Form

Study Title: **A Prospective, Single-Blinded, Dose-Response Study of SCS Therapy using Paraesthesia-Free Waveform Patterns in Patients with Chronic Neuropathic Low Back Pain**

Protocol Number: **GRS2017-001**

I _____ the undersigned hereby voluntarily consent to my involvement in the research project titled "A Prospective, Single Centre Study using Subthreshold Waveform in SCS Patients with Chronic Neuropathic Low Back Pain". I acknowledge that the nature, purpose, risks and alternative treatments have been fully explained to my satisfaction by Dr Marc Russo. I have also been provided with an Information Sheet regarding the research.

- Although I understand that the purpose of this research study is to improve the quality of medical care, it has also been explained that my involvement may not be of any direct benefit to me.
- I have been given the opportunity to have a member of my family or another person present while the study is explained to me.
- I have been told that no information regarding my medical history will be divulged and the results of any tests involving me will not be published so as to reveal my identity.
- I understand that access will be required to my medical records for the purpose of this study as well as for quality assurance, auditing and in the event of a serious adverse event.
- I understand that if I become pregnant during the study I will be invited to consent to access to information regarding any pregnancy and its outcome.
- I understand that I am free to withdraw from the study at any stage without prejudice to future treatment. If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.
- I am 18 years of age or over.
- I consent to my GP being notified of my participation in this study and of any clinically relevant information noted by the Study Doctor in the conduct of the trial.
- I declare that all my questions have been answered to my satisfaction.
- I have read or have had read to me in my first language and I understand the Participant Information Sheet, version G, dated 18th March 2020.

Declaration by researcher*: A verbal explanation of the research project, its procedures and risks has been given to the participant and I believe that the participant has understood that explanation.

NAME OF PARTICIPANT: _____

SIGNATURE OF STUDY PARTICIPANT: _____ **DATE:** _____

NAME OF INVESTIGATOR: _____

SIGNATURE OF INVESTIGATOR: _____ **DATE:** _____